European Manual of Medicine
Series Editors: W. Arnold · U. Ganzer

Alexander Herold
Paul-Antoine Lehur
Klaus E. Matzel
P. Ronan O'Connell *Editors*

Coloproctology

Second Edition

Springer

European Manual of Medicine

Series editors

Wolfgang Arnold
München, Germany

Uwe Ganzer
Düsseldorf, Germany

Presenting state-of-the-art procedures in all clinical medicine disciplines, the European Manual of Medicine book series aims to educate postgraduate students and residents in accordance with the U.E.M.S. charter on training medical specialists in the European Union. Each volume is a comprehensive reference devoted to a specific discipline, and the editors are internationally renowned specialists from different European Countries. The contents cover both diagnostic and therapeutic methods which are subdivided into essential procedures (those that are commonly employed in all European countries) and helpful procedures (which might be of further interest as well). The reader-friendly layout allows quick retrieval of information, and concise checklists and algorithms throughout each volume clearly present the pathway from patient complaint to diagnosis. This text book series is ideal for any practitioner in the European Union looking to gain a thorough understanding of the latest procedures in their field of interest. The European Union of Medical Specialists (U.E.M.S.) represents national associations of medical specialists in the European Union and its associated countries. Active at the European level since 1958, the UEMS promotes the free movement of European medical specialists while ensuring the highest quality of medical care for European citizens. More information can be found online at: www.uems.net

More information about this series at http://www.springer.com/series/4640

Alexander Herold • Paul-Antoine Lehur
Klaus E. Matzel • P. Ronan O'Connell
Editors

Coloproctology

Second Edition

Springer

Editors
Alexander Herold
End- und Dickdarm-Zentrum Mannheim
Mannheim, Germany

Paul-Antoine Lehur
Clinique de chirurgie digestive et endocrinienne
Institut des maladies de l'appareil digestif, Hotel Dieu
Nantes, France

Klaus E. Matzel
Chirurgische Klinik mit Poliklinik
Universitaet Erlangen
Erlangen, Germany

P. Ronan O'Connell
UCD School of Medicine
St Vincent's University Hospital
Dublin, Ireland

European Manual of Medicine
ISBN 978-3-662-53208-9 ISBN 978-3-662-53210-2 (eBook)
DOI 10.1007/978-3-662-53210-2

Library of Congress Control Number: 2017938030

© Springer-Verlag Berlin Heidelberg 2017
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.
The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer-Verlag GmbH Germany
The registered company address is: Heidelberger Platz 3, 14197 Berlin, Germany

Foreword from the Series Editors

To date, the goal of the Series Editors – namely to contribute to the dissemination of a medical-scientific standard recognized by the majority of European countries by publishing the European Manual of Medicine (EMM) – has been realized by the editors and authors of "Coloproctology" with great success.

The uniformly structured chapters, the easy-to-follow presentation of the difficult content, the revealing illustrations, and the summarizing flowcharts for the diagnosis and therapy of each clinical image not only allow residents in continuing training to rapidly familiarize themselves with the subject matter, but also provide experienced coloproctology practitioners with a concise overview of recent advances in this subfield of surgery.

The individual chapters are complemented by a compact bibliography focusing on the most important publications to quickly bring readers up to date on the latest state of research.

The volume "Coloproctology" has become the subject of growing interest, both within Europe and without, which also convinced us of the need to prepare the second, revised and expanded edition you now hold in your hands.

The Series Editors wish to thank the publisher Springer Verlag and particularly Ms. Sandra Lesny, Claus-Dieter Bachem, Michael Koy, and Rahul Kumar Sharma, once again, not only for their unflagging commitment to the EMM Project, but also and especially for the individual support they provided for the editors of the separate volumes.

Munich/Düsseldorf
Autumn 2016

Wolfgang Arnold
Uwe Ganzer

Preface

This book forms the latest addition to the *European Manual* series published by Springer, and is the second edition of the *European Manual of Coloproctology*. It will be the first standard and recommended textbook of the European Society of Coloproctology. The editors have again brought together authors, each of whom has both an international reputation within coloproctology or an allied specialty and a desire to see ever-improving standards in coloproctology across Europe.

The individual chapters of this book are written by experienced colleagues in the field, and the publication aims to establish uniform European standards with regard to the requirements of the EBSQ exams. In addition, it is a most valuable source of information for researchers and clinicians in the field allied disciplines. The manual will also be of assistance to the many practicing coloproctologists across Europe and beyond who undertake continued professional development.

This book covers all topics in coloproctology: anatomy, physiology, anal disorders, dermatology, functional disorders, inflammatory bowel disease, endometriosis, appendicitis, benign and malignant tumors, presacral tumors, laparoscopy, endoscopy, perioperative management, intestinal failure, abdominal wall reconstruction, and emergencies and pain syndromes. All chapters give a comprehensive overview on etiology, incidence, epidemiology, diagnostics, medical and surgical treatment, access, complications, and individual special considerations. Finally, all data were presented with the best available level of evidence.

In bringing together authors from all over Europe, the result is a book that provides great breath of knowledge and diversity of clinical practice. The editors trust that the reader will find in it a concise view of current European coloproctology that will be of value both in preparation for EBSQ examination and for those engaged in continued professional development.

Mannheim, Germany — Alexander Herold
Nantes, France — Paul-Antoine Lehur
Erlangen, Germany — Klaus E. Matzel
Dublin, Ireland — P. Ronan O'Connell

Contents

Contributors

Felix Aigner, MD Charité Universitätsmedizin Berlin, Campus Virchow-Klinikum, Department for General, Visceral and Transplant Surgery, Berlin, Germany

Donato F. Altomare, MD Department of Emergency and Organ transplantation, Azienda Ospedaliero Universitaria Policlinico Bari, Bari, Italy

Malika Bennis, MD Digestive Surgery, Saint-Antoine, Paris, France

Gian Andrea Binda, MD Department of Gynecology, Galliera Hospital, Genoa, Italy

Christian Buchli, MD, PhD Karolinska University Hospital, Center of Digestive Diseases, Karolinska Institutet, Stockholm, Sweden

Gordon L. Carlson, BSc, MD, FRCS Salford Royal NHS Foundation Trust, Intestinal Failure Unit, Manchester, UK

N. Chereau, MD Digestive Surgery, Saint Antoine, Paris, France

Gingert Christian, MD Surgery and Orthopedics, Kantonsspital Schaffhausen, Schaffhausen, Switzerland

Faculty of Health (Department of Medicine), University of Witten/Herdecke, Witten, Germany

Philip J. Conaghan, MA, BM BCh, DM, FRCS Department of Colorectal Surgery, Royal Berkshire Hospital, Reading, UK

André D'Hoore, MD, PhD Department of Abdominal Surgery, University Hospitals of Surgery, Leuven, Belgium

Ian R. Daniels, BMedSci, MB BCh, FRCS Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon & Exeter Hospital, Exeter, Devon, UK

Peter Dawson, MS, FRCS West Middlesex and Chelsea and Westminster Hospitals, London, UK

Honorary Senior Lecturer Imperial College, London, UK

Sanjeev Dayal, MD Peritoneal Malignancy Institute, Basingstoke, UK

Daniel Dindo, MD, PhD Surgical Center Zurich, Hirslanden Clinic, Zurich, Switzerland

Adam Dziki, MD, PhD Department of General and Colorectal Surgery, University Hospital, Lodz, Poland

Eloy Espin, MD, PhD, EBSQ-col General Surgery Department, Hospital Valle de Hebron, Universitat Autonoma de Barcelona, Barcelona, Spain

Alessandro Fasciani, MD Department of Gynecology, Galliera Hospital, Genoa, Italy

Eric Frampas, MD, PhD Central Department of Radiology and Medical Imaging, Nantes Cedex 1, France

Christian Gingert, MD Surgery and Orthopedics, Kantonsspital Schaffhausen, Schaffhausen, Switzerland

Faculty of Health (Department of Medicine), University of Witten/ Herdecke, Witten, Germany

Laura Gruner, MD Praxis für Gastroenterologie und Ernährungsmedizin am End-und Dickdarmzentrum, Mannheim, Germany

Dieter Hahnloser, MD, CHUV Centre Hospitalier Universitaire Vaudois, Service de Chirurgie Viscerale, Lausanne, Switzerland

Alexander Herold, MD End- und Dickdarmzentrum Mannheim, Consultant Medical University Mannheim, Mannheim, Germany

Franc H. Hetzer, MD Surgery, Kantonsspital Schaffhausen, Schaffhausen, Switzerland

Christoph Holmer, MD Department of General, Visceral and Vascular Surgery, Charité – Universitätsmedizin Berlin, Berlin, Germany

Martin Hübner, MD Department of Visceral Surgery, University Hospital Lausanne (CHUV), Lausanne, Switzerland

Evangelos Kalaitzakis, MD, PhD Bispebjerg University Hospital, Endoscopy Unit, Digestive Disease Center, Copenhagen, Denmark

Peter Kienle, MD, PhD Department of Surgery, University Medicine Mannheim, Mannheim, Germany

Brian Kirby, MD, FRCPI Department of Dermatology, St Vincent's University Hospital, Dublin, Ireland

Charles H. Knowles, MB, BChir, PhD, FRCS National Centre for Bowel Research and Surgical Innovation, Queen Mary, University of London and Barts Health NHS Trust, London, UK

Heiner Krammer, MD Praxis für Gastroenterologie und Ernährungsmedizin am End-und Dickdarmzentrum, Mannheim, Germany

Martin E. Kreis, MD Department of General, Visceral and Vascular Surgery, Charité – Universitätsmedizin Berlin, Berlin, Germany

Klaus Krogh, DMSc, PhD Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus C, Denmark

Jean-Jacques Labat, MD, PhD Institut fédératif de pelvi-périnéologie, Nantes, France

David Laharie, MD, PhD Service d'hépato-gastroentérologie, Hôpital Haut-Lévêque, CHU de Bordeaux, Pessac, France

Soeren Laurberg, DMSc Department of Surgery, Aarhus University Hospital, Aarhus C, Denmark

Jérémie H. Lefevre, MD, PhD Digestive Surgery, Saint-Antoine, APHP, Université Pierre et Marie Curie, Paris VI, Paris, France

Paul-Antoine Lehur, MD, PhD Clinique de chirurgie digestive et endocrinienne, Institut des Maladies de l'Appareil Digestif (IMAD), Nantes Cedex 01, France

Lily Maguire, MD Peritoneal Malignancy Institute, Basingstoke, UK

Anna Martling, MD, PhD Karolinska University Hospital, Center of Digestive Diseases, Karolinska Institutet, Section of Coloproctology, Stockholm, Sweden

Klaus E. Matzel, MD, PhD Chirurgische Klinik, Universität Erlangen, Erlangen, Germany

Søren Meisner, MD Endoscopy Unit, Digestive Disease Center, Bispebjerg University Hospital, Copenhagen, Denmark

Guillaume Meurette, MD, PhD Institut fédératif de pelvi-périnéologie, Nantes, France

Brendan Moran, MD Peritoneal Malignancy Institute, Basingstoke, UK

Neil J. Mc C. Mortensen, MD, FRCS Colorectal Surgery, Oxford University Hospitals, Oxford, UK

Franka Neumer, MD Praxis für Gastroenterologie und Ernährungsmedizin am End-und Dickdarmzentrum, Mannheim, Germany

P. Ronan O'Connell, MD, FRCSI School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland

St Vincent's University Hospital, Dublin, Ireland

Tom Øresland, PhD GI Surgery, Akershus University Hospital, Lørenskog, Norway

Y. Parc, MD, PhD Department of Digestive Surgery, Hôpital Saint-Antoine, AP-HP, Université pierre et Marie Curie, Paris, France

J. Pimentel, MD, PhD Colorectal Unit, University Hospital of Coimbra/ Faculty of Medicine, Coimbra, Portugal

Florian Poullenot, MD Service d'hépato-gastroentérologie, Hôpital Haut-Lévêque, CHU de Bordeaux, Pessac, France

Friederike Remmen, MD End- und Dickdarm-Zentrum Mannheim, Mannheim, Germany

Harald R. Rosen, MD, FEBSQ Vienna Private Clinic, Vienna, Austria

Thomas H.K. Schiedeck, MD Department of General and Visceral Surgery, Clinic Ludwigsburg, Ludwigsburg, Germany

Alberto Serventi, MD Department of Gynecology, Galliera Hospital, Genoa, Italy

Kieran Sheahan, MB, FRCPI FRCPATH Histopathology, St. Vincent's University Hospital, Dublin, Ireland

Laurent Siproudhis, MD, PhD Gastroenterology Unit, Chu Pontchaillou, Rennes Cedex 09, France

Neil J. Smart, MBBS(Hons), PhD FRCSEd Exeter Surgical Health Services Research Unit, Royal Devon & Exeter Hospital, Exeter, Devon, UK

Mattias Soop, MD, PhD Irving National Intestinal Failure Unit, Salford Royal NHS Foundation Trust, Manchester, UK

Emmanuel Tiret, MD Digestive Surgery, Saint-Antoine, APHP, Université Pierre et Marie Curie, Paris VI, Paris, France

Thilo Wedel, MD Institute of Anatomy, Center of Clinical Anatomy, Christian-Albrechts University Kiel, Kiel, Germany

History of the Division of Coloproctology

1

Klaus E. Matzel

In most European countries, colorectal surgery is not a certified subspecialty. However, many countries have colorectal societies and annual meetings that focus on colorectal disease [1] (Table 1.1). A survey among national representatives of the European Society of Coloproctology (ESCP) [2] showed that formal fellowships in colorectal surgery exist in only 10 countries (Czech Republic, Denmark, Germany, Ireland, Israel, Italy, Netherlands, Russia, Sweden, United Kingdom), and 6 countries have board certification in colorectal surgery (Czech Republic, Denmark, Germany, Ireland, Israel, Russia). Five countries have a formal examination (Czech Republic, Ireland, Israel, Romania, Russia), including oral (in four countries), multiple choice (in three), and practical sections (in two). As much as the health care systems and hospital organizations vary among European countries, so too does colorectal training. Therefore, because colorectal subspecialization is becoming increasingly common, addressing the challenge of standardization is in the best interests of all of practitioners in the field.

K.E. Matzel, MD, PhD
Chirurgische Klinik, Universität Erlangen,
Maximiliansplatz, 91054 Erlangen, Germany
e-mail: Klaus.Matzel@uk-erlangen.de

1.1 Union Européenne des Médecins Spécialistes, Section of Surgery, Division of Coloproctology

The Division of Coloproctology is one of several subspecialties composing the Section of Surgery within the Union Européenne des Médecins Spécialistes (UEMS) [2]. Its aim is to develop, through the European Board of Surgery Qualification Examination, a diploma acceptable across Europe as a whole.

The UEMS was founded in 1958 and today is represented by national associations from EU member states and others, including Norway and Switzerland. Armenia, Israel, and Turkey are associate members, and Georgia is an observer-member. The UEMS operates as the official EU body to defend and foster the professional interests of medical specialists. To this end, a crucial aim is the study and promotion of training of the highest order.

In 1962 the UEMS identified sections representing principal specialties, among which the Section of Surgery represented General Surgery. Over the years, the Section of Surgery developed two man strategies. The first was the creation of accreditation and certification in General Surgery. This resulted in the formation of the European Board of Surgery, which developed a diploma in General Surgery titled the "European Board of Surgery Qualification" (EBSQ). Freedom of movement and employment

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_1

Table 1.1 Colorectal specialization in European countries according to responders to a survey among the national representatives of the ESCP (December 2014) [1]

Country	National colorectal society	Annual colorectal meeting	Specialized colorectal training	Colorectal fellowship	Board of colorectal surgery
Austria	No	Part of General Surgery	No	No	No
Belgium	Yes	Part of General Surgery	No	No	No
Bulgaria	No	Independent	No	No	No
Czech Republic	Yes	Independent	Yes	Yes	Yes
Denmark	Yes	Part of General Surgery	Yes	Yes	Yes
Egypt	Yes	Independent	No	No	No
Finland	No	Part of General Surgery	Yes	No	No
France	Yes	Independent	No	No	No
Germany	Yes	Independent	Yes	Yes	Yes
Greece	–	–	–	–	–
Hungary	Yes	Biannual	No	No	No
Iceland	Yes	Part of General Surgery	No	No	No
Ireland	Yes	Independent	Yes	Yes	Yes
Israel	Yes	Independent	Yes	Yes	Yes
Italy	Yes	Independent	No	Yes	No
Latvia	Yes	Independent	No	No	No
Lithuania	Yes	Independent	No	No	No
Netherlands	Y	Part of General Surgery	Yes	Yes	No
Norway	No	Independent	No	No	No
Poland	Yes	Independent	No	No	No
Portugal	Yes	Independent	Yes	No	No
Romania	Yes	Independent	Yes	No	No
Russia	Yes	Part of General Surgery	Yes	Yes	Yes
Serbia	Yes	Part of General Surgery	No	No	No
Slovenia	Yes	Part of General Surgery	No	No	No
Spain	Yes	Both*	Yes	No	No
Sweden	Yes	Both*	Yes	Yes	No
Switzerland	Yes	Both*	No	No	No
Turkey	Yes	Independent	No	No	No
Ukraine	–	–	–	–	–
United Kingdom	Yes	Independent	Yes	Yes	No

*Independent, separate speciality meeting as well as a meeting at the annual meeting of general/visceral surgery societies.

throughout the European Union requires that the Certificate of Completion of Surgical Training (CCST) of every EU member state be recognized by the others. The second strategy was the differentiation of General Surgery into its constituent specialties, of which there are now several, each becoming a division or section. The first to be formed was Vascular Surgery, which established the EBSQ (Vascular) Diploma in 1996; the second was Coloproctology, formed in 1998 [3].

EBSQ specialties now include General Surgery, Endocrine Surgery, Transplantation, Trauma Surgery, Hepato-Pancreatic-Biliary (HPB) Surgery, Surgical Oncology, Breast Surgery, and Esophagus, Cardiac, and Stomach Surgery. Today the UEMS consists of 42 specialist sections, 10 multidisciplinary joint committees, and over 20 divisions.

1.2 EBSQ Coloproctology Diploma

The founding members of the Division of Coloproctology came from 12 European countries (Table 1.2). The first president and secretary were, respectively, the professors John Christiansen (Denmark) and John Nicholls (UK). In 2004 professors Lars Pahlman (Sweden) and Klaus Matzel (Germany) became president and secretary, respectively. Since 2011 Professor Matzel has been president, and Professor Dieter Hahnloser and Professor Franc Hetzer (both from Switzerland) have been the secretaries and Mr. Janindra Warusavitarne (UK) is in charge of the web presentation since 2014.

The first certification examination, with six candidates, took place in Malmö, Sweden, in 1998. The examinations are now held during the annual meeting of the ESCP and up to twice a year at national meetings, if requested by a national society. The EBSQ (Coloproctology) Diploma remains the only recognized pan-European certification in the specialty of coloproctology and one of the few outside the USA and Canada. Indeed, its acceptance has grown over the years, with 383 surgeons from 26 countries holding the diploma by mid 2016 [1] (Fig. 1.1).

1.3 EBSQ Coloproctology Examination

The Division of Coloproctology recommends 7 years of common trunk training, with dedicated specialist training in Coloproctology requiring a minimum of 2 more years in a European training center (ideally by those who already hold an EBSQ Coloproctology Diploma). All training should be in hospitals recognized by national authorities as "appropriate for training."

Table 1.2 Founding members of the Division of Coloproctology in 1998

C. Baeten, The Netherlands
J. Christiansen, Denmark
J. Deasey, Ireland
F.M. Devesa, Spain
H. Järvinen, Finland
J.-C. Givel, Switzerland
T. Hager, Germany
J-C. Marti, Switzerland
M. Martikainen, Finland
H. Myrvold, Norway
J. Nicholls, UK
H. Ortiz, Spain
L. Pahlman, Sweden
R. Parc, France
M. Pescatori, Italy
R. Schiessel, Austria
R. Sjödahl, Sweden

Candidates wishing to obtain the EBSQ Coloproctology Diploma must satisfy two criteria: Par I, Eligibility; and Part II, Examination.

In Part I, candidates establish eligibility by submitting a curriculum vitae detailing their training in general surgery and coloproctology; a signed CCST; a signed affidavit from two trainers; and their log book enumerating their index procedures. Candidates who are within 3 months of obtaining a CCST may take the Part II examination, but they are awarded the EBSQ (Coloproctology) Diploma only when they have obtained their CCST. Currently, four groups of procedures (A–D; see below) are recognized; these are subdivided into a total of 13 operative categories. Certain operations are regarded as index procedures (categories 2, 9, and 13, as detailed in Table 1.3;). These procedures define a specialist colorectal surgeon, and the minimal number of surgeries should be performed for each of these categories. To be eligible, a candidate must complete the minimal numbers of operations in 5 of 6 categories in group A, 4 of 5 categories in group C, and all of group D, totaling 10 of 13 categories.

(A) Proctology: Trainees should perform a minimum of 100 proctological procedures, at

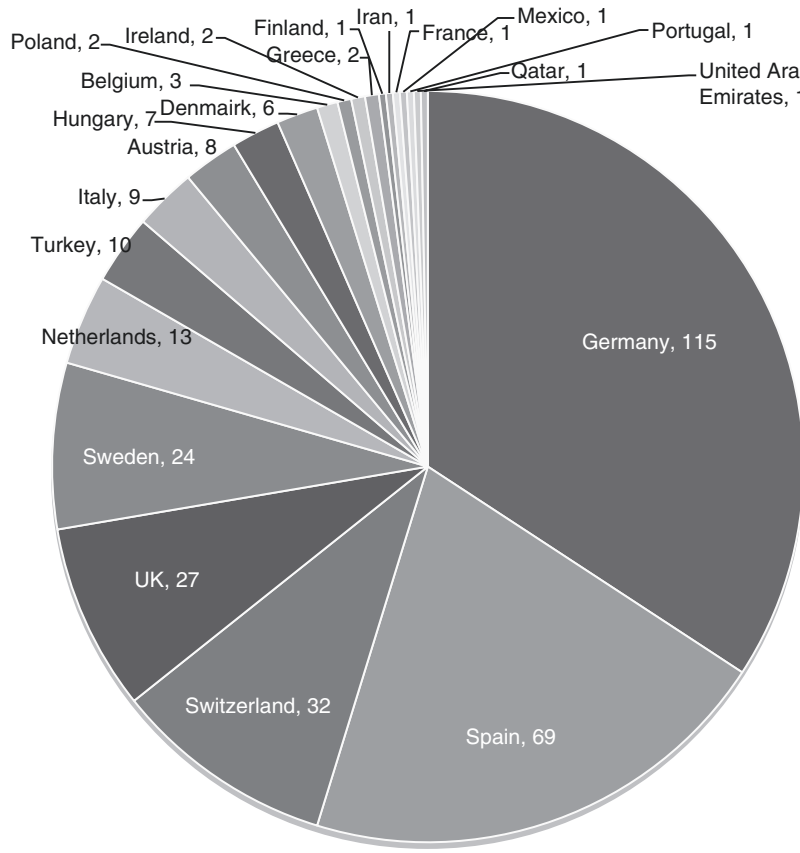


Fig. 1.1 EBSQ Coloproctology Diplomas per country (as of mid 2016)

least one third of which are under the direct supervision of a trainer. Minimal numbers should be achieved in five of the six sections. Anal fistula repair is regarded as an index procedure, and a minimum of 30 of these procedures should be performed by the candidate.

(B) Endoscopy: In some European countries, colonoscopy is not performed by colorectal surgeons. This has no negative impact on the application. In countries where colonoscopy is performed by colorectal surgeons, a minimal number of procedures should be performed by the candidate, including the number to be performed under supervision.

(C) Colorectal resection: Trainees should perform a minimum of 130 colorectal resections through either open or laparoscopic surgery. Minimal numbers of procedures should be performed in four of the five sections detailed above. Anterior resection of the rectum is regarded as an index procedure, and a minimum of 30 operations should be performed. Sigmoid colectomy per se (e.g., for cancer or diverticulitis) does not constitute an anterior resection. Anterior resections and low anterior resections generally involve a rectal disease (e.g., cancer).

(D) Stoma formation: Formation of a stoma is regarded as an index case, and trainees should create a minimum of 20 stomas.

Applications sent to the EBSQ administration office are reviewed by members of the European Board of Coloproctology. If the applicant fulfills the prerequisites, he or she is eligible to sit Part II of the EBSQ examination.

Part II is a formal examination that includes (1) a written section in the form of a quiz, presenting an evolving case (60 min); (2) an academic section in which the candidate discusses a recent journal article after being given 60 min

Table 1.3 Index procedures required for the EBSQ coloproctology examination

Category	Type of procedure	Minimal total number performed[a]	Minimal number performed while supervised by a trainer[b]
(A) Proctology			
1.	Procedures for hemorrhoids	30	5
2.	**Anal fistula repair**	**30**	**10**
3.	Other proctological operations	20	5
4.	Transanal procedures	10	5
5.	Surgical procedures for incontinence	5	5
6.	Prolapse procedures	5	3
(B) Endoscopy			
7.	Colonoscopy/flexible sigmoidoscopy	150[c]	–[c]
(C) Colorectal resection			
8.	Colonic resection[d]	40	20
9.	**Anterior resection (with anastomosis)**[d]	**30**	**15**
10.	Perineal rectal excision	5	5
11.	Total colectomy[d]	10	5
12.	Rectal resection with colo-anal/ileoanal anastomosis[d]	25	5
(D) Stoma formation			
13.	**Stoma procedure**	**20**	**10**

[a]Minimal total number of procedures performed during which the trainee performed the operation as operating surgeon, with or without a trainer directly supervising the procedure. This number includes the minimal number of procedures supervised by a trainer.
[b]Minimal number of procedures performed by a trainee as the operating surgeon and directly supervised (taught) by a trainer scrubbed in for the procedure
[c]Training supervision and requirements to be determined by individual countries' endoscopic training requirements
[d]Open or laparoscopic technique, including low anterior resections with colorectal anastomosis (excluding colo-anal anastomosis, set as category 12)

to study it; and (3) a general section in which colorectal topics are discussed on the basis of clinical scenarios and clinical and radiologic images.

The topics for these three sections are selected to cover a broad spectrum of coloproctology, including colorectal diseases and proctologic cases. The academic and general sections are oral examinations, each lasting 30 min, and are overseen by two examiners. These sections can be undertaken in the applicant's native language, if requested beforehand. The written section and the paper selected for the academic discussion are in English.

Standardized scoring sheets are used to exclude subjective interpretation by the examiners. The relative weight of the written examination is 50 % and the oral sections are 25 % each. The minimal requirement to pass is 66 % of the maximal available points and not less than 60 % in each section.

As mentioned earlier, the main EBSQ examination always takes place during the annual meeting of the ESCP [4] not only because of its logistical convenience—many examiners are in attendance—but also because the ESCP has always supported the development of a pan-European qualification in coloproctology.

1.4 Aims of the Division of Coloproctology

In light of the diversity of surgical training and education, the aim of the UEMS Section of Surgery, Division of Coloproctology, is to develop, through the EBSQ examination, a diploma that is acceptable throughout Europe.

The difficulties are partly political, since health care systems differ enormously from country to country. At present, a pragmatic approach has been adopted: the Division of Coloproctology acknowledges differences in training but, for eligibility, still requires that training encompasses the recommended experience described in Part I. Over time, the index procedures will be adjusted in response to an evolving spectrum of surgical activities in the specialty.

The diploma is not yet officially recognized by every European nation as the specialty examination for coloproctology, although it has gained professional acceptance and value in several countries. In Germany the diploma is accepted as an equivalent to the German qualification of visceral surgery and as a prerequisite to apply for acceptance to the Centre of Competence/Excellence in Colorectal Surgery. Since 2006 Swedish accreditation in Coloproctology has used the same format as the EBSQ Examination, and in Spain the examination is given almost annually in conjunction with the annual meeting of the Spanish Society of Coloproctology.

Beginning in 2015, holders of the diploma receive the title Fellow of the european society of coloproctology (ESCP) (in distinction to Member). Furthermore, holding the EBSQ Diploma is considered an advantage when applying for an ESCP study grant. These initiatives are expected to increase further interest in and acceptance of the EBSQ Examination in Coloproctology.

As stated earlier, coloproctology is not yet recognized by most European countries as a specialty or even a subspecialty within General Surgery. A future challenge will be to attain official acceptance of the EBSQ Coloproctology Diploma at the national level. It is also important to consider what constitutes a training unit among the various European nations. At present, eligibility for the examination is based only on expertise acquired in a specified colorectal center. While acknowledging differences in health care policy, it is the Division of Coloproctology's aim to formulate and implement pan-European guidelines.

References

1. Hahnloser D, Williams JG, Matzel KE. Training colon and rectal surgeons in Europe. Seminars in Colon and Rectal Surgery 2015;26(3):150–154.
2. www.escp.eu.com.
3. www.uems.eu.
4. www.uemssurg.org/divisions/coloproctology.

Anatomy of the Colon, Rectum, Anus, and Pelvic Floor

2

Thilo Wedel

2.1 Introduction

The large intestine is the last segment of the gastrointestinal tract and is subdivided into the colon and the rectum (colorectum). While the digestion and absorption of nutrients mainly take place in the upper gastrointestinal tract and small intestine, the large intestine is responsible for the following alimentary functions:

- Resorption of water and electrolytes (body fluid homeostasis)
- Utilization of nutrients resistant to digestive enzymes (intraluminal bacterial fermentation)
- Further segmental propulsion of ingesta (peristalsis)
- Storage and controlled evacuation of feces (continence and defecation)

The last two functions are maintained by a complex interaction of the rectal ampulla and anal canal with the internal and external anal sphincter muscles and the musculature of the pelvic floor.

T. Wedel, MD
Institute of Anatomy, Center of Clinical Anatomy,
Christian-Albrechts University Kiel,
Otto-Hahn-Platz 8, 24118 Kiel, Germany
e-mail: t.wedel@anat.uni-kiel.de

2.2 Colon

The colon has various anatomic characteristics that are distinct from the small intestine:

- Three bands of thickened longitudinal muscle layer (teniae coli)
- Saccular pouches (haustra)
- Fixed transverse mucosal folds extending over approximately two thirds of the inner circumference (semilunar folds)
- Tatty tags within the tela subserosa (epiploic appendices)

2.2.1 Structure of the Colonic Wall

2.2.1.1 Mucosa

The epithelial lining and the underlying lamina propria mucosae and muscularis mucosae constitute the mucosal layer. The single-layered epithelium forms densely distributed crypts containing columnar absorptive enterocytes, abundant goblet cells, and enteroendocrine cells. Between the epithelial crypts extends the lamina propria mucosae, comprising fibroblasts, immunocompetent cells, nerve fibers, and lymphatic and capillary networks embedded in loosely arranged connective tissue fibers. Solitary lymphatic follicles contact the epithelial lining and frequently protrude into the submucosa. The mucosa is delimited from the submucosa by a thin muscular

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_2

sheet, the lamina muscularis mucosae, comprising up to six layers of smooth muscle cells running parallel and perpendicular to the bowel axis.

2.2.1.2 Submucosa

The submucosa makes up half of the total wall thickness and mainly consists of connective tissue and disseminated fatty nodules, providing both tensile strength and a sliding plane between the mucosa and tunica muscularis. The submucosal layer contains fibroblasts and immunocompetent cells (e.g., lymphocytes and macrophages) and is richly supplied with blood vessel networks (submucosal vascular plexus) and ganglionated nerve fiber meshes (submucosal nerve plexus).

2.2.1.3 Tunica Muscularis

The tunica muscularis comprises two distinct layers of smooth muscle cells separated by an intermuscular connective tissue space containing the myenteric nerve plexus. While the inner circular muscle layer is of uniform thickness, the outer longitudinal muscle layers is much thinner overall and clustered in three major bands: the tenia omentalis, tenia libera, and tenia mesenterialis. Together these are the teniae coli.

2.2.1.4 Serosa

The serosa constitutes a mesothelial lining of flattened epithelial cells and resembles the visceral peritoneal surface. It is absent at retroperitoneal parts of the colon (the cecum and the ascending and descending colon). Subserosal connective tissue underlies the serosal lining and contains blood vessels, nerve fibers, and disseminated fatty nodules called epiploic appendices.

2.2.2 Colonic Segments

The colon is usually 1.4–1.6 m long and forms a frame-like arch extending throughout the entire abdominal cavity. According to its course, the colon comprises five segments.

2.2.2.1 Cecum and Appendix Vermiformis

The cecum is a blind saccular pouch with a luminal diameter ranging between 6 and 9 cm located in the right iliac fossa. Normally, most of the cecum lies retroperitoneally and is fixed by ileocecal plicae. However, its position may vary considerably when an mesentery remains after incomplete secondary retroperitonealization of the ascending colon (mobile cecum). The ileum enters the cecum at its medial border, forming a sphincter-like opening called the ileocecal valve (Bauhin valve). The orifice comprises a superior and inferior mucosal lip protruding into the cecal cavity; these are the result of a thickening of the circular muscle layer.

The worm-like appendix vermiformis is a blind tube, usually 7–12 cm long, with an outer diameter of 3–8 mm. The base of the appendix is located below the ileocecal valve at the medial side of the cecum, where the teniae coli fuse. The appendix is attached to the ileocecal segment by a mesoappendix containing the appendicular artery, a branch of the ileocolic artery. Its flexible position varies, mostly in a retrocecal (two thirds) or intrapelvic (one third) location. Other variations, such as a subcecal, preileal, or postileal location, are only rarely encountered. In contrast to the colonic wall, in the appendix the two muscle layers are of equal thickness, intermingle with each other, and do not allow relevant dilation of the organ. Both the mucosa and submucosa are densely packed with lymphatic follicles that extend throughout the entire circumference of the appendix.

2.2.2.2 Ascending Colon

The ascending colon, like the other colonic segments, has a smaller diameter than the cecum, ranging between 4 and 7 cm. It extends retroperitoneally from the right lower abdomen up to the right colonic flexure located underneath the right liver lobe (hepatic flexure) and ventrally to the anterior renal fascia (Gerota's fascia) covering the right kidney. The right colonic flexure is fixed by peritoneal folds emerging from neighboring organs: the right renocolic, hepatocolic, and right phrenicocolic ligaments.

2.2.2.3 Transverse Colon

The transverse colon lies intraperitoneally and is loosely suspended by the transverse mesocolon and the gastrocolic ligament, allowing highly

varying positions and length. Along its course from the right to the left colonic flexure, it contacts the liver, gallbladder, duodenum, pancreas, stomach, greater omentum, and small intestine. Blood and lymphatic vessels supply the transverse colon via the transverse mesocolon. The topographic position of the left colonic flexure is higher than the right one and relates to the spleen (splenic flexure) and the left kidney. The left colonic flexure is fixed by the splenocolic, left renocolic, and left phrenicocolic ligaments.

2.2.2.4 Descending Colon

The descending colon extends from the left colonic flexure along the left side of the dorsal abdominal wall. Its diameter ranges between 3 and 5 cm. Similar to the ascending colon, the descending colon is retroperitoneally fixed and attached to the anterior renal fascia (Gerota's fascia).

2.2.2.5 Sigmoid Colon

The intraperitoneally located sigmoid colon continues the descending colon and extends from the left iliac fossa into the pelvic cavity to the upper rectum. Its course is *S*-shaped but may vary greatly depending on its length, which ranges between 12 and 60 cm. Because of the flexible mesosigmoid, the sigmoid colon is very mobile and can easily change its position. Thus, during defecation it may be pushed down and compress the anterior rectal wall, eventually causing incomplete rectal evacuation (sigmoidocele/outlet obstruction). The mesosigmoid radix starts from the inner border of the greater psoas muscle; crosses the left ureter, left genital blood vessels, and the aortic bifurcation; and reaches caudally the level of the third sacral vertebra. It contains the blood and lymphatic vessels supplying the sigmoid colon.

2.2.3 Blood Supply of the Colon

The colon, derived from both the midgut and hindgut, receives its blood supply from branches of the superior and inferior mesenteric arteries (Fig. 2.1).

2.2.3.1 Superior Mesenteric Artery

The superior mesenteric artery supplies the cecum, appendix, ascending colon, and two thirds of the transverse colon.

Ileocolic Artery

The ileocolic artery continues the superior mesenteric artery past the outlet of the ileal arteries. It usually divides into a superior branch for the ascending colon and an inferior branch for the cecum (colic branch) and the appendix (appendicular artery).

Right Colic Artery

The right colic artery (diameter, 2.9 ± 0.6 mm) has an inconstant origin: it arises directly from the superior mesenteric artery, the ileocolic artery, or the middle colic artery. It supplies the ascending colon and the right colonic flexure. In 70 % of individuals, however, a clearly identifiable right colic artery is not present, in which case the right colon receives its blood supply via the colic branch of the ileocolic artery and the right branch of the middle colic artery.

Middle Colic Artery

The middle colic artery (diameter, 3.3 ± 0.8 mm) is always present, arises from the initial infrapancreatic segment of the superior mesenteric artery, and passes within the transverse mesocolon right to the midline. In 50 % of individuals, before reaching the transverse colon, the arterial trunk divides upward into left and right branches to reach the transverse colon and the colonic flexures, respectively.

2.2.3.2 Inferior Mesenteric Artery

The inferior mesenteric artery (diameter, 4.4 ± 0.5 mm) supplies the left third of the transverse colon, the descending and sigmoid colons, and most of the rectum (see "Blood Supply of the Rectum and Anus" later in the chapter).

Left Colic Artery

The left colic artery (diameter, 3.1 ± 1.0 mm) arises from the left side of the inferior mesenteric artery, crosses the left kidney, and divides upward into an ascending branch that passes into the left

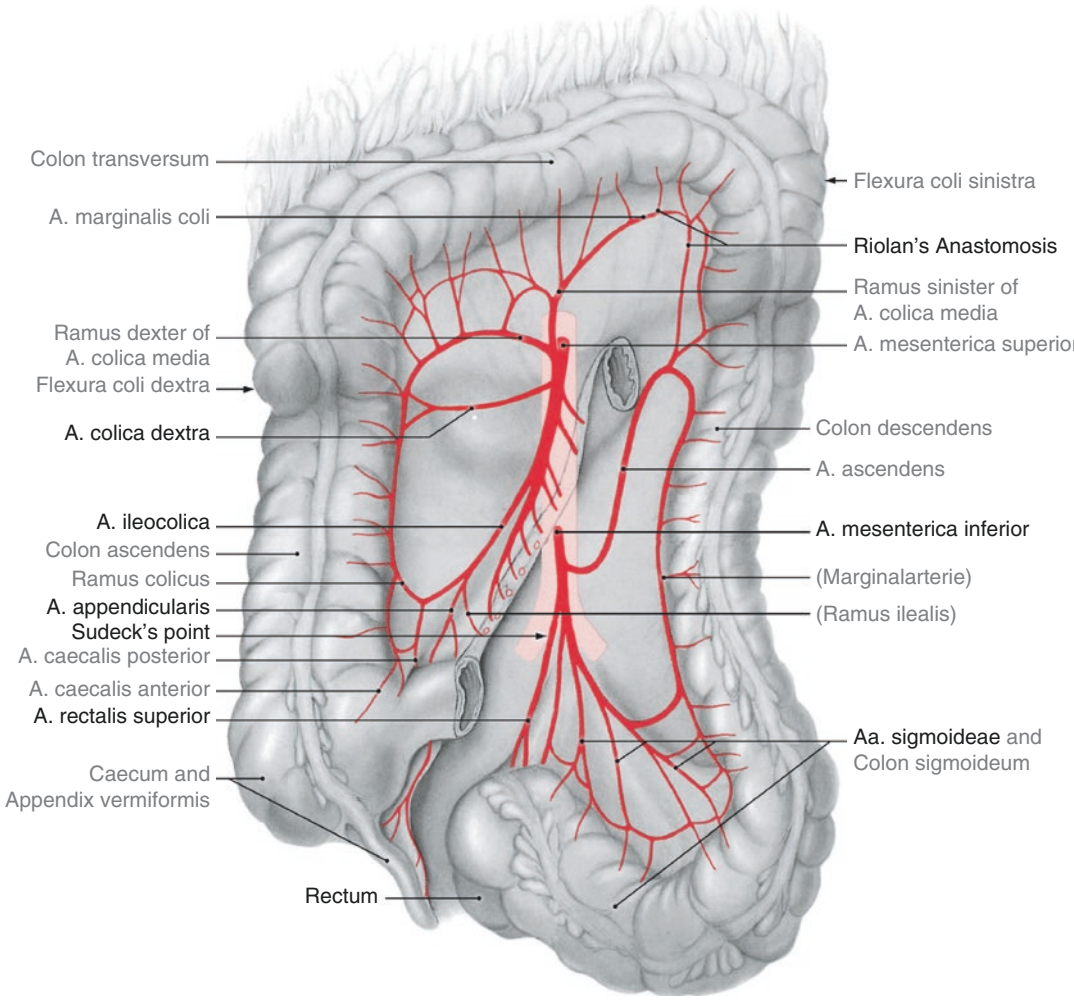


Fig. 2.1 Arterial supply of the colon

colic flexure and a descending branch that passes into the descending and sigmoid colons. In 16% of individuals these branches originate directly from the inferior mesenteric artery (in the absence of a left colic artery).

Sigmoid Arteries

The sigmoid arteries (diameter, 3.0±0.5 mm) number between two and five. They branch from the inferior mesenteric artery and cross the left ureter and gonadal vessels, passing within the mesosigmoid to reach the sigmoid colon. Branches anastomose to the left colic artery and the superior rectal artery via primary or secondary arcades (the marginal artery of the colon). This anastomosis is also called Sudeck's point.

2.2.3.3 Marginal Artery of the Colon

The marginal artery of the colon (Drummond's artery) is formed by the dividing arcades of the ileocolic, right, middle, left colic, and sigmoid arteries. The artery runs parallel and adjacent to the colon within the mesentery and gives rise to the vasa recta and brevia, which directly enter the colonic wall. In addition to the anastomosis between the middle and left colic artery via the marginal artery, a large branch may be present, connecting the superior and inferior mesenteric

arteries directly; this is also called the arch of Riolan (Griffith's point).

2.2.4 Lymphatic Drainage of the Colon

Colonic lymph nodes are subdivided into four groups:

- Epiploic lymph nodes on the serosal surface and within the epiploic appendices
- Paracolic lymph nodes adjacent to the colonic wall
- Intermediate lymph nodes along the colic blood vessels
- Preterminal lymph nodes along the main trunks of the superior and inferior mesenteric arteries

Preterminal lymph nodes drain into para-aortic lymph nodes located at the origin of these visceral arteries and are referred to as the highest lymph node station of the colon.

2.2.4.1 Venous Drainage of the Colon

Venous blood from the colon is collected by branches draining into the superior mesenteric vein (ileocolic vein, right colic veins, middle colic vein) and inferior mesenteric vein (left colic vein, sigmoid veins). In most cases the right and middle colic veins are joined by the right gastroepiploic and pancreaticoduodenal veins, forming the so-called gastrocolic trunk of Henle.

2.2.5 Nerve Supply of the Colon

2.2.5.1 Sympathetic Nerves

The cecum, ascending colon, and two thirds of the transverse colon are supplied by sympathetic nerves originating from the 5th to the 12th thoracic segments. Preganglionic nerve fibers pass via the greater and lesser splanchnic nerves to the celiac and superior mesenteric plexuses, where they switch over to final neurons. Nerve fibers (postganglionic) of these neurons reach the colonic wall via the periarterial plexus along the superior mesenteric artery.

The left one third of the transverse colon, the descending colon, and sigmoid colon are supplied by sympathetic nerves from the lumbar and upper sacral spinal segments. Preganglionic nerve fibers travel via lumbar splanchnic nerves to the inferior mesenteric plexus and via sacral splanchnic nerves to the superior and inferior hypogastric plexus. Postganglionic nerve fibers enter the colonic wall via the periarterial plexus along the inferior mesenteric artery.

The sympathetic input mediates relaxation of the colonic wall and contraction of both the ileocecal valve and the vascular musculature. Afferent nerve fibers are primarily responsible for the sensation of visceral pain.

2.2.6 Parasympathetic Nerves

The cecum, ascending colon, and two thirds of the transverse colon are supplied by parasympathetic nerve fibers derived from the vagus nerve. These vagal nerve fibers travel via the celiac and superior mesenteric plexuses into the colonic wall, where they switch to intramural ganglion cells.

The left one third of the transverse colon, the descending colon, and the sigmoid colon are supplied by parasympathetic nerves originating from the second to the fourth sacral segments (the sacral parasympathetic input). The parasympathetic nerve fibers pass through the inferior and superior hypogastric plexus, via the pelvic splanchnic nerves, and reach the colonic wall, following the branches of the inferior mesenteric artery.

The parasympathetic input mediates contraction of the colonic wall musculature, relaxation of the internal anal sphincter, and secretomotor functions. Sensations of distension and pain are carried by afferent parasympathetic nerve fibers (Fig. 2.2).

2.2.6.1 Enteric Nervous System

While the connections between the central nervous system and the intestine are established by

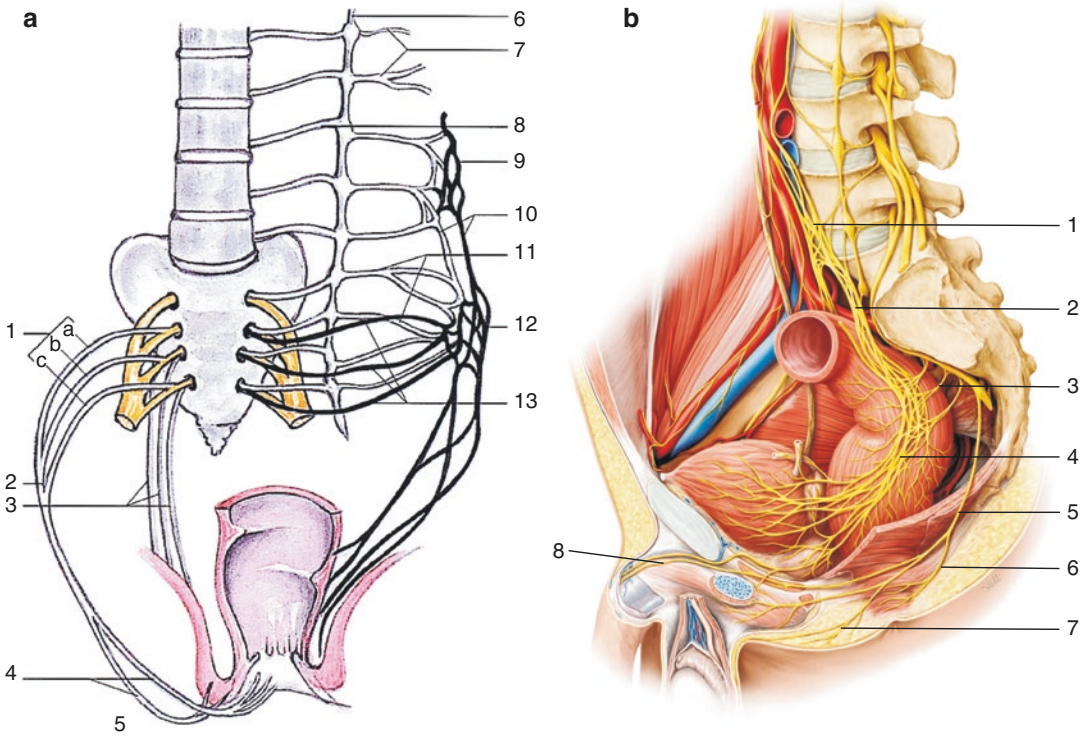


Fig. 2.2 Nerve supply of the anorectum and pelvic floor. (**a**) Somatic and autonomic innervation of the anorectum and pelvic floor. *1* sacral nerves (**a** S2, **b** S3, **c** S4), *2* pudendal nerve, *3* levatory nerves, *4* inferior rectal nerves, *5* somatic innervation of the pelvic floor and external anal sphincter, *6* sympathetic trunk, *7* lumbar splanchnic nerves, *8* grey communicans nerve, *9* superior hypogastric plexus, *10* hypogastric nerves, *11* sacral splanchnic nerves, *12* inferior hypogastric plexus, *13* pelvic splanchnic nerves. (**b**) Somatic and autonomic innervation of the anorectum and pelvic floor in men. *1* superior hypogastric plexus, *2* hypogastric nerves, *3* sacral splanchnic nerves, *4* inferior hypogastric plexus, *5* pudendal nerve, 6 inferior rectal nerves, *7* posterior scrotal nerves, *8* dorsal nerve of the penis

extrinsic sympathetic and parasympathetic nerves to modulate gut activities, the enteric nervous system resides within the bowel wall and is responsible for coordinating major intestinal functions such as motility and secretion. In addition to sympathetic and parasympathetic mediators, a broad spectrum of nonadrenergic, noncholinergic neurotransmitters is released by intrinsic intramural nerve cells to establish local reflex circuits, which provide control of intestinal motor functions virtually independent from higher nervous inputs.

The enteric nervous system nerves comprises ~150 million neurons ("little brain of the gut") and is organized in different nervous networks (plexus) composed of clusters of nerve cells (enteric ganglia) and interconnecting nerve fiber strands. The major plexuses are located in the intermuscular space between the longitudinal and circular muscle layers (myenteric plexus), within the submucosa (external and internal submucosal plexuses), and within the mucosa (mucosal plexus) (Fig. 2.3).

In addition to the nerve plexus, both the circular and longitudinal muscle layers and the intermuscular space contain a network of interstitial cells of Cajal (ICCs). These interdigitating cells are intercalated between nerve fibers and smooth muscle cells and generate the slow-wave activity of the colonic musculature; they are also referred to as intestinal pacemaker cells. Moreover, they are actively involved in intestinal neurotransmission by mediating neuronal inputs to smooth muscle cells.

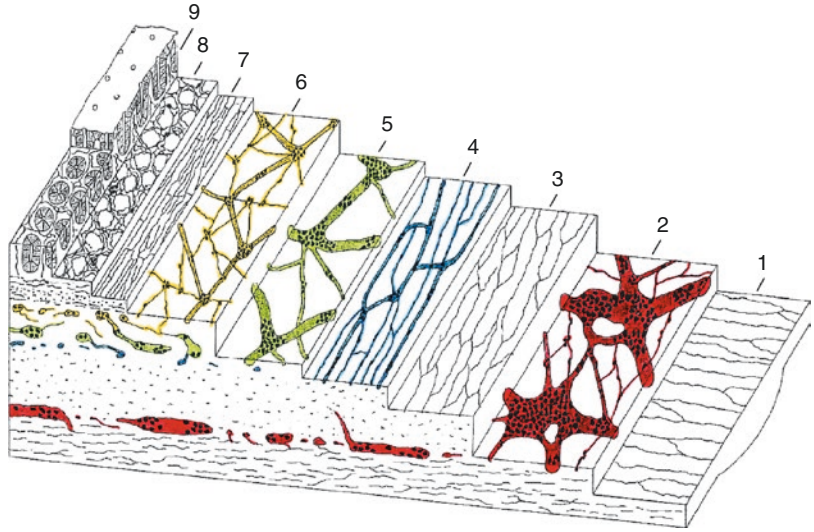


Fig. 2.3 Topographical organisation of the enteric nervous system in the human colon. *1* plexus of the longitudinal muscle layer, *2* myenteric plexus, *3* plexus of the circular muscle layer, *4* external submucosal plexus, *5* intermediate submucosal plexus, *6* internal submucosal plexus, *7* plexus of the lamina muscularis mucosae, *8* mucosal plexus (subglandular portion), *9* mucosal plexus (periglandular portion). Ganglionated plexus appear in color, *dark dots* represent enteric nerve cells

2.3 Rectum and Anus

The rectum is the final segment of the large intestine and has a twofold function:

- Retention of feces and closure of the gastrointestinal tract (continence)
- Controlled evacuation of feces (defecation)

The rectum is 15–19 cm long and extends from the third sacral vertebra to the perineum. It is the most dorsally located intrapelvic organ, descending along the sacrococcygeal concavity (sacral flexure) and passing through the pelvic floor at the anorectal junction (perineal flexure, anorectal angulation).

The rectum is divided into two segments:

- Rectal ampulla
- Anal canal

In contrast to the colon, the rectum is characterized by the following anatomic peculiarities:

- Confluence of teniae coli to a continuous longitudinal smooth muscle layer
- Absence of epiploic appendices
- Presence of permanent semilunar transverse folds, the most constant middle fold (a Kohlrausch fold), and a superior and inferior fold (Houston's folds)
- Extraperitoneal position of the lower and dorsal parts of the organ

2.3.1 Rectal Ampulla

The rectal ampulla is the widest part of the rectum, with a perimeter varying between 8 and 16 cm. Its ventral wall is covered by visceral peritoneum reflecting on to the bladder and seminal vesicles in males (rectovesical pouch) and onto the uterus and upper posterior vaginal wall in females (rectouterine pouch, Douglas's pouch). The rectal musculature is arranged in a folding grille-like pattern, enabling the wall to adequately adjust to the highly variable filling state.

2.3.2 Anal Canal and Anus

The anal canal (pars analis recti) is 2.5–4 cm long with a perimeter of 5–9 cm. It forms a 90–100°

angle with the rectum (the anorectal angle), which is caused by the constant traction of the puborectal sling (see the section "Pelvic floor" later in the chapter). The inner lining of the anal canal varies along its course to the anus (Fig. 2.4).

2.3.2.1 Inner Surface of the Anal Canal

The upper part of the anal canal is covered with a pink intestinal mucosa (the colorectal zone). At the transitional zone the wet columnar epithelium gives way to the dry squamous epithelium, displaying a histological mosaic of cylindrical, cubic, and flat epithelial cells. Macroscopically, the transitional zone is characterized by 8–12 vertical anal columns (Morgagni's columns), each of which contains a terminal branch from the superior rectal artery. The anal columns are separated by the anal sinuses, which form pocket-like mucosal folds at their lower ends, called anal valves or crypts. The row of alternating anal columns and sinuses corresponds to the dentate line (pectinate line, crypt line), which is considered to be the junction between the endodermal (cloacal) and ectodermal (proctodeal) parts of the anal canal.

Between the dentate line and the anocutaneous line, the pale anoderm (squamous zone) extends for ~1.5 cm to the anal verge. The anoderm is lined by a nonkeratinized, stratified squamous epithelium devoid of glands and hairs but richly equipped with sensory nerve endings that are highly sensitive to touch, pain, and temperature. A whitish-bluish line (lineal alba, Hilton's line) is occasionally visible at the lower end of the anal canal, corresponding to the underlying bulge of the internal anal sphincter.

While the "surgical" anal canal comprises the entire length of the canal, from the anorectal junction down to the anal verge, the "anatomic" anal canal is defined by the lower part extending from the dentate line to the anocutaneous line.

2.3.2.2 Anus

Below the anocutaneous line, the anal canal gives way to the anus. The hairless perianal skin is a dull brown color and radially folded because of the contraction of the corrugator ani muscle. The skin contains sweat, sebaceous, and apocrine glands and is supplied by perianal blood vessels originating from the inferior rectal artery.

2.3.2.3 Internal Anal Sphincter

The internal anal sphincter comprises elliptical bundles of smooth muscle and corresponds to the thickened, tube-like end of the circular muscle layer of the rectum (Fig. 2.4). The muscle is 5–8 mm thick and 2–3 cm long. In relation to the anal canal, the internal anal sphincter extends from the anorectal junction down to the anocutaneous line; the most prominent part projects on to the white linea alba (Hilton's line). Normally the lower border is overlain by the subcutaneous part of the external anal sphincter. Because of its permanent involuntary contraction, the internal anal sphincter is readily palpable as a rigid cylinder, in particular when the striated external anal sphincter is completely relaxed (e.g., under anesthesia).

2.3.2.4 Conjoined Longitudinal Muscle (Corrugator Ani Muscle)

The longitudinal muscle layer of the rectum also changes its morphology as it approaches the anal canal (Fig. 2.4). Diverging bundles of smooth muscle fibers extend between the internal and external anal sphincters toward the perianal region and are joined by striated muscle fibers from the puborectalis ("conjoined" longitudinal) muscle. Distally, the muscular fibers become increasingly fibroelastic and enter the perianal skin with small tendons, producing radial wrinkles (hence "corrugator" ani muscle). The most peripheral muscular septa radiate outward and pass between the subcutaneous and superficial parts of the external anal sphincter into the ischioanal fossa. By inserting in the superficial perineal fascia, these fibers contribute to the separation of the ischioanal space from the subcutaneous perianal space.

2.3.2.5 Corpus Cavernosum Recti

The submucosa of the upper part of the anal canal contains a specific arrangement of arteriovenous anastomoses best described as the corpus cavernosum recti (annulus haemorrhoidalis, glomera venosa haemorrhoidalia) (Fig. 2.4). Branches

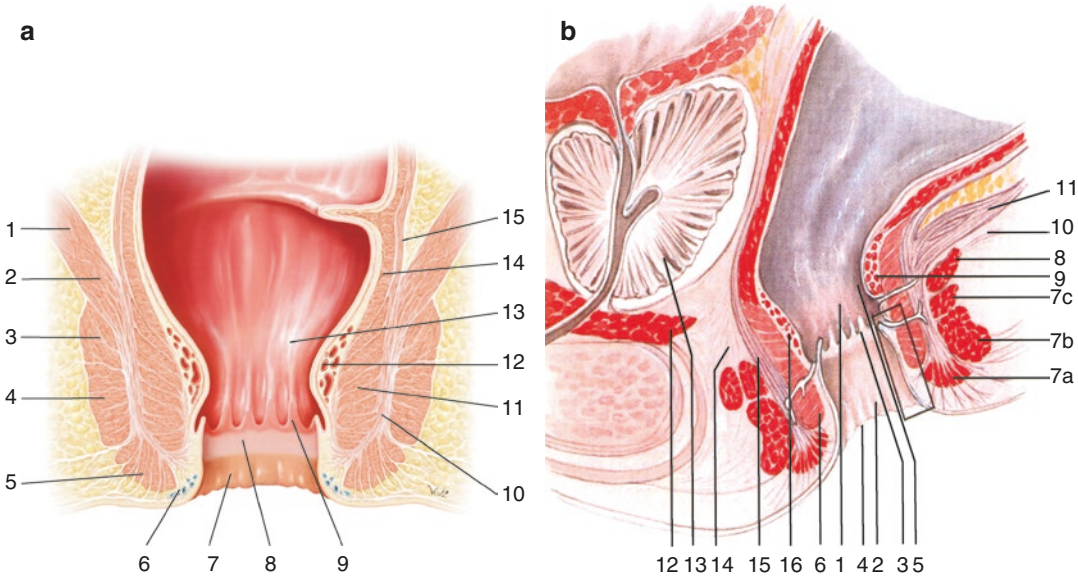


Fig. 2.4 Rectum and anal canal. (**a**) Frontal section of the anorectum. *1* levator ani muscle (iliococcygeal muscle), *2* levator ani muscle (puborectal muscle), *3–5* external anal sphincter (deep, superficial, subcutaneous part), *6* perianal veins, *7* perianal skin, *8* anoderm, *9* anal columns and crypts, *10* conjoined longitudinal muscle (corrugator ani muscle), *11* internal anal sphincter, *12* corpus cavernosum recti, *13* anorectal junction, *14* circular rectal muscle layer, *15* longitudinal rectal muscle laycanal, *3* anal crypts, *4* anocutaneous line, *5* anorectal junction, *6* internal anal sphincter, *7* external anal sphincter (a subcutaneous part, (**b**) superficial part, (**c**) deep part), *8* puborectal muscle, *9* corpus cavernosum recti, *10* anococcygeal ligament, *11* levator ani muscle, *12* deep transverse perineal muscle, *13* prostate, *14* prerectal muscle fibres, *15* corrugator ani muscle, *16* anal canal muscle

from the superior rectal artery reach the corpus cavernosum recti from the right (7 and 11 o'clock, in the lithotomy position) and left (3 o'clock) sides and release their oxygenated arterial blood into the cavernous tangles, which are bare of capillaries. The position of the arterial branches supplying the corpus cavernosum recti corresponds to the typical topographic distribution pattern of hemorrhoids originating from the corpus cavernosum recti. The blood is drained by veins, which penetrate through the internal anal sphincter and are collected in the external rectal venous plexus. The subfascially located plexus drains into the inferior, medial, and superior rectal veins.

As a result of transsphincteric blood drainage, the blood filling the corpus cavernosum recti is determined by the degree of contraction of the internal anal sphincter. Its constant tonus smoothly compresses the draining veins, resulting in a physiologic cushion-like swelling of the corpus cavernosum recti. Normally, the corpus cavernosum recti extends from the anorectal junction down to the dentate line and is fixed by the anal canal muscle.

2.3.2.6 Proctodeal Glands

The proctodeal glands are of ectodermal origin and form at the junction between the cloacal and proctodeal parts of the anal canal. They mostly originate in the intermuscular space between the internal and external anal sphincters, run through the internal anal sphincter muscle, and open into the anal crypts (Fig. 2.4b). However, they may also bridge the intermuscular space and reach into the external anal sphincter. The tubular excretory ducts are lined with cubic epithelium, and the alveolar secretory parts are branched and covered with a columnar epithelium of a primarily eccrine secretion type. The glands are surrounded by lymphatic tissue arranged in periglandular follicles. The number of proctodeal glands ranges between 5 and 15. Most of the glands are encountered along the dorsal anal commissure; they are less frequently found at the

lateral anal region and are only occasionally present at the ventral anal commissure. This topographic distribution resembles the preferential location of perianal fistula and abscesses considered to develop from infected proctodeal glands. As rudimentary anal skin appendages, proctodeal glands are not consistently present; in about one third of individuals only small subepithelial crypts end blindly within the submucosa.

2.3.3 Pelvic and Perirectal Fasciae

While the inner pelvic wall is covered by the parietal pelvic fascia, the pelvic organs – including the rectum – are sheathed by the visceral pelvic fascia (endopelvic fascia). Both fasciae are connected by condensed connective tissue structures traditionally described as ligaments (e.g., lateral rectal ligaments, rectal stalks, paraproctium). Originally, they were considered to function as support structures for the pelvic viscera. From both anatomic and embryological points of view, however, these ligaments do not provide substantial mechanical fixation of the pelvic organs and instead primarily serve as access routes for their vascular and nervous supplies.

2.3.3.1 Rectal Fascia and Mesorectum

The part of the visceral pelvic fascia that sheathes the rectum is called the rectal fascia. The rectal fascia is composed of a connective tissue sheath bare of blood vessels and nerves, and constitutes a morphologic barrier, thereby preventing early penetration of a rectal neoplasia into adjacent organs. Clinically, the rectal fascia is also termed *mesorectal fascia*, as the fascial envelope encloses perirectal fatty tissue containing the major routes of blood supply to and lymphatic drainage from the rectal wall – comparable to the mesenteries of the other intestinal segments. Accordingly, the perirectal fatty tissue corresponds to the mesorectum, which is most developed at the dorsal side of the rectum, displaying two mesorectal "cheeks."

Between the mesorectal fascia and the parietal pelvic fascia opens the retrorectal space. This avascular and nerve-free, slit-like space corresponds to the access route for the dorsal mobilization of the rectum during total mesorectal excision. The retrorectal space extends down to the pelvic floor, where the mesorectal fascia fuses with the parietal pelvic fascia (Waldeyer's fascia). Between the parietal pelvic fascia and the sacrum opens another space, called the presacral space, which contains sacral arteries and veins and the origin of parasympathetic pelvic splanchnic nerves covered by the presacral fascia (Fig. 2.5).

2.3.3.2 Rectoprostatic/Rectovaginal Septum

The ventral part of the mesorectal fascia comes into close contact with the dorsal urogenital fascia to form the rectoprostatic or rectovaginal septum. In males the rectoprostatic septum (Denonvilliers's fascia) covers the prostate, seminal vesicles, and ductus deferens, separating them from the anterior rectal wall. The mesenchymal layer of the rectoprostatic septum contains nerve branches of the inferior hypogastric plexus, in particular the urogenital neurovascular bundles (Walsh's bundles), and approaches the prostate and seminal vesicles dorsolaterally.

2.3.3.3 Paraproctium

Laterally, the mesorectal fascia reflects toward the pelvic wall to provide access to minor blood and lymphatic vessels and, in particular, to autonomic nerves diverging from the inferior hypogastric plexus into the rectal wall. This loosely arranged connective tissue between the pelvic wall and the rectum (the "T-junction") corresponds to the paraproctium, often referred to as lateral rectal ligaments or rectal stalks, approaching the rectal wall from a dorsolateral direction.

2.3.4 Blood Supply of the Rectum and Anus

As a hindgut derivate the rectum is mainly supplied by the terminal branch of the inferior mesenteric artery, the superior rectal artery (diameter, 3.0 ± 1.1 mm), which contributes more than 80 % of the rectal blood supply (Fig. 2.6). Passing within the mesorectum, the artery divides in two to three large branches surrounding the posterolateral rectal wall. The branches ramify between

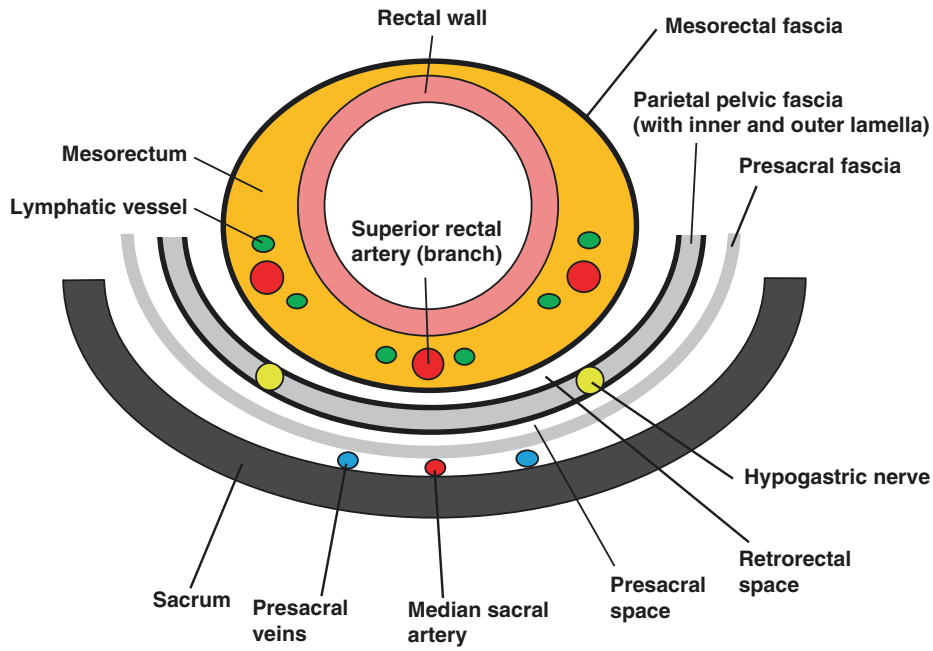


Fig. 2.5 Pelvic and perirectal fasciae. This schematic illustration of the pelvic and perirectal fasciae delimits their different perirectal spaces and highlights the topography of autonomic nerves, blood vessels, and lymphatic vessels/nodes

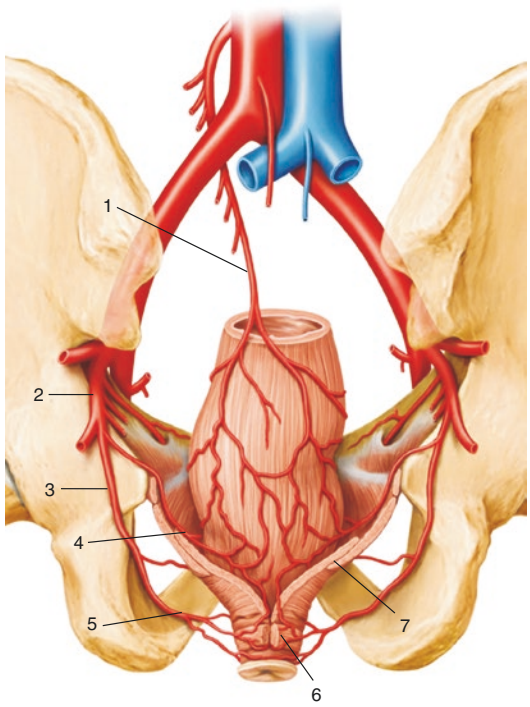


Fig. 2.6 Blood supply of the rectum and anal canal: rectal arteries. *1* superior rectal artery (from inferior mesenteric artery), *2* internal iliac artery, *3* pudendal artery, *4* medial rectal artery, *5* inferior rectal artery, *6* external anal sphincter, *7* levator ani muscle

the muscle layers, enter the submucosa, and descend to the anal columns, where they open into the corpus cavernosum recti. By contrast, the medial rectal arteries, originating from the internal iliac arteries, are inconstant and bilaterally present in only 10% of individuals. Their contribution is rather small, and anastomoses with the superior and inferior rectal arteries are poorly developed. The lower anal canal and the internal anal sphincter are supplied by anal arteries from the inferior rectal arteries. They approach the anal region from the pudendal arteries, which are located within Alcock's canal, via the ischioanal fossa and divide into ventral and dorsal branches. Functional anastomoses are established between the inferior and superior rectal arteries within the anal canal. The posterior wall of the anal canal and the internal anal sphincter are also supplied by the median sacral artery.

2.3.5 Lymphatic Drainage of the Rectum and Anus

Similar to the blood supply, the main lymphatic drainage of the rectum is achieved by intramural

lymphatic vessels passing to inferior mesenteric lymph nodes via the mesorectum. The lymphatic drainage may take place along the paraproctium into the internal iliac lymph nodes, but this occurs only if the mesorectal fascia is penetrated in advanced tumor stages. Lymphatic vessels of the lower anal canal and the perianal region project to superficial inguinal lymph nodes.

2.3.6 Nerve Supply of the Rectum and Anus

Whereas the rectum and upper anal canal are supplied by autonomic nerves, the lower anal canal and the anus receive somatic input via the pudendal nerves (Fig. 2.2).

2.3.6.1 Autonomic Nerves

Lumbar sympathetic nerves pass along the inferior mesenteric and superior rectal arteries, forming considerably rigid periarterial nervous networks, the inferior mesenteric and superior hypogastric plexuses. From the superior hypogastric plexus originate the left and right hypogastric nerves, which enter the pelvic cavity embedded within the two lamellae of the parietal pelvic fascia (Fig. 2.5). They approach the rectal wall laterally and diverge into an intrapelvic nervous network called the inferior hypogastric plexus (pelvic plexus). Sacral parasympathetic nerves join the inferior hypogastric plexus via pelvic splanchnic nerves (nervi erigentes), intermingle with their sympathetic counterparts, and commonly enter the rectal wall to establish connections with the intramural enteric nervous system.

The inferior hypogastric plexus also provides the autonomic nerve supply for the intrapelvic urogenital organs that maintain sexual and lower urinary tract functions. The autonomic nerves are at risk during rectal resection, in particular during lateral (paraproctium) and ventral (rectoprostatic/rectovaginal septum) mobilization of the rectal wall.

2.3.6.2 Somatic Nerves

The lower anal canal is supplied by perianal branches of the pudendal nerves. In contrast to the autonomically innervated rectum and upper anal canal, the anodermal segment is highly sensitive to touch, pressure, pain, and temperature because of densely distributed somatosensory nerve endings.

2.4 Pelvic Floor

The pelvic floor comprises both striated and smooth muscles covered by fasciae (the rhabdo- and lissomusculofibrous systems), providing a twofold function:

- Closure of the pelvic cavity to provide support for intrapelvic organs
- Controlled opening for bladder and rectum evacuation and parturition

Because of its physiological weakness (less muscle strength, less nervous input, wider urogenital opening) and because of the stressful strain that occurs during parturition, the female pelvic floor is generally more susceptible to insufficiency. This may result in descending perineum syndrome, pelvic organ prolapse, and evacuation disorders.

2.4.1 Levator Ani Muscle

The levator ani muscle – a broad, flattened, and funnel-shaped muscle attached to the pelvic wall – forms most of the pelvic floor. Ventrally, the muscular sheet leaves a midline gap for the urethra and vagina (urogenital hiatus) and the anal canal (anal hiatus). The levator ani muscle comprises various muscular parts (Fig. 2.7):

2.4.1.1 Ileococcygeal Muscles

The ileococcygeal muscles arise from the tendinous arc formed by the obturator fascia, attach to the coccyx (the last two sacral vertebrae), and fuse in a midline raphe. The muscular sheet is thin and often displays intramuscular, slit-like gaps, particularly in females, which may give way to the propagation of ischiorectal abscesses (supralevatory spread).

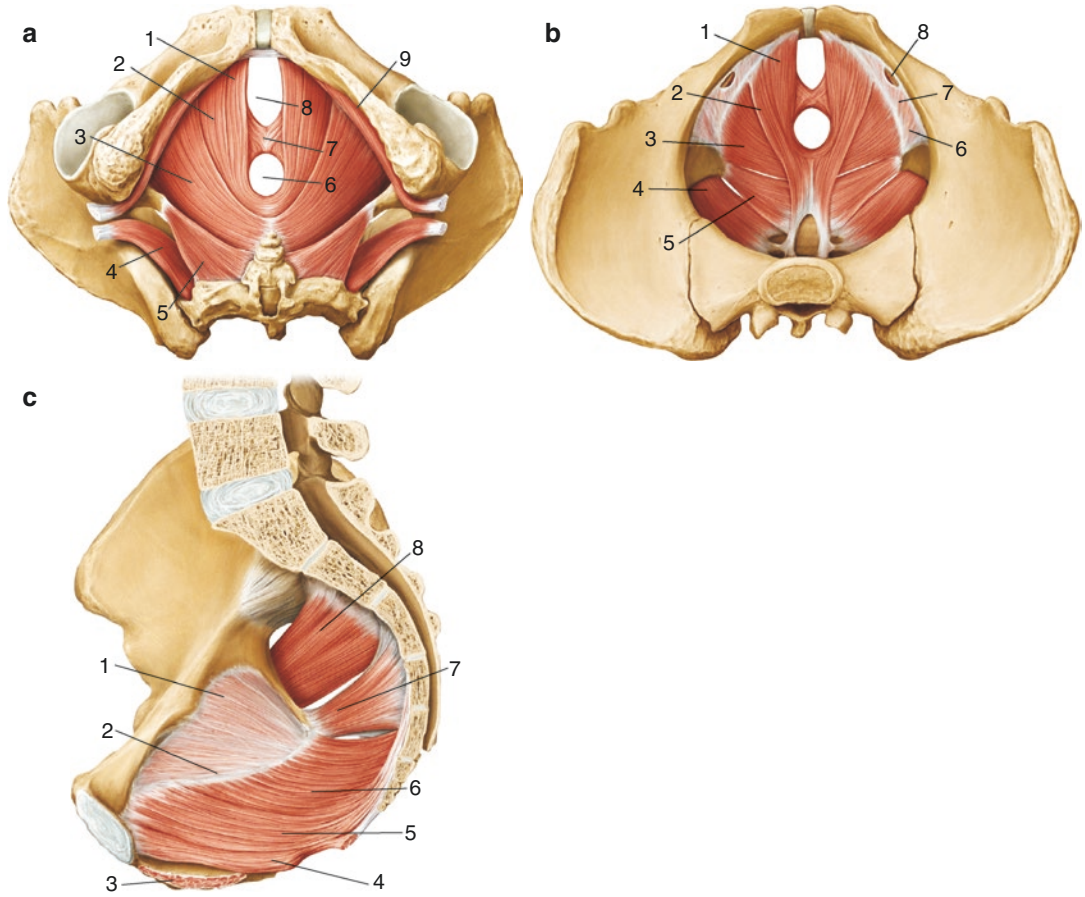


Fig. 2.7 Pelvic floor. (**a**) Pelvic floor muscles in women after removal of the urogenital diaphragm (caudal view). *1* puborectal muscle, *2* pubococcygeal muscle, *3* iliococcygeal muscle, *4* piriformis muscle, *5* coccygeal muscle, *6* anal hiatus, *7* prerectal muscle fibres, *8* urogenital hiatus, *9* internal obturator muscle. (**b**) Pelvic floor muscles in women after removal of the urogenital diaphragm (cranial view). *1* puborectal muscle, *2* pubococcygeal muscle, *3* iliococcygeal muscle, *4* piriformis muscle, *5* coccygeal muscle, *6* internal obturator muscle covered by obturator fascia, *7* tendinous arc, *8* obturator canal. (**c**) Pelvic floor muscles (right pelvis, medial view). *1* internal obturator muscle covered by obturator fascia, *2* tendinous arc, *3* deep transverse perineal muscle, *4* puborectal muscle, *5* pubococcygeal muscle, *6* iliococcygeal muscle, *7* coccygeal muscle, *8* piriformis muscle

2.4.1.2 Pubococcygeal Muscle

The pubococcygeal muscle extends above the ileococcygeal muscles from the pubic bone to the sacrum, where it forms a tendinous plate attached to the coccygeal bone. Some fibers decussate to the periurethral musculature and insert into the walls of the vagina (pubovaginal muscle) and rectum (puboanal muscle). The puboanal fibers blend with fibers of the longitudinal rectal muscle to form the conjoined longitudinal muscle.

2.4.1.3 Puborectal Muscle

The puborectal muscle is the most prominent muscle of the pelvic floor. Inseparable from the pubococcygeal muscle at its origin, the muscle bends at the anorectal junction to form a sling behind the rectum. Contraction results in a compression of the anal canal by pulling the anorectal junction toward its *punctum fixum* (the pubic bone), thereby reducing the anorectal angle. The puborectal sling is intimately fused with the deep part of the external anal sphincter. From the cau-

dal part of the muscle, prerectal fibers decussate to insert into the perineal tendinous center.

2.4.1.4 Coccygeal Muscles

The coccygeal muscles lie dorsocranial to the levator ani muscle and extend from the ischial spine to the lateral margins of the coccyx along the sacrospinal ligaments. Lying in the same plane as the levator ani muscle, they complete the muscular pelvic diaphragm at its posterior end.

2.4.2 External Anal Sphincter

Below the levator ani muscle, the anal canal is surrounded by the external anal sphincter (Fig. 2.4). The muscle forms an elliptical cylinder about 15 mm thick and is divided by septa into three parts. Although the external anal sphincter is a striated skeletal muscle, its fibers mainly comprised slow-twitch type I fibers, mediating a prolonged contraction suitable for maintaining an adequate basal tonus.

2.4.2.1 Subcutaneous Part

The subcutaneous part circumscribes the anal orifice deep to the skin below the lower border of the internal anal sphincter. Some fibers are anteriorly attached to the perineal tendinous center and posteriorly to the anococcygeal ligament.

2.4.2.2 Superficial Part

The superficial part lies above and lateral to the subcutaneous part. Because of its firm attachment to both the perineal tendinous center and the anococcygeal ligament, this part is shaped like an ellipse. The dorsal region frequently displays a crypt-like recess, thereby favoring the development of anal fissures at the coccygeal midline.

2.4.2.3 Deep Part

The deep part is the thickest and most cranially located segment surrounding the internal anal sphincter. Its fibers blend inseparably with the puborectal muscle and are not attached posteriorly to the coccyx. Whereas in males all three parts of the external anal sphincter are equally present along the entire circumference, in females the external anal sphincter muscle is anteriorly reduced to one third of its posterior thickness, in particular because of the less developed deep part.

2.4.3 Smooth Pelvic Muscles

In addition to striated muscles mainly composed of slow-twitch type I fibers (rhabdomusculofibrous system), the pelvic floor is also equipped with several smooth muscle elements (lissomusculofibrous system) predominantly located along the medial border of the levator sling. Smooth muscle fibers also extend from the rectal wall to the vagina (rectovaginal muscle), to the membranous part of the urethra (rectourethral muscle, Roux muscle), and to the coccyx along the anococcygeal ligament (rectococcygeal muscle, retractor recti muscle, Treitz muscle).

2.4.4 Nerve Supply of the Pelvic Floor

All striated muscles of the pelvic floor are innervated from sacral spinal segments ($S_{2–4}$) (Fig. 2.2). The somatomotor supply of the levator ani muscle and the external anal sphincter is provided by inferior rectal branches of the pudendal nerve and by direct branches from the sacral plexus. The smooth musculature is supplied by autonomic nerve fibers originating from the inferior hypogastric plexus (pelvic plexus) (Fig. 2.2).

2.4.5 Blood Supply of the Pelvic Floor

The pelvic floor is supplied by branches from the pudendal artery and the inferior rectal and perineal arteries. Furthermore, the median and lateral sacral arteries contribute from the dorsal side and the obturator arteries from the lateral sides.

2.4.6 Anal Continence Organ

The pelvic floor muscles contribute substantially to the maintenance of anal continence. However, closure of the anal canal is a complex function achieved

through the synergistic interaction of different anatomic components, which together resemble an anal continence "organ." Maintenance of anal continence requires both autonomic and somatic nervous control, and is mediated by various structures:

- Puborectal sling, providing kink-like compression
- External anal sphincter, providing a lace-like closure
- Internal anal sphincter, providing a ring-like narrowing
- Corpus cavernosum recti, providing a cushion-like closure
- Anodermal segment, providing a highly discriminative somatic sensation of luminal content
- Rectal ampulla, providing a visceral sensation of luminal content before defecation

2.4.7 Pelvic Spaces

The musculofibrous systems of the pelvic floor divide the region between the peritoneal cavity and the perineal skin into three different compartments (Fig. 2.8).

2.4.7.1 Subperitoneal Space

The subperitoneal space is delimited by the pelvic peritoneum from above and ends at the pelvic diaphragm (supradiaphragmatic/supralevatory compartment). It contains loosely arranged connective tissue, which condenses around the pelvic organs to form the paracystium, paraprostatium, paracolpium, parametrium, and paraproctium. Toward the lateral pelvic wall the space widens to give access to the neurovascular supply of the pelvis, pelvic organs, and lower extremities. Autonomic nerve fibers (hypogastric nerves, the inferior hypogastric plexus) descend from both sides, passing through the subperitoneal space in a dorsoventral direction to approach the intrapelvic organs.

2.4.7.2 Ischioanal Space and Perineal Body

Below the pelvic diaphragm extends the ischioanal fossa (infradiaphragmatic/infralevatory compartment). The space is shaped like a pyramid, with its base toward the perineal skin and its apex at the junction of the internal obturator and levator ani muscles, covered by the obturator and inferior pelvic diaphragmatic fasciae. A duplicate of the obturator fascia (Alcock's canal) sheathes the internal pudendal vessels and pudendal nerve,

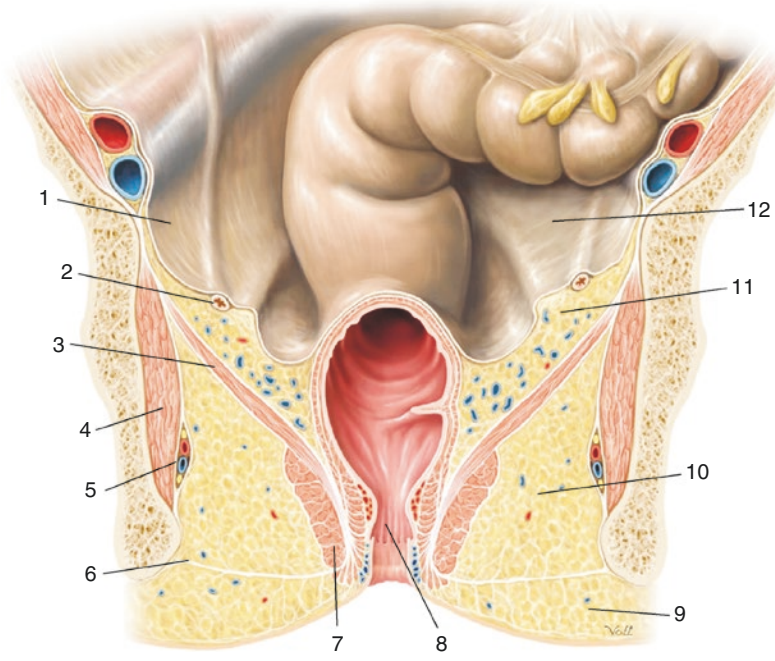


Fig. 2.8 Pelvic spaces. Frontal section of the pelvis (ventral view). *1* parietal peritoneum, *2* ureter, *3* levator ani muscle covered by superior and inferior pelvic diaphragmatic fascia, *4* obturator muscle covered by obturator fascia, *5* pudendal nerve and vessels ensheathed by doubling of obturator fascia (Alcock's canal), *6* superficial perineal fascia (transverse septum), *7* external anal sphincter, *8* anal canal, *9* perianal space (subcutaneous layer), *10* ischioanal space (infradiaphragmatic/infralevatory compartment), *11* subperitoneal space (supradiaphragmatic/supralevatory compartment), *12* peritoneal cavity

releasing their branches into the ischioanal fossa to reach the perineal structures. The ventral part of the ischioanal fossa surrounds the urethra and the vagina and is caudally closed by the urogenital diaphragm. The dorsal part surrounds the anal canal and extends toward the sacrotuberal ligaments and the gluteus maximus muscle. The ischioanal fossa is filled with loosely arranged areolar fat (corpus adiposum perinei). Because the anococcygeal ligament does not completely separate both sides of the ischioanal fossa, infralevatory abscesses may easily spread from one side to the other (an infralevatory "horseshoe" abscess).

The perineal body corresponds to the common tendinous insertion area of the external anal sphincter, the bulbospongious muscles, and transverse perineal muscles. The inferior continuation of the rectogenital septum is intimately connected to the perineal body.

2.4.7.3 Perianal Space

Toward the perianal region the ischioanal fossa is caudally delimited by a thin fascia called the superficial perineal fascia, which forms from the diverging tendinous endings of the conjoint longitudinal muscle. The perianal space extends below this connective tissue plane. This space corresponds to the subcutaneous layer underlying the perianal skin and contains small fat lobules separated by rigid connective tissue septa.

Suggested Reading

1. Aigner F, Gruber H, Conrad F, Eder J, Wedel T, Zelger B, Engelhardt V, Lametschwandtner A, Wienert V, Böhler U, Margreiter R, Fritsch H. Revised morphology and hemodynamics of the anorectal vascular plexus: impact on the course of hemorrhoidal disease. Int J Colorectal Dis. 2009;24:105–13.
2. Fritsch H, et al. Clinical anatomy of the pelvic floor. Adv Anat Embryol Cell Biol. 2004;175:1–64.
3. Heald BJ, Moran BJ. Embryology and anatomy of the rectum. Semin Surg Oncol. 1998;15:66–71.
4. Kinugasa Y, Murakami G, Uchimoto K, Takenaka A, Yajima T, Sugihara K. Operating behind Denonvilliers' fascia for reliable preservation of urogenital autonomic nerves in total mesorectal excision: a histologic study using cadaveric specimens, including a surgical experiment using fresh cadaveric models. Dis Colon Rectum. 2006;49:1024–32.
5. Lange J, Mölle B, Girona J. Chirurgische Proktologie. Heidelberg: Springer; 2006.
6. Lienemann A, et al. Functional imaging of the pelvic floor. Eur J Radiol. 2003;47:117–22.
7. Loeweneck H, Feifel G. Lanz Wachsmuth – Praktische Anatomie, Ein Lehr- und Hilfsbuch der anatomischen Grundlagen ärztlichen Handelns, 2. Band, 6. Teil, Bauch. Heidelberg: Springer; 2003.
8. Michels NA, et al. Variant blood supply to the descending colon, rectosigmoid and rectum based on 400 dissections. Its importance in regional resections: a review of medical literature. Dis Colon Rectum. 1965;8:251–78.
9. Platzer W. Pernkopf-Anatomie, Atlas der topographischen und angewandten Anatomie des Menschen, 2. Band, Brust, Bauch und Extremitäten. 3rd ed. München: Urban & Schwarzenberg; 1989.
10. Sakaguchi T, Suzuki S, Morita Y, Oishi K, Suzuki A, Fukumoto K, Inaba K, Kamiya K, Ota M, Setoguchi T, Takehara Y, Nasu H, Nakamura S, Konno H. Analysis of anatomic variants of mesenteric veins by 3-dimensional portography using multidetector-row computed tomography. Am J Surg. 2010;200(1):15–22.
11. Schemann M, Neunlist M. The human enteric nervous system. Neurogastroenterol Motil. 2004;16 Suppl 1:55–9.
12. Schünke M, et al. Prometheus, LernAtlas der Anatomie, Band 2: Hals und Innere Organe. Stuttgart: Thieme; 2005.
13. Schünke M, et al. Prometheus, LernAtlas der Anatomie, Band 1: Allgemeine Anatomie und Bewegungssystem. Stuttgart: Thieme; 2005.
14. Standring S. Gray's anatomy, the anatomical basis of clinical practice. 39th ed. New York: Churchill Livingstone; 2004.
15. Stelzner F. Chirurgie an den viszeralen Abschlußsytemen. Stuttgart: Thieme; 1998.
16. Stelzner S, Holm T, Moran BJ, Heald RJ, Witzigmann H, Zorenkov D, Wedel T. Deep pelvic anatomy revisited for a description of crucial steps in extralevator abdominoperineal excision for rectal cancer. Dis Colon Rectum. 2011;54:947–57.
17. Stoker J, et al. Pelvic floor imaging. Radiology. 2001;218:621–41.
18. Tillmann B. Atlas der Anatomie. Heidelberg: Springer; 2004.
19. Wedel T, et al. Organization of the enteric nervous system in the human colon demonstrated by whole-mount immunohistochemistry with special reference to the submucous plexus. Ann Anat. 1999;181:327–37.

Physiology of Colon, Rectum, and Anus

3

Klaus Krogh and Soeren Laurberg

3.1 Functions of the Colon and Rectum

The main functions of the human colon and rectum are:

- Transport and storage of feces
- Absorption of water and electrolytes
- Absorption of short-chain fatty acids (SCFAs)

Most absorption of water, electrolytes, and SCFAs occurs in the right colon, whereas the main function of the left colon is storage and evacuation of feces. Feces are transported in the large bowel as a result of muscular contraction in the walls of the colon and rectum. A knowledge of the physiology of large-bowel motility is important in understanding the various pathological changes that may effect large-bowel function.

K. Krogh, DMSc, PhD (✉)
Department of Hepatology and Gastroenterology,
Aarhus University Hospital,
Norrebrogade, Aarhus C 8000, Denmark
e-mail: klaukrog@rm.dk

S. Laurberg, DMSc
Department of Surgery, Aarhus University Hospital,
Tage Hansensgade, Aarhus C 8000, Denmark
e-mail: slaurberg@yahoo.com

3.2 Colonic and Rectal Muscle Physiology

3.2.1 Resting Membrane Potential

Smooth muscle cells within the circular and longitudinal colorectal muscle layers are arranged in bundles connected by gap junctions. Bundles fuse at many points, making each muscle layer function as a syncytium. The resting membrane potential of colorectal smooth muscle cells (−50 to −60 mV) is not constant; rather, it undergoes small undulating changes called slow waves. Slow waves are generated by the interstitial cells of Cajal (pacemaker cells).

Slow waves do not cause colorectal contractions but influence the frequency of spike potentials. Spike potentials are action potentials that occur when the resting membrane potential becomes more positive than about −40 mV. During spike potentials, calcium enters the smooth muscle cells, causing contraction.

Several factors influence the occurrence of spike potentials, either by depolarization, making the membrane potential more positive, and thus the cells more excitable, or by hyperpolarization, making it more negative and the cells less excitable. Depolarization of the membrane potential is caused by stretching of the muscle cells, acetyl choline, and several gastrointestinal hormones. Hyperpolarization is caused by epinephrine and norepinephrine.

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_3

3.2.2 Colonic Muscle Contraction

Colorectal contractions are either phasic or tonic:

- *Phasic contractions* last a few seconds and cause the intraluminal pressure to increase. They are well defined, having a definite beginning and ending. Phasic contractions are the mechanical response of smooth muscle cells to spike potentials.
- *Tonic contractions* are less well-defined, last longer – usually several minutes or more – and may or may not be associated with increased intraluminal pressure.

Transit of colonic contents is often not associated with detectable pressure changes and may be due to changes in colonic tone. Two types of tone have been described:

- *Tetanic tone* is generated by the fusion of phasic contractions and is thus dependent on phasic activity and electrical spike potentials.
- *Specific tone* is not associated with spike activity or phasic activity and is probably regulated by chemical processes.

3.2.3 Colonic Motility

The following patterns of phasic colonic contractions have been identified:

- Single nonpropagating contractions
- Antegrade pressure waves
- Retrograde pressure waves
- Periodic colonic motor activity

Single nonpropagating contractions are frequent and usually involve short segments of the colonic wall. Their main function is to mix the luminal content, thereby promoting absorption.

Antegrade pressure waves (mass or high-amplitude propagating contractions) normally occur a few times each day, usually originating in the cecum or ascending colon, and span large parts of the colon, propelling contents aborally. The development of high-resolution fiber optic manometry has allowed detailed description of colonic contractions, including mass contractions. Mass contractions occur mostly during waking hours, especially upon awakening or after meals. The latter constitutes the colonic component of the gastrocolic response. The main function of mass contractions is colonic transport, and their frequency and amplitude are reduced in patients with slow-transit constipation. Colonic mass contractions may progress into the rectum and result in defecation.

The function of *retrograde pressure waves* and *periodic colonic motor activity* (discrete bursts of periodic contractions, either propagating or localized) is unknown. High-resolution fiber optic manometry has revealed that the number of retrograde contractions is increased in patients with chronic constipation.

Colonic tone in humans remains to be described in more detail. However, both tetanic and specific tonic activities occur.

3.2.4 Rectal Motility

Rectal motility patterns resemble colonic patterns, but there are certain differences. The following *phasic rectal contractions* have been identified:

- Isolated contractions
- Short clusters of contractions
- Powerful phasic contractions

The physiological significance of *isolated contractions* and *short clusters of contractions* (often with a low amplitude and a frequency of approximately five or six contractions per minute) is as yet unknown.

Powerful phasic contractions within the rectum have been called the rectal motor complex (RMC). The RMC is usually seen every 60–120 min; it lasts several minutes and its contractions have a frequency of 3–10 per minute (Fig. 3.1). Accordingly, it has a strong resemblance to phase 3 of the migrating motor complex within the small bowel. It is often located in a very short segment of the rectum; it can, however,

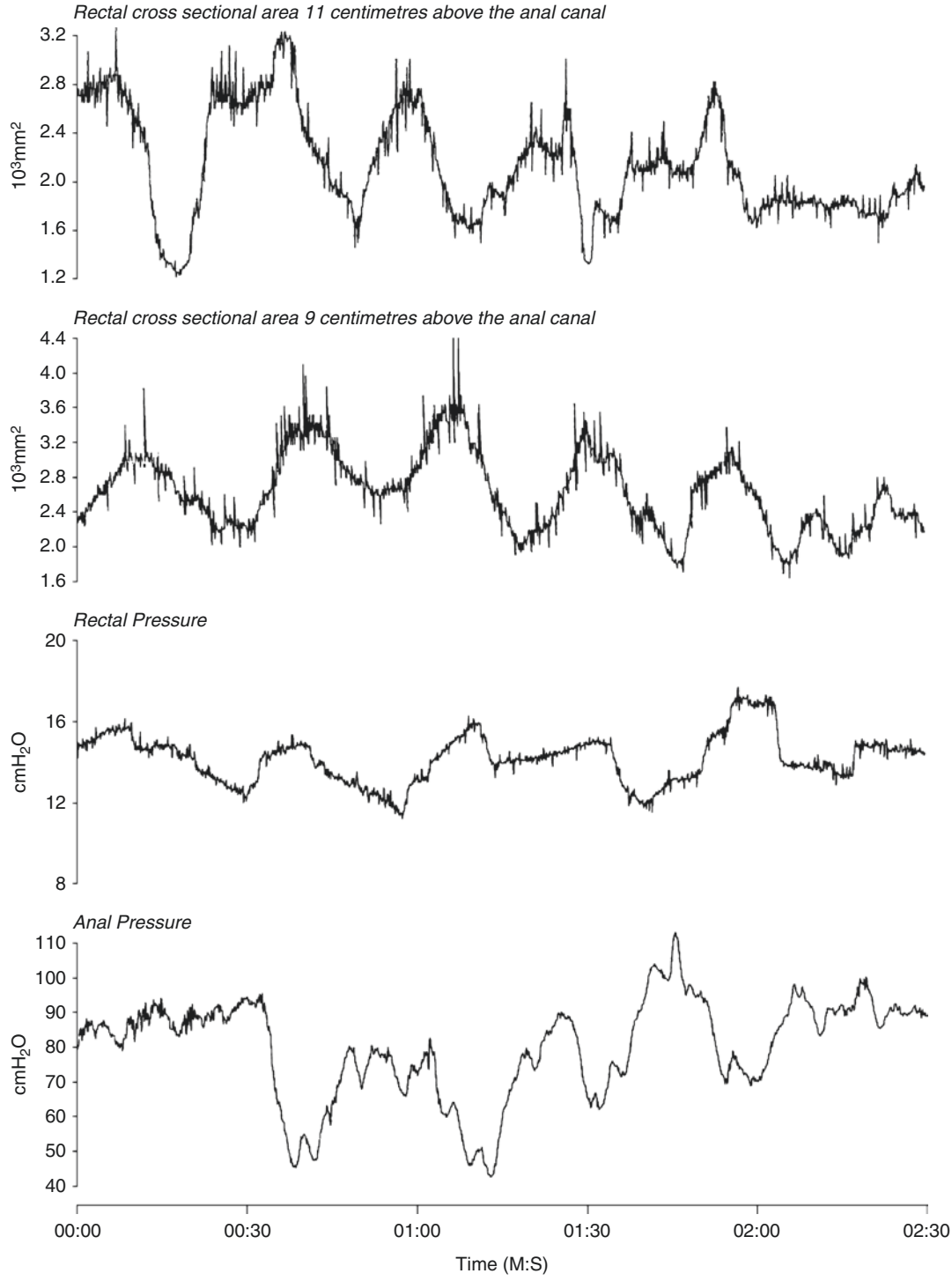


Fig. 3.1 Rectal motor complex

propagate orally or aborally. Because the RMC often is associated with contractions of the colon and the anal canal, it has been proposed that its main function is to prevent defecation.

Two types of change in *rectal tone* have been described:

- Rapid-volume waves
- Slow-volume waves

Rapid-volume waves last less than 2 min and are associated with increased luminal pressure. They are not affected by eating. *Slow-volume waves* last more than 2 min and are not associated with changes in intraluminal pressure, but their frequency increases after a meal. Slow waves may increase rectal sensation of luminal contents. Increased rectal tone during defecation may change the rectum from a capacious reservoir to a conduit.

3.2.5 Postprandial and Diurnal Changes

Colorectal tone and the frequency of both colonic mass contractions and haustral colonic contractions increase within a few minutes after a meal. The effect is more pronounced in the left than in the right colon, and it usually lasts 30–60 min. This *gastrocolic response* is mediated by sympathetic nerves and by the release of cholecystokinin and perhaps gastrin. The effect is to move contents over large distances of the colorectum, often resulting in defecation.

Sleep has a strong inhibitory effect on colonic mass contractions, haustral contractions, and colorectal tone. However, during rapid eye movement sleep and especially upon awakening, colonic tonic and phasic activity increases. The RMC is more frequent during sleep and may contribute to nocturnal continence.

3.2.6 Neural Control of Colorectal Motility

Colorectal motility is controlled by various factors:

- Enteric nervous system (ENS)
- Prevertebral sympathetic ganglia
- Autonomic system within the brain stem and spinal cord
- Higher cortical centers
- Circulating hormones
- Immune system

3.2.6.1 Enteric Nervous System

Enteric nerves within the intermuscular plexus (Auerbach's plexus) mainly control colorectal motility, and those within the submucosal plexus (Meissner's plexus) mainly control mucosal secretion and blood flow. Neurotransmitters found in the ENS can either stimulate (acetylcholine, serotonin, histamine, cholecystokinin, angiotensin, motilin, and gastrin) or inhibit (dopamine, noradrenalin, glucagon, vasoactive intestinal polypeptide, enkephalin, and somatostatin) motility. Receptors for histamine and serotonin have been classified into subgroups. Agonists and antagonists have been developed and may have a clinical role in the future.

The ENS generally consists of three types of neurons:

- Sensory neurons
- Interneurons
- Motor neurons

Sensory neurons, specialized to detect mechanical stimuli, temperature, or chemical properties, interact through multiple *interneurons* with *motor neurons* to either stimulate or inhibit smooth muscle contraction. Interneurons also integrate stimuli from the ENS with the extrinsic nerve system and hormones. Reflexes within the ENS can thus be activated by both local and extrinsic stimuli. Thus efferent parasympathetic fibers within the vagal and splanchnic nerves can stimulate motility over large distances of the gastrointestinal tract.

3.2.6.2 Prevertebral Sympathetic Ganglia

Sympathetic nerve fibers and *prevertebral sympathetic ganglia* are considered the most important mediators of the gastrocolic response, which

mediates colorectal phasic and tonic activity after a meal. *Parasympathetic activity* within the ENS depolarizes colorectal smooth muscle cells through the release of acetylcholine and stimulates colorectal motility. If parasympathetic innervation is lost, colorectal reflex activity is reduced. A clinically important example is severe defecation disorders caused by reduced left colonic and rectal reflex activity and tone after damage to the splanchnic nerves or spinal cord lesions of the conus medullaris or cauda equina.

Sympathetic activity causes hyperpolarization of colorectal smooth muscle cells, reducing colonic phasic activity and tone. The clinical effects of sympathetic denervation have not been studied in detail, but observational studies indicate that it has a minor effect on colorectal transport.

3.2.6.3 Autonomic System

Nonconscious sensory information is mediated through parasympathetic afferents in the vagal nerve or through the splanchnic nerves to the sacral spinal cord. Painful stimuli are conveyed through sympathetic afferents via a three-neuron chain from the colon to the brain: the cell body of the primary afferent is located in the dorsal root ganglia of the spinal cord. This synapses with dorsal horn neurons and conveys information through the spinothalamic or spinoreticular tracts to the thalamus and reticular formation. From there, a third neuron connects to higher sensory centers such as the anterior cingulate cortex.

The colon and rectum are insensitive to most stimuli; however, they are very sensitive to stretching. The subjective experience of rectal sensation is a feeling of rectal fullness and an urge to defecate. By contrast, colonic distension produces pain and colic. The location of rectal stretch receptors is controversial. The rectal mucosa contains no specific receptor type, which probably explains the poor discriminatory quality of rectal sensation.

3.2.6.4 Higher Cortical Centers

Higher brain centers that influence colonic motility include the frontal regions of the cerebral cortex, the stria terminalis, the amygdala, and the hypothalamus. The effects on colorectal motility are mainly inhibitory; thus a loss of supraspinal control of the sacral reflex center may cause increased left colonic and rectal reflex activity and tone (Fig. 3.2).

3.2.6.5 Hormonal and Immune System Control

Thyroid hormone stimulates colorectal motility and epinephrine reduces it. The unique ability of the immune system to recognize specific antigens makes immunoneuronal integration important for bowel function. Once the immune system within the bowel wall becomes sensitized to specific antigens, a second exposure to that antigen causes mast cells to release histamine and other messengers. Histamine acts on intestinal H_2 receptors, stimulating electrolyte, water, and mucus secretion, and promotes strong contractions, called "power propulsion," spanning large distances within the bowel. Consequently, potentially harmful antigens are quickly cleared from the lumen.

3.3 Colorectal Transit Time

Total and segmental colorectal transit times show great individual variation. Healthy asymptomatic subjects may have total colorectal transit times of up to 4 days. Left colonic and rectal transit time is usually longer than right colonic transit time. In healthy subjects, stool frequency and consistency probably correlate better with rectosigmoid transit time than with total colonic transit time. However, stool weight per day correlates with colonic transit time.

Stool weight in healthy people consuming a normal diet in Europe or North America is usually between 100 and 150 g/day. In rural Uganda it is up to 500 g/day. Dietary fibers, mainly bran, that do not undergo anaerobic bacterial fermentation retain water within stools. Accordingly, bran increases stool weight and reduces colonic transit time in most individuals. It is, however, important that extra fiber does not reduce colonic transit times in women with severe idiopathic constipation; it may even further prolong transit times in patients with severely prolonged colonic transit times caused by spinal cord lesions.

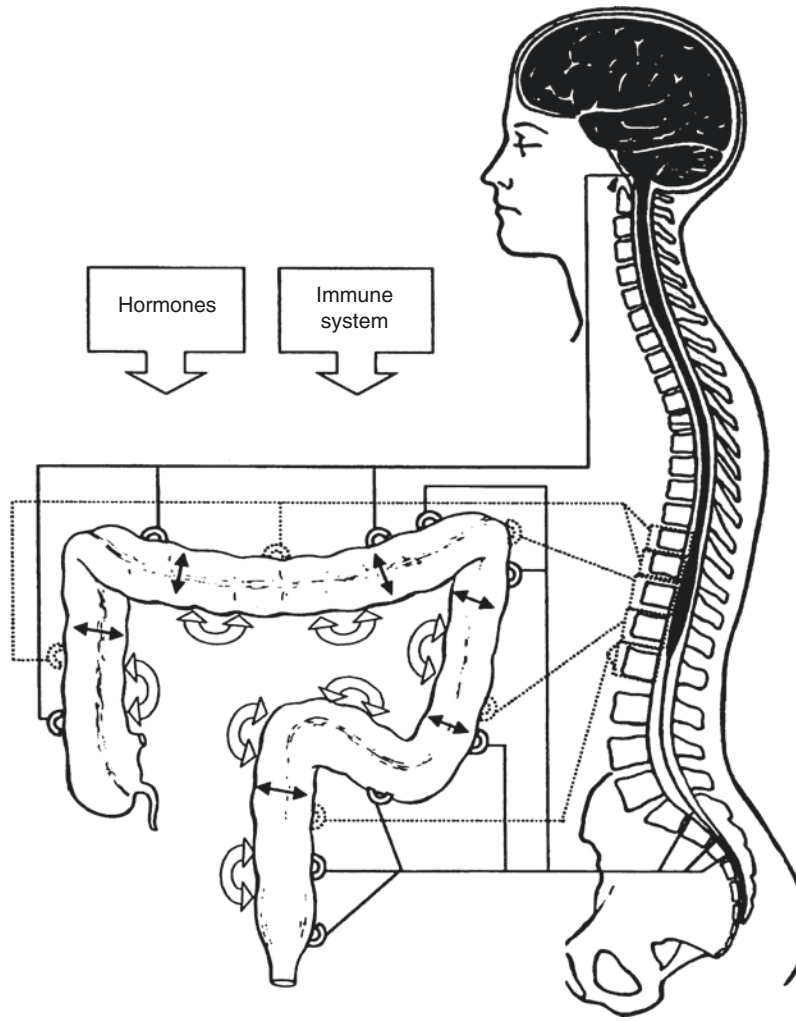


Fig. 3.2 Control of colorectal motility. *White arrows*: the enteric nervous system; *solid lines*: parasympathetic innervation; *broken lines*: sympathetic innervation

3.4 Anorectal Physiology

The main functions of the rectum and anal canal are:

- To maintain fecal continence
- To allow defecation at an appropriate time and place

The following factors are important in maintaining anal continence:

- Internal anal sphincter muscle (IAS)
- External anal sphincter muscle (EAS)
- Puborectalis muscle
- Rectal compliance
- Anorectal sensitivity
- Anorectal motility

3.4.1 Internal Anal Sphincter

The IAS is a continuation of the circular muscle layer of the rectum and consists of smooth muscle cells. Its main function is to contribute to the *anal resting pressure*. Anal resting pressure is extremely variable between individuals and tends to decrease with age and parity. The resting pressure undulates in a slow-wave pattern of low amplitude and frequency. An ultra-slow-wave pattern of greater amplitude may also be present. Their physiological significance is unknown.

3.4.2 External Anal Sphincter

The EAS comprises striated muscle. Its main function is to generate the anal squeeze pressure. The EAS is partly under voluntary control from Onuf's nucleus in the ventral horn of the sacral spinal cord via the pudendal nerve and the perineal branch of the S4 nerve.

3.4.3 Puborectalis Muscle

The striated puborectalis muscle creates an angle of approximately 80° at the anal rectal junction; this angle is considered to contribute to anal continence.

3.4.4 Rectal Compliance

Rectal compliance is defined as the relationship between rectal pressure and rectal volume, or the cross-sectional area (change in volume [ΔV]/change in pressure [ΔP] or change in cross-sectional area [ΔCSA]/ΔP). Reduced rectal compliance is considered the most important factor causing fecal incontinence following radiotherapy.

3.4.5 Anorectal Sensitivity

In contrast to the rectum, the mucosa of the anal canal has many sensory receptors. Thus the anal canal is extremely sensitive to touch, pin pricks, temperature, and movement. Even moderately reduced anal sensitivity – for instance, that caused by diabetic neuropathy – may cause fecal incontinence.

3.4.6 Anorectal Motility

Coordination of motility between the rectum and anal canal is central to both continence and efficient evacuation.

3.4.6.1 Rectoanal Reflexes

The *anal sampling* and the *rectoanal inhibitory* reflexes are important to continence. The anal sampling reflex (Fig. 3.3) allows contents of the rectum to come into contact with the anal mucosa and thereby determine the nature of the rectal contents (i.e., solid or liquid stool or gas). After a short relaxation of the anal upper canal, anal pressure normalizes, forcing the contents back into the rectum.

The rectoanal inhibitory reflex mediates relaxation of the IAS during rectal distension (Fig. 3.4). It is conducted through intramural nerve fibers but may be enhanced by parasympathetic stimuli from the sacral spinal cord. The rectoanal inhibitory reflex is absent in Hirschsprung's disease.

3.5 Defecation

Defecation is normally preceded by colonic mass movements that bring colonic contents to the rectum. Distension of the rectal wall may further stimulate contractions of the colon and rectum through an intrinsic reflex mediated by the ENS and by the parasympathetic *defecation reflex*, which involves the sacral segments of the spinal cord. Phasic rectal contractions occur and rectal tone increases, changing the rectum from a capacious reservoir to a conduit. Filling of the rectum stimulates the rectoanal inhibitory reflex, relaxing the IAS. Relaxation of the puborectalis muscle creates an obtuse angle, overcoming the anal flap valve mechanism, and defecation occurs if the EAS is relaxed. The process is enhanced by increasing abdominal pressure through a Valsalva maneuver. Under normal circumstances, defecation can be postponed by voluntary contraction of the EAS. The defecation reflex then gradually subsides and rectal compliance increases. The amount of luminal transport before and during defecation varies considerably. If the defecation reflex is interrupted, colorectal transport upon defecation is significantly reduced (Fig. 3.5).

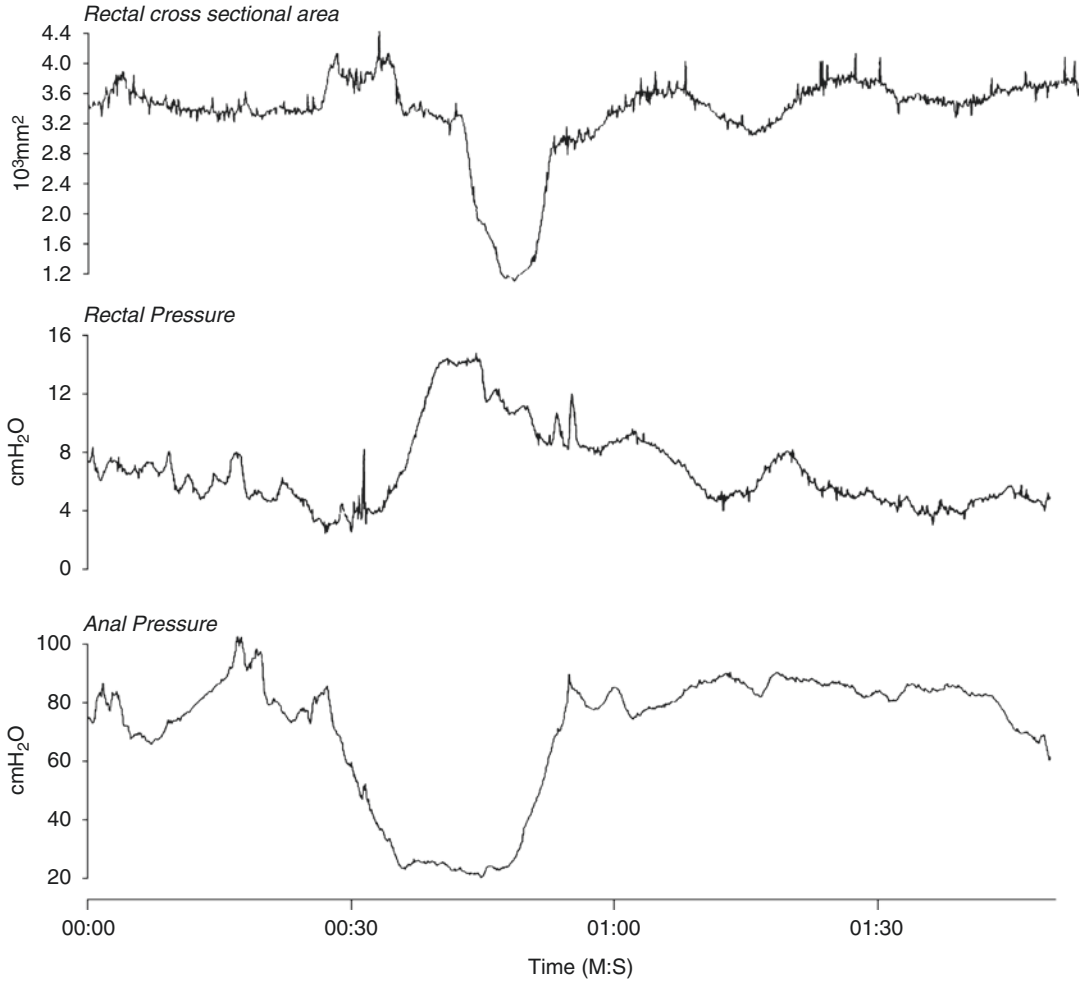


Fig. 3.3 Anal sampling reflex

3.6 Physiological Assessment of the Colon and Rectum

3.6.1 Colonic Motility

Most studies of colorectal motility have been performed using pressure transducers connected to a luminal catheter. These are either perfused, low-compliance systems or use pressure-sensitive strain gauges. Perfused catheters are especially suited for studies of sphincters because they measure contractions that obstruct their side holes. This restricts their usefulness in nonsphincteric regions. Furthermore, ambulatory studies cannot be performed and the association between changes in pressure and luminal cross-sectional area is poor. Intraluminal pressure-sensitive strain gauges are better suited for chronic measurements, and ambulatory systems are available, but they are expensive and placement requires colonoscopy. High-resolution colonic manometry based of fiber optics has given new and detailed insight into colorectal motility in healthy patients and in patients with constipation. The method is, however, extremely expensive and only available in a few centers.

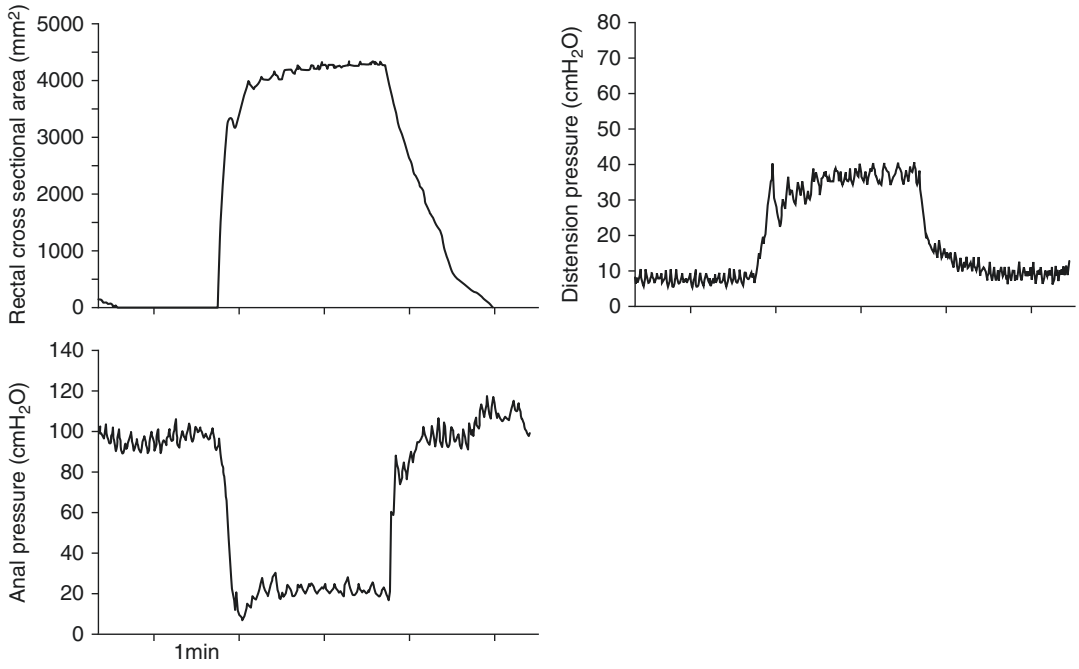


Fig. 3.4 Rectoanal inhibitory reflex

3.6.1.1 Colorectal Transit Times

Colorectal transit times can be determined by:

- Transit of radio-opaque markers
- Scintigraphy
- Capsule methods

Radio-opaque markers are counted either in stools or on plain abdominal films (Fig. 3.6). Markers can be taken as a single dose and followed by a single film after a fixed time interval (often 3–4 days), as a single dose followed by multiple films after fixed time intervals, or as multiple doses followed by a single film (often after 7 days). The first method can distinguish between constipated patients and healthy subjects but does not give any quantitative information about total or segmental colorectal transit times. If markers are followed by multiple films or if markers are taken on multiple days followed by a single film, total and segmental transit times can be determined.

Scintigraphy can be used to determine transit times throughout the gastrointestinal tract. Scintigraphy is superior for measuring gastric and small-bowel transit but less good for measuring colorectal transit. Colonic transit times vary greatly among individuals, and many patients with subjective complaints of constipation have normal colorectal transit times.

Capsule methods include the wireless motility capsule (WMC) and the Motilis 3D-Transit system. The WMC is widely available and easy to use. It provides information on pH, pressure, and temperature, thereby allowing gastric emptying, small-intestine transit time, and total colorectal transit time to be assessed. The WMC does not allow assessment of segmental colorectal transit times. The Motilis 3D-Transit is based on tracking an electromagnet throughout its passage through the gastrointestinal tract. The method allows a fully ambulatory description of regional gastrointestinal transit times and holds promise for describing specific contraction

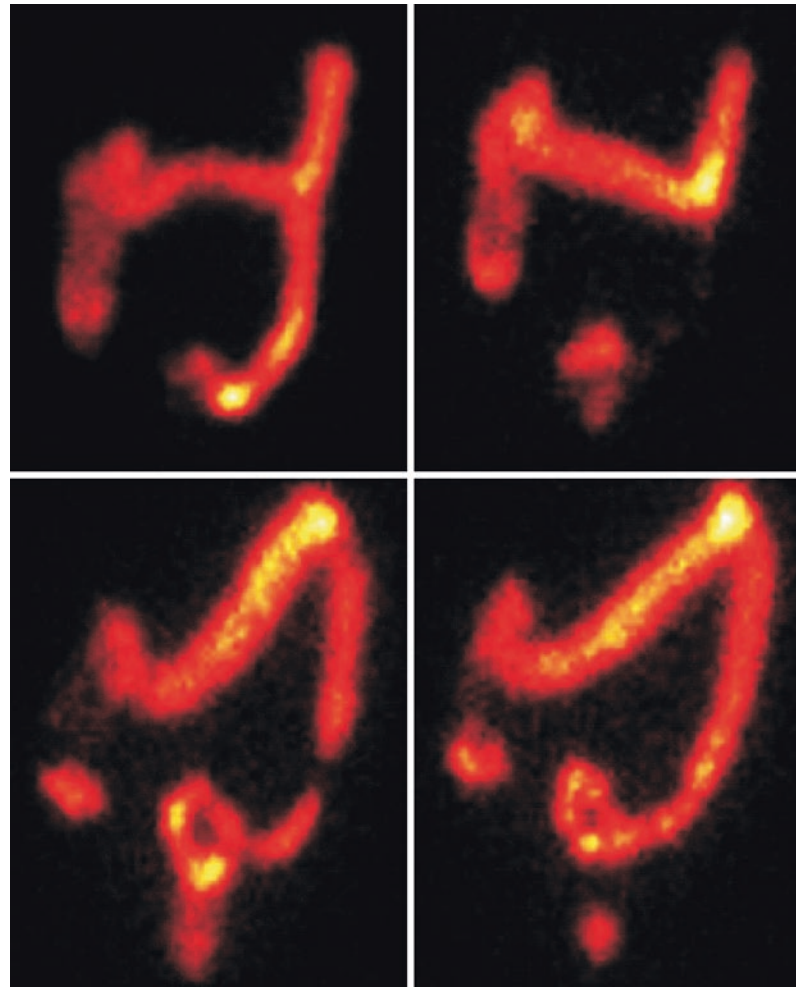


Fig. 3.5 Colorectal transport: scintigraphy before (*left*) and after (*right*) defecation. Normal (*top*) and in a patient with a sacral spinal cord lesion (*bottom*)

patterns, including colorectal mass movements. The method is, however, still only for experimental use.

3.6.1.2 Colorectal Emptying

Movement of colorectal contents during defecation can be assessed by means of evacuation proctography. However, this is a highly nonphysiological test and does not give any detailed quantitative measurement of colorectal transport. Isotope proctography with radio-labeled material inserted into the rectum allows quantitative description of rectal emptying. It also is a nonphysiological test because the isotope is not mixed with the feces and because the test does not give information about the movement of colonic contents.

3.6.1.3 Rectal Compliance and Tone

Compliance is the parameter most often used to describe colorectal distensibility. It is usually defined as ΔV or ΔCSA divided by ΔP. Rectal compliance computed from pressure–volume curves during rectal distension is commonly used to describe rectal wall properties in research and clinical practice. Measurement of rectal cross-sectional area during distension is of value mainly in a research setting.

Rectal tone may be measured by use of a barostat that measures changes in the intraluminal

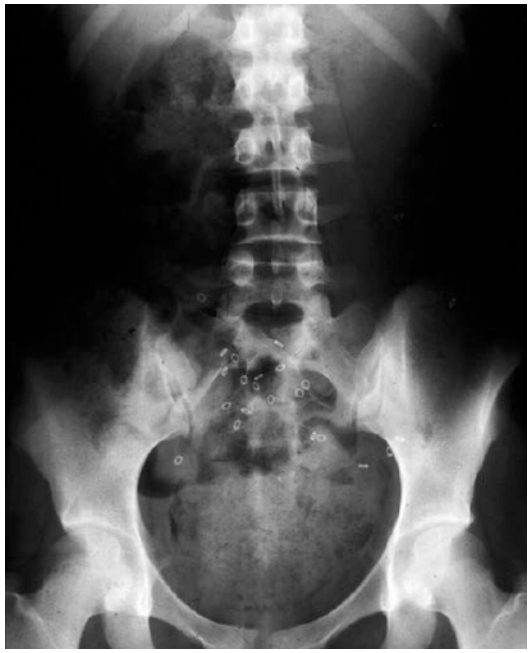


Fig. 3.6 Radio-opaque markers used to determine colorectal transit time

volume of a balloon at constant pressure. It is difficult to distinguish whether changes are caused by tone in the rectal wall as a result of muscle contraction, increased connective tissues, or other factors. The method is best suited for studies of changes in rectal tone, for instance, after a meal.

3.6.1.4 Rectal Sensibility

Rectal sensibility is usually evaluated by distension with either a balloon or a condom. The method is extremely imprecise because of elongation of the balloon within the rectum. A large bag made from a low-compliance material reduces the error from elongation and provides more reproducible data.

Multimodal rectal stimulation with distension, electricity, and temperature allows the analysis of various subtypes of rectal sensory receptors. Rapid balloon distension of the rectum and anal canal holds promise for future evaluation of the cerebral response to anorectal stimuli and may be a more physiological stimulus than electrostimulation.

3.6.2 Anal Manometry

Anal manometry may be performed using:

- A solid-state pressure transducer
- Balloon manometry
- A perfused system

Normal parameters vary greatly depending on the technique used and the population studied. Nevertheless, anal manometry is a standard part of the investigation of fecal incontinence. The functional lumen imaging probe was introduced for detailed evaluation of the distensibility of the anal sphincter complex (Fig. 3.7). Whether resistance to dissension is a physiologically more important parameter than pressure remains to be proven.

3.7 Absorption of Water and Electrolytes

Under normal circumstances, approximately 1,500–2,000 mL of fluid pass from the ileum to the colon each day. The fluid contains sodium, potassium, chloride, and bicarbonate. Most water is absorbed, especially in the right colon, and only 100–150 mL is lost in the stool. Furthermore, the colon has a significant absorptive reserve capacity: approximately 5–6 L. Overall, the colon absorbs sodium and chloride and secretes potassium and bicarbonate. Sodium absorption and bicarbonate secretion are active processes against the negative electrical potential difference between mucosal cells and the lumen. Potassium secretion is mainly dependent on potential, but there may also be active transport.

The chemical composition of luminal contents and stretching of the wall activate receptors in the colonic wall. Through the release of messengers from motor neurons to the neuroepithelial junctions, water and electrolyte transport through the epithelium cells is stimulated or inhibited. Messengers that act at the neuroepithelial junctions include acetylcholine and vasoactive intestinal peptide (antiabsorptive messengers) and

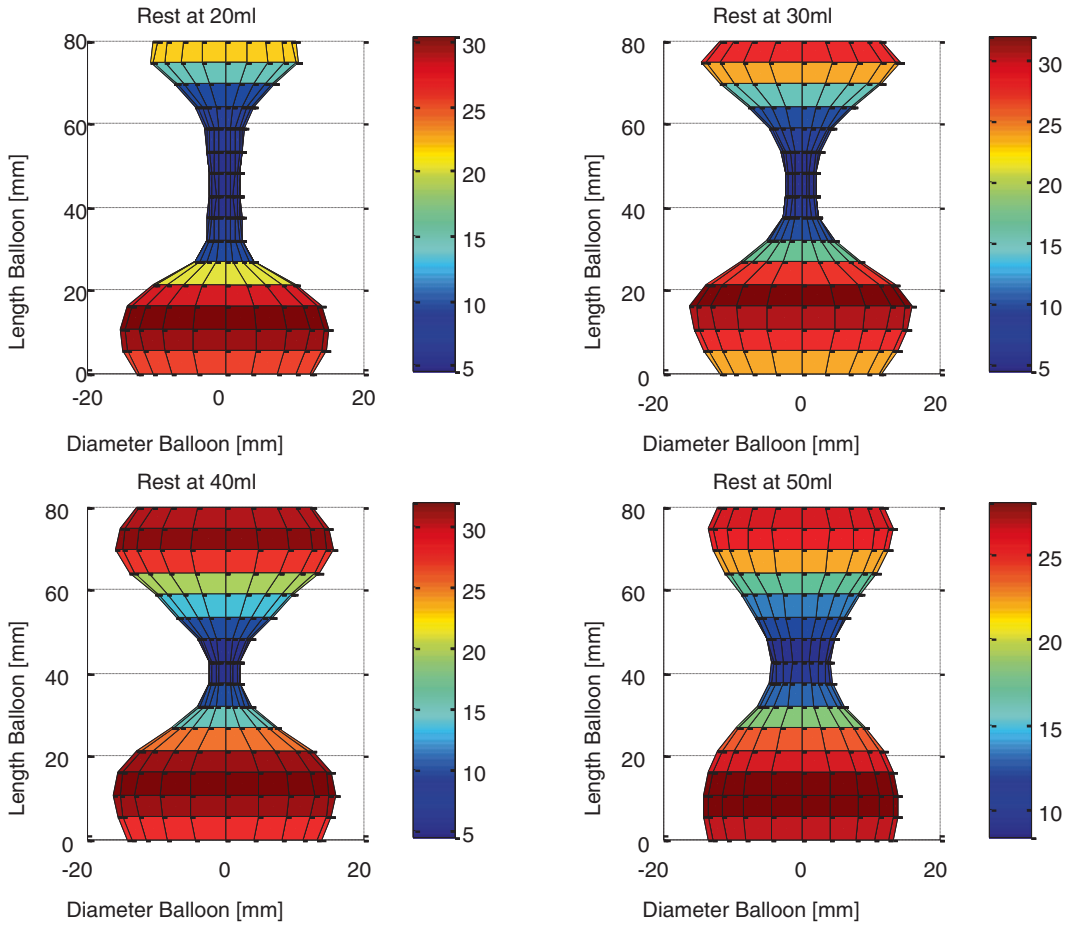


Fig. 3.7 Distension of the anal canal with a functional lumen imaging probe. The distension profile of the anal canal is illustrated at four distension volumes, from 20 to 40 mL. The color tone illustrates the diameter with *dark blue* as the smallest and *reddish-brown* as the largest diameter. The middle part of the anal canal is the least distensible because it remains closed until a distension volume of 40 mL is achieved

somatostatin and neuropeptide Y (proabsorptive messengers).

Release of norepinephrine from sympathetic nerve cells acts through alpha receptors to increase water, sodium, and chloride absorption. This mechanism may be disrupted in autonomic diabetic neuropathy. Release of acetylcholine from parasympathetic fibers within the vagal or sacral nerves reduces water and sodium absorption in the colon. Mineralocorticosteroids, glucocorticoids, and somatostatin stimulate colonic sodium transport, whereas mineralocorticosteroids also stimulate potassium secretion.

3.8 Absorption of SCFAs

Dietary fibers are complex macromolecular plant substances that are resistant to hydrolysis by human digestive enzymes. SCFAs (mostly acetic, propionic, and butyric acids) are produced by anaerobic bacterial fermentation of dietary fiber. Most SCFAs are produced and absorbed in the right colon. SCFAs are readily absorbed by colonic mucosa, are precursors for mucosal lipid synthesis, and provide a major source of energy for colonocytes. SCFAs stimulate colonic sodium absorption.

Suggested Reading

1. Bouchoucha M, Devroede G, Arhan P, Strom B, Weber J, Cugnenc P, Denis P, Barbier J. What is the meaning of colorectal transit time measurement? Dis Colon Rectum. 1992;35:773–82.
2. Brock C, Nissen TD, Gravesen FH, Frøkjaer JB, Omar H, Gale J, Gregersen H, Svendsen O, Drewes AM. Multimodal sensory testing of the rectum and rectosigmoid: development and reproducibility of a new method. Neurogastroenterol Motil. 2008;20:908–18.
3. Dinning PG, Wiklendt L, Maslen L, Patton V, Lewis H, Arkwright JW, Wattchow DA, Lubowski DZ, Costa M, Bampton PA. Colonic motor abnormalities in slow transit constipation defined by high resolution, fibre optic manometry. Neurogastroenterol Motil. 2015;27:379–88.
4. Farmer A, Scott S, Hobson AR. Gastrointestinal motility revisited: the wireless motility capsule. UEG J. 2013;1:413–21.
5. Haase AM, Gregersen T, Schlageter V, Scott MS, Demierre M, Kuchera P, Dahlerup JF, Krogh K. Pilot study trialling a new ambulatory method for the clinical assessment of regional gastrointestinal transit times using multiple electromagnetic capsules. Neurogastroenterol Motil. 2014;26:1783–91.
6. Haas S, Brock C, Krogh K, Gram M, Nissen TD, Lundby L, Laurberg S, Drewes AM. Cortical evoked potentials in response to rapid balloon distension of the rectum and anal canal. Neurogastroenterol Motil. 2014;26:862–73.
7. Krogh K, Ryhammer AM, Lundby L, Gregersen H, Laurberg S. Comparison of methods used for measurement of rectal compliance. Dis Colon Rectum. 2001;44:199–206.
8. Lestar B, Pennickx F, Kerremans R. The composition of anal basal pressure. Int J Colorectal Dis. 1989;4:118–22.
9. Sorensen G, Liao D, Lundby L, Fynne L, Buntzen S, Gregersen H, Laurberg S, Krogh K. Distensibility of the anal canal in patients with idiopathic fecal incontinence: a study with the functional lumen imaging probe. Neurogastroenterol Motil. 2014;26:255–63.
10. Whitehead WE, Delvaux M, the Working Team. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. Dig Dis Sci. 1997;2:223–4.
11. Wood JD, Alpers DH, Andrews PLR. Fundamentals of neurogastroenterology. Gut. 1999;45(suppl II):II6–16.

Hemorrhoids

4

Felix Aigner

Abbreviations

ATZ	Anal transitional zone
CCR	Corpus cavernosum recti
DG-HAL	Doppler-guided hemorrhoidal artery ligation
SRA	Superior rectal artery

4.1 Introduction

Hemorrhoidal disease is one of the most common benign disorders of the lower gastrointestinal tract. Hemorrhoids per se are vascular cushions forming a gas-tight seal at the anorectal junction and contribute to the physiological continence mechanism. Enlargement of these hemorrhoidal cushions and subsequent sliding into the anal canal or through the anus cause clinical symptoms such as bleeding, mucosal discharge, or pruritus and are the most common complaints defining hemorrhoidal disease and leading to patient referral to a coloproctologist. Treatment options comprise conservative and surgical therapies applied according to a patient's complaints. Asymptomatic hemorrhoids do not require surgical treatment.

4.2 Anatomy

The vascular plexus within the subepithelial space of the anal transitional zone (ATZ) has been described as "corpus cavernosum recti" (CCR) and claimed to provide mechanical rather than nutritional functions, resembling the morphological features of erectile tissues (Fig. 4.1).

Several anatomic investigations have demonstrated the existence of arteriovenous communications between the terminal branches of the superior rectal artery (SRA) and the CCR [13, 19]. This subepithelial vascular plexus is known to be a complex system of thin-walled tortuous venous structures supported by smooth muscle and fibroelastic tissue scaffolding [9]. These vascular structures, surrounded by fibromuscular tissue, have been described as so-called anal glomerula, corresponding to the anal cushions [18]. Anatomic investigations suggest the existence of a specialized functional vascular network at the anorectal region, similar to that of the penile corpora cavernosum. Others hypothesized the presence of some kind of regulating veins in the CCR [2]. Anatomic studies provide clear morphological and functional evidence for distinct vascular glomerula equipped with

F. Aigner, MD
Department of Surgery, Charité Universitätsmedizin Berlin, Campus Virchow-Klinikum,
Augustenburger Platz 1, 13353 Berlin, Germany
e-mail: felix.aigner@charite.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_4

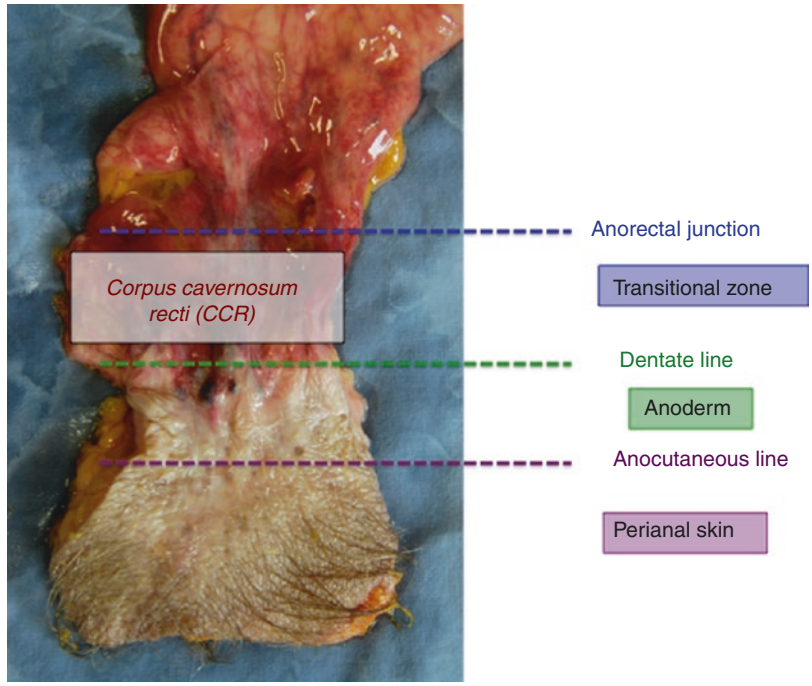


Fig. 4.1 Anatomic description of the anorectal junction. The rectum specimen is cut longitudinally

sphincter-like constrictions; these are most likely responsible for regulating the filling and drainage of the CCR [2, 18]. Data suggest that the CCR possesses an intrinsic active contractile mechanism that is able to ensure effective blood transport through the CCR [2]. Disruption of this intrinsic blood flow regulation and concomitant replacement of smooth muscle tissue with connective tissue seem to be key factors in the pathogenesis of hemorrhoidal disease.

4.3 Symptoms

The most common complaints of patients with hemorrhodial disease are bleeding upon defecation, pruritus, anal seepage or soiling, anal pain, and mucoanal prolapse. For symptomatic assessment, the individual burden of suffering is essential, since asymptomatic piles or skin tags are not an indication for treatment of hemorrhoids.

4.4 Etiology

The pathogenesis of hemorrhoidal disease is multifactorial and controversial [19]:

1. The hyperplasia theory describes disturbance of the drainage of the CCR as a result of increased sphincter resting tone, on the one hand, and prolapse of the ATZ into the anal canal, on the other.
2. The varicose vein theory has been abandoned because patients with portal hypertension do not show an increased incidence of hemorrhoidal disease.
3. The anal sliding lining theory is associated with the first theory: increased intraabdominal pressure (during pregnancy or upon straining during dfaecation, especially by constipated patients) results in distension and rupture of submucosal smooth muscle fibers and subsequent prolapse of the ATZ.

4.5 Classification

The traditional Goligher classification is applied for grading hemorrhoidal disease:

Grade 1 hemorrhoids do not prolapse at examination and are only visible through a proctoscope.

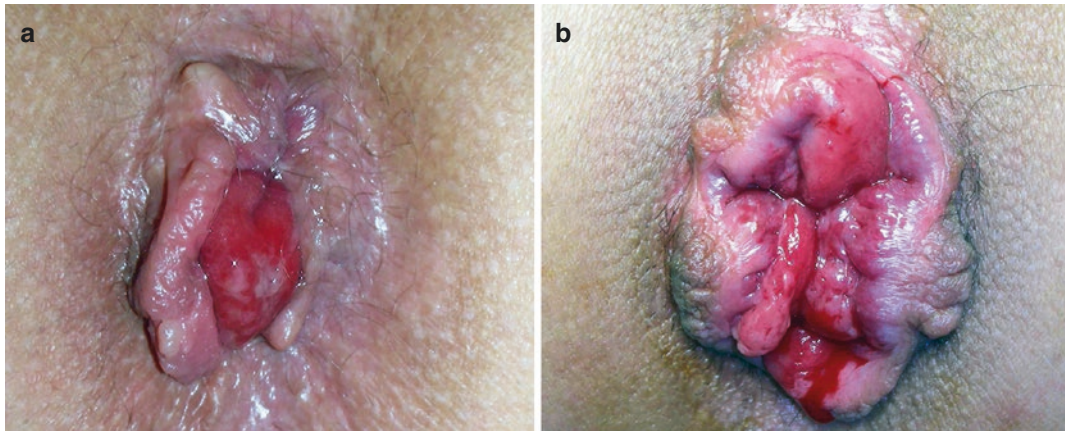


Fig. 4.2 Segmental (**a**) and circular (**b**) hemorrhoidal prolapse of patients with grade 3 hemorrhoidal disease

Grade 2 hemorrhoids prolapse during defecation but reduce spontaneously.
Grade 3 hemorrhoids prolapse and need manual repositioning.
Grade 4 hemorrhoids prolapse but cannot be reduced digitally into the anal canal by the patient.

From a clinical point of view, the Goligher classification is rather rigid, since other symptoms such as mucosal prolapse, fecal incontinence, and segmental or circular prolapse of the hemorrhoidal tissue (Fig. 4.2a, b) are not included. The classification according to Müeller-Lobeck [10] also differentiates between acute thrombosed (grade 4a) and chronic fibrosing (grade 4b) hemorrhoids.

4.6 Diagnosis

History taking is the most important step toward a diagnosis of hemorrhoidal disease and should include a question about pretreatment for hemorrhoidal complaints. Individual complaints and burden of disease should be taken into account. Questions about pain and discomfort upon defaecation, pruritus, bleeding, soiling, mucosal discharge, and any kind of preexisting fecal incontinence, as well as the extent of prolapsing tissue, are mandatory.

The position of the patient during examination and surgical intervention depends on the investigator's preference and does not matter from a clinical point of view (either the left lateral, lithotomy, or jacknife position). Inspection of the perianal region should determine the presence of anal fissures, fistula openings, and erythema. A digital rectal examination using the examinor's index finger should exclude tumor masses, polypoid structures, rectoceles, and internal fistula openings and should assess the anal resting and squeeze pressures. The Valsalva maneuver can induce any kind of prolapse and facilitates the differentiation bewteen hemorrhoidal and rectal prolapse.

Rigid proctoscopy and rectosocopy visualizing at least 15 cm of the rectum is a standard requirement before treatment. Colonoscopy is recommended whenever the history suggests anything more than hemorrhoidal symptoms (e.g., colorectal cancer).

4.7 Treatment

4.7.1 Conservative Treatment

Preventive treatment for hemorrhoidal disease should be considered as concomitant therapy (e.g., stool softeners, a fiber-rich diet, sufficient fluid intake, and avoiding excessive straining during defecation), independent of the hemorrhoidal grade. Drugs (e.g., suppositories, ointments, creams, flavonoids) can reduce hemorrhoidal symptoms. The effect is characterized

by the anti-inflammatory, analgesic, and local anaesthetic properties of the drugs. Topical steroids should be applied only for short periods to avoid atrophy of the perianal skin and anoderm. A series of prospective randomized trials highlighted the healing effect of diosmin (flavonoid) regarding the end points of pain, bleeding, and pruritus in terms of hemorrhodial disease [6].

4.7.2 Surgical Treatment

The leading indication for invasive techniques is the individual burden of hemorrhoidal disease, rather than grade of hemorrhoidal prolapse, since it is assumed that the associated symptoms are partly independent of the anatomic derangement (Table 4.1). Nonresecting minimally invasive techniques can be performed on an outpatient basis, with low morbidity. The major target is an induced inflammatory stimulus (e.g., sclerosing injection or rubber band ligation), resulting in "controlled" scarring and thereby fixation of the ATZ and the prolapsed mucosa to the rectal wall.

4.7.3 Sclerosing Injection

Slerotherapy is widely used for grade 1 and 2 hemorrhoids and consists of submucosal injection of a tissue-irritating agent (ethoxysclerol or 5% phenol in almond oil), which causes fibrosis and fixation of the hemorrhoidal zone to the rectal wall [8].

Table 4.1 Surgical treatment of hemorrhoidal disease

Nonresection techniques
Sclerosing injection
Rubber band ligation
Infrared coagulation
Laser hemorrhoidoplasty
Ligation-based techniques
Hemorrhoidal artery ligation without mucopexy
Resection techniques
Stapled hemorrhoidopexy
Conventional hemorrhoidectomy
Milligan-Morgan
Parks
Ferguson
Fansler-Arnold

4.7.3.1 Technique

The needle is inserted into the rectal submucosa above the hemorrhoidal pedicle, and 2–3 mL are injected at each site, depending on the agent and its concentration. It is important not to inject directly into the CCR, the muscularis recti, or the internal sphincter muscle. Depending on the agent and its concentration, up to three injection sites are possible during one session. The injection procedure can be repeated at monthly intervals until symptoms (e.g., bleeding) have ceased. The complication rate is rather low (0.7–6.5%) [10]; however, recurrence is common in the long term (up to 70%).

4.7.4 Rubber Band Ligation

This method is the most commonly applied treatment for grade 1 and 2 hemorrhoids [3]. Rubber band ligation of the rectal mucosa above the hemorrhoidal pedicle causes ulceration and scarring of the respective area, resulting in fixation of the ATZ.

4.7.4.1 Technique

Rubber bands are applied through a proctoscope (several modifications of the applicator are available), with or without simultaneous injection of sclerosing agents both to avoid early rejection of the rubber band by the contraction of the smooth muscularis mucosae and to provide an additional sclerosing effect to the banded rectal mucosa. Up to three applications can be made during one session, which can be repeated at monthly intervals on an outpatient basis. The most common pitfall is setting the ligation too close to or below the dentate line, which causes immediate pain and subsequent perianal thrombosis caused by painful hypercontraction of the sphincter muscles. Bleeding—especially after rejection of the rubber band and necrotic rectal mucosa on postintervention days 5–7—might be the cause for readmission, and a 25% recurrence rate of haemorrhoidal complaints within 5 years of follow-up are common.

4.7.5 Infrared Coagulation

Application of infrared energy causes localized submucosal coagulation and necrosis with consecutive inflammation and, again, fixation of the ATZ. Recurrence rates are similar to those for rubber band ligation; however, the lack of pain during this procedure favors infrared coagulation. This technique may cause local necrosis, and its use has been widely abandoned in Europe [3].

4.7.6 Laser Hemorrhoidoplasty

Laser hemorrhoidoplasty uses an 980-nm laser diode to deliver energy to the submucosal branches of the SRA that supply blood to the hemorrhoids. The laser energy is applied in a pulsed fashion, resulting in photocoagulation of the arterial branches and fixation of the rectal mucosa and submucosa to the muscular layer. Authors have demonstrated that this is a safe, effective, and painless technique for the treatment of symptomatic grade 2–3 hemorrhoids with minimal or moderate mucosal prolapse, and it is suitable as ambulatory treatment [4]. These early results are positive, but more confirming studies are mandatory.

4.7.7 Ligation-Based Techniques

Ligation techniques, such as Doppler-guided hemorrhoidal artery ligation (DG-HAL), were introduced to reduce the arterial inflow to the CCR and thus preserve the hemorrhoidal zone as part of the continence system. In addition to inappropriate application of this surgical alternative for higher grade hemorrhoids, high recurrence rates of up to 38 % after DG-HAL [5] are the result of technical failure of the ligation technique itself. Doppler-guided ligations can be set too high above the ATZ, missing the targeted submucosal branches of the SRA. However, prolapsing hemorrhoids have been proposed to be insufficiently treated by solely interrupting the arterial inflow without repositioning the ATZ by mucopexy in DG-HAL. To overcome the shortcomings of the DG-HAL procedure, suture ligation has been modified to address the pexy of the hemorrhoidal prolapse by fixing it above the dentate line (Fig. 4.3). Many terms for this technique have been established, including "rectoanal repair," "transanal hemorrhoid mucopexy," and "anal lifting."

4.7.7.1 Technique

Mucopexy with or without DG-HAL is performed using a specific proctoscope equipped with a Doppler probe. The proctoscope has a sliding part comprising the operating window and a Doppler probe for better proximal and distal movement without repositioning the proctoscope during the mucopexy. The detected arteries are directly ligated with a Z-stitch at the site of the best Doppler signal. Once the arteries are transfixed, the sites of greatest prolapse are treated by targeted mucopexy using the slide in the proctoscope. Recent studies conclude that repositioning of the ATZ remains the key step in treating prolapsing hemorrhoids [17]. Detecting submucosal arterial signals might be confusing for the operating surgeon because the distribution pattern of the terminal branches of the SRA varies [1]. The Doppler transducer is supposedly not that crucial to the marked beneficial effect of this tissue-preserving technique [17]. Advantages of mucopexy and fixation of the ATZ with or without DG-HAL are a short hospital stay, low postoperative pain and analgesic consumption, and quick recovery and return to daily activities. DG-HAL is safe and efficacious, with a low level of postoperative pain. It can be safely considered for the primary treatment of grade 2 and 3 hemorrhoids. Recurrence rates depend on the addition of mucopexy to DG-HAL and range between 3 % and 60 % (pooled recurrence rate, 17.5 %) [15].

4.8 Resection Techniques

4.8.1 Stapled Hemorrhoidopexy

The rationale of this technique includes repositioning the ATZ by circular excision of redundant rectal mucosa (at least resection of a 2.5-cm-high

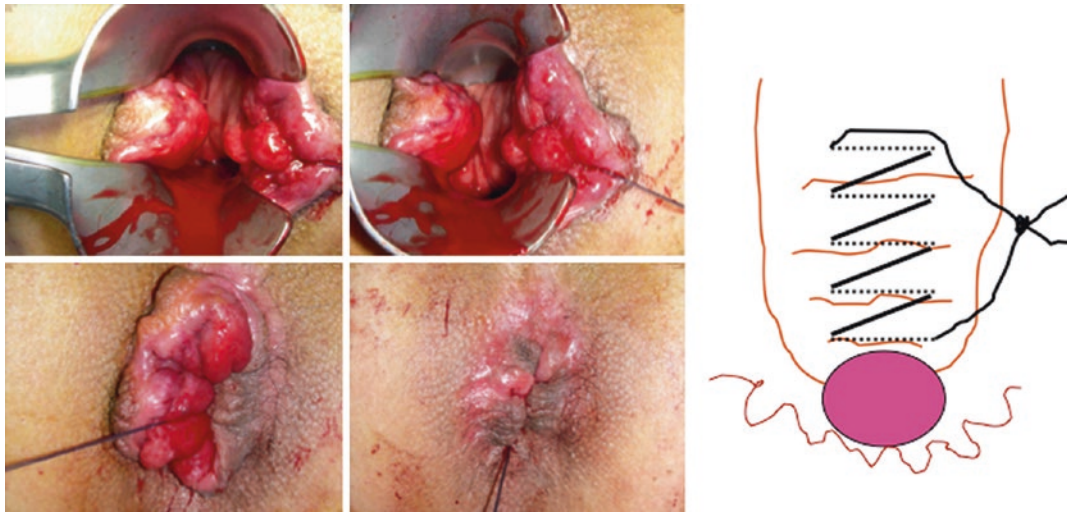


Fig. 4.3 Mucopexy technique (rectoanal repair) with repositioning of the anal transitional zone

mucosal cuff) with the use of a circular stapling device, thus reducing hemorrhoidal prolapse and improving venous drainage of the CCR.

4.8.1.1 Technique

The level of circular resection is targeted by a submucosal purse-string suture set approximately 3.5–4 cm above the dentate line, with the staple line finally located 1.5–2 cm above this anatomic borderline between the rectum and anal canal. In women, caution must be taken not to capture the posterior vaginal wall within the stapling line, which might happen after grasping too much rectal wall within the purse-string suture.

This technique is appropriate for grade 3 hemorrhoids without a large external component (skin tags) or circular mucosal prolapse, as well as grade 4 hemorrhoids after primary conservative treatment (deswelling and repositioning). Meta-analyses comparing stapled hemorrhoidopexy with conventional hemorrhoidectomy favored stapled hemorrhoidopexy because of its shorter operation times, faster recovery of bowel function, shorter hospital stay, less postoperative pain, and higher patient satisfaction as a minimally invasive technique, but it does result in higher recurrence rates over the long term [7]. Adverse effects of this technique are bleeding from the staple line and pain inthe case of stapling too deep, beyond the dentate line. Urgency is an underestimated adverse event of stapled haemorrhoidopexy because of reduction of the compliance and capacity of the distal rectum.

4.8.2 Conventional Hemorrhoidectomy

The principle of all conventional hemorrhoidectomy techniques is to excise hypertrophied prolapsing hemorrhoidal tissue, including external components (skin tags), caused by chronic prolapse of grade 3 and 4 hemorrhoids. The key to success with these techniques is not defined through radicality, but rather not touching the internal sphincter muscle and preserving sufficient anoderm bridges to avoid postoperative stenosis and functional disorders.

4.8.2.1 Technique

The difference between the Milligan-Morgan, Parks, and Ferguson techniques lies in how the operation is finished. In the Milligan-Morgan technique the excisional areas are left open for secondary wound healing (Fig. 4.4), whereas Parks describes a semiclosed and Ferguson a closed hemorrhoidectomy technique, including reconstruction of the anoderm (Parks) and/or

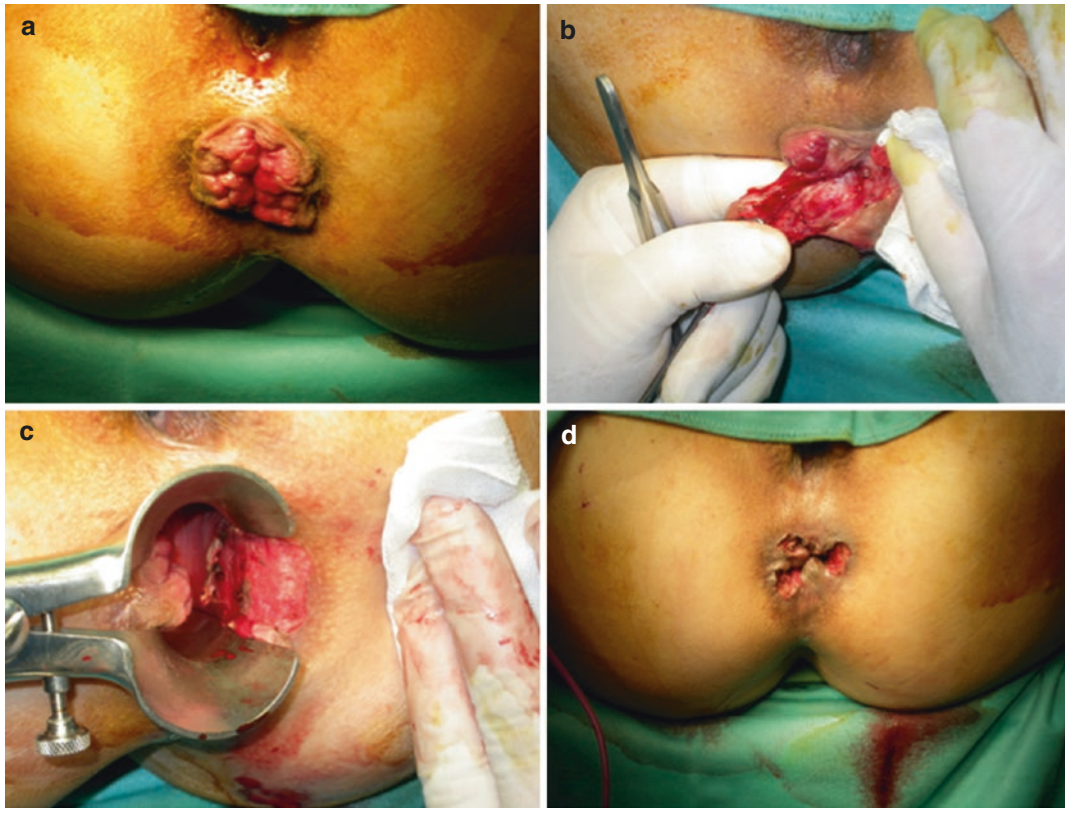


Fig. 4.4 Conventional hemorrhoidectomy (Milligan-Morgan). Preoperative aspect (**a**), resection of the hemorrhoidal tissue with preservation of the internal sphincter muscle (**b**), open wound healing (**c**), and hemorrhoidectomy at three sites of prominent hemorrhoidal prolapse (**d**)

perianal skin (Ferguson) with absorbable sutures. The vascular pedicle is occluded with conventional stitch sutures or bipolar sealing devices; the latter result in less postoperative bleeding and pain [16]. The Milligan-Morgan technique is associated with low recurrence rates (<5 % [7]) but significantly more postoperative pain and anal stenosis, especially following excessive excisions. The advantage of the reconstructive techniques (Parks, Ferguson) is the anatomic reconstruction of the anorectal junction. However, a slightly increased rate of postoperative septic complications resulting from the closure of a potentially infected anal wound and a technically more challenging operation should be taken into account. The Fansler-Arnold technique for fixed circular hemorrhoidal prolapse describes a complete reconstruction of the anoderm using a flap technique during hemorrhoidectomy.

Summarizing all surgical techniques, a tailored approach to hemorrhoidectomy should be applied on an individual basis since the traditional Goligher classification does not discriminate between segmental and complete circular hemorrhodial prolapse (e.g., in grade 3 hemorrhoids; Fig. 4.2). Thus partial hemorrhoidectomies are justified regarding avoidance of overtreatment in patients where additional mucosal prolapse or bleeding hemorrhoids can best be treated by ligation-based techniques. A treatment algorithm is presented in Fig. 4.5.

4.8.3 Pre- and Postoperative Care

Mechanical bowel preparation is not necessary and a small enema is sufficient on the morning of surgery. Some surgeons perfer no bowel

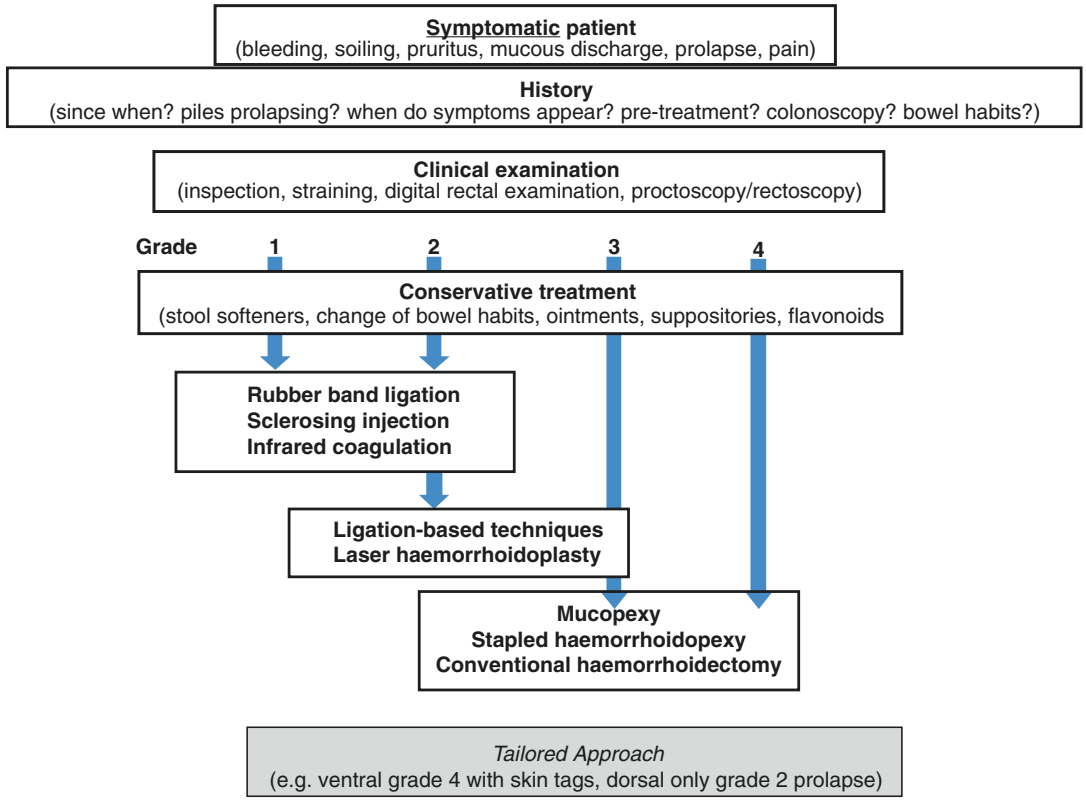


Fig. 4.5 Treatment algorithm for hemorrhoidal disease

preparation at all. The use of prophylactic antibiotics is not based on evidence, and they do not provide any benefit. Anal tamponade is not recommended. The best postoperative treatment of the wounds after conventional hemorrhoidectomy is daily showering, sitz baths, and cleansing with water after defecation. Stool softeners should be administered to avoid straining during defecation (the major cause of hemorrhodial disease). Use of urinary catheters is possible; however, urinary retention after anal surgery is not negligible, especially when tamponades are used. Hemorrhoidal surgery can be performed on an outpatient basis, especially when using minimally invasive techniques such as rubber band ligation, sclerotherapy, and laser hemorrhoidoplasty for grade 1 and 2 hemorrhoids. However, patients must be sufficiently instructed to be readmitted in the case of an emergency. Close communication with the operating surgeon is mandatory.

Regarding perioperative use of heparin, the author suggests referencing practice parameters for the prevention of venous thrombosis [14].

4.8.4 Complications and Their Management

4.8.4.1 Pain

- Pain is often temporary, complicated if long-lived, extraordinarily heavy, or occurring after an interval with no pain.
- Conventional hemorrhoidectomy techniques are more frequently associated with pain.
- Pain following rubber band ligation or stapled hemorrhoidopexy is often correlated with unnecessary distal ligation or stapling of the sensitive anoderm.
- Examination under anesthesia might be necessary in patients with persistent pain following hemorrhoidectomy.

- Regular use of a fixed analgesic regime is mandatory (at least recommended).

4.8.4.2 Postoperative Bleeding

- Patients with hemorrhage within 48 h postoperatively should be readmitted in the case of persistent bleeding.
- Postoperative bleeding rarely requires early surgical intervention.
- Intraoperative bleeding from the staple line in stapled hemorrhoidopexy should be treated with additional Z-stitches at the end of the operation (there is up to a 35 % incidence of hemorrhage requiring surgical intervention [11]).

4.8.4.3 Urinary Retention

- Urinary retention is often correlated with postoperative pain or excessive intraoperative intravenous fluid consumption, anal tamponades, or preexisting urinary retention (e.g., in prostate hypertrophy).
- A perioperative urinary catheter might be useful.

4.8.4.4 Anorectal Sepsis

- Local septic complications are rare following conventional hemorrhoidectomies, but they are significantly more common after stapled hemorrhoidopexy [7].
- Treatment is the same as for cryptoglandular abscesses and fistulae.
- Life-threatening Fournier gangraene is rare but is associated with high mortality.

4.8.4.5 Anal Stenosis

- Anal stenosis is rare but frequently occurs in cases of excessive resection of the sensitive anoderm.
- Anal stenosis can be treated with anal dilation or anoplastic interventions (e.g., a house flap).

4.8.4.6 Fecal Incontinence

- Fecal incontinence is an underestimated side effect of resection techniques (occurs in up to 30 % [12]).
- Urge incontinence especially occurs following stapled hemorrhoidopexy (caused by the reduced capacity and compliance of the rectal ampulla).
- Passive incontinence with loss of the internal sphincter muscle can occur following excessive resection of the rectal wall.
- Caution must be taken with patients with preexisting fecal incontinence or weak sphincter tone (thus favoring tissue-preserving ligation techniques).

4.8.4.7 Recurrence

- Recurrence must be differentiated from residual complaints of incomplete resolution of the prolapse.
- A long-term cure is appreciated (up to one third of patients experience recurrent symptoms in the long run).
- Recurrence occurs more frequently following ligation techniques than resection techniques.

4.8.5 Special Conditions

4.8.5.1 Acute Thrombosed Haemorrhoidal Prolapse (Anal Prolapse, Grade 4A [10])

Emergency hemorrhoidectomies are rarely indicated. Patients with acute thrombosed hemorrhoidal prolapse should be examined and perianal thrombosis excluded. The primary target is to reposition the prolapse to allow deswelling of the edematous anorectal mucosa/skin. Therefore, conservative treatment (analgesic, anti-inflammatory, and cooling treatments) is to be recommended rather than excessive resection in the edematous anal region. Early elective surgical intervention might be scheduled in the following days (remember tailored hemorrhoidectomy). In the majority of cases no further surgery is needed (e.g., after childbirth).

4.8.5.2 Inflammatory Bowel Disease

Hemorrhoidal disease in patients with Crohn's disease should be surgically treated with the greatest caution and reluctance (if possible and if the patient is in a stage of remission).

4.8.5.3 Immunocompromised Patients

Attention must be paid to the prolonged healing process in immunosuppressed patients (e.g., those with human immunodeficiency virus and after transplant). Antibiotic prophylaxis is recommended.

4.8.5.4 Pregnancy

Surgical treatment of hemorrhoidal disease in pregnant women should be performed with the greatest reluctance. Perianal thrombosis originating from the anal verge frequently occur during pregnancy and can be treated with excision under local anesthesia or conservatively.

4.8.5.5 Recurrent Hemorrhoidal Disease

Causes are incomplete removal of the primary prolapse or recurrent complaints after a period of remission. Recurrence after minimally invasive techniques (sclerosing injection, rubber band ligation, ligation-based techniques) can feasibly be treated the same way again; however, the subsequent treatment is less effective. Repeated stapled hemorrhoidopexy should be appraised critically because of possible septic complications or urge incontinence. Recurrence following conventional techniques should be treated with ligation-based methods instead, unless re-resection is performed to spare as much of the anoderm as possible (anal stenosis).

References

1. Aigner F, Bodner G, Conrad F, Mbaka G, Kreczy A, Fritsch H. The superior rectal artery and its branching pattern with regard to its clinical influence on ligation techniques for internal hemorrhoids. Am J Surg. 2004;187:102–8.
2. Aigner F, Gruber H, Conrad F, Eder J, Wedel T, Zelger B, et al. Revised morphology and hemodynamics of the anorectal vascular plexus: impact on the course of hemorrhoidal disease. Int J Colorectal Dis. 2009;24:105–13.
3. Aigner F, Haunold I, Salat A. Stadiengerechte Therapie des Hämorrhoidalleidens. Coloproctology. 2013;35:281–94.
4. Crea N, Pata G, Lippa M, Chiesa D, Gregorini ME, Gandolfi P. Hemorrhoidal laser procedure: short- and long-term results from a prospective study. Am J Surg. 2014;208(1):21–5.
5. Giordano P, Overton J, Madeddu F, Zaman S, Gravante G. Transanal hemorrhoidal dearterialization. A systematic review. Dis Colon Rectum. 2009;52:1665–71.
6. Ho YH, Foo CL, Seow-Choen F, Goh HS. Prospective randomized controlled trial of a micronized flavonidic fraction to reduce bleeding after haemorrhoidectomy. Br J Surg. 1995;82(8):1034–5.
7. Jayaraman S, Colquhoun PHD, Malthaner RA. Stapled versus conventional surgery of hemorrhoids. Cochrane Database Syst Rev. 2006;(4):Art.No.: CD005393. doi:101002/14651858. CD005393.pub2.
8. Johanson JF. Optimal nonsurgical treatment of hemorrhoids: a comparative analysis of infrared, rubber band ligation and injection sclerotherapy. Am J Gastroenterol. 1992;87:1600.
9. Loder PB, Kamm MA, Nicholls RJ, Phillips RK. Haemorrhoids: pathology, pathophysiology and aetiology. Br J Surg. 1994;81(7):946–54.
10. Müller-Lobeck H. Ambulante Hämorrhoidaltherapie. Chirurg. 2001;72:667–76.
11. Ommer A, Hinrichs J, Möllenberg H, Marla B, Walz MK. Long-term results after stapled hemorrhoidopexy: a prospective study with a 6-year follow-up. Dis Colon Rectum. 2011;54(5):601–8.
12. Ommer A, Wenger FA, Rolfs T, Walz MK. Continence disorders after anal surgery – a relevant problem? Int J Colorectal Dis. 2008;23(11):1023–31.
13. Parnaud E, Guntz M, Bernard A, Chome J. Normal macroscopic and microscopic anatomy of the hemorrhoidal vascular system. Arch Fr Mal Appar Dig. 1976;65(7):501–14.
14. Prophylaxis of venous thrombembolism. Version 18.3.2009; S3-Leitlinie. AWMF Leitlinien-Register Nr. 003/001:50–4.
15. Pucher PH, Sodergren MH, Lord AC, Darzi A, Ziprin P. Clinical outcome following Doppler-guided haemorrhoidal artery ligation: a systematic review. Colorectal Dis. 2013;15(6):284–94.
16. Sakr MF. LigaSure versus Milligan-Morgan hemorrhoidectomy: a prospective randomized clinical trial. Tech Coloproctol. 2010;14(1):13–7.
17. Schuurman J, Borel Rinkes I, Go P. Hemorrhoidal artery ligation procedure with or without doppler transducer in grade II and III hemorrhoidal disease a blinded randomized clinical trial. Ann Surg. 2012;255:840–5.
18. Stelzner F, Staubesand J, Machleidt H. The corpus cavernosum recti—basis of internal hemorrhoids. Langenbecks Arch Klin Chir Ver Dtsch Z Chir. 1962;299:302–12.
19. Thomson WH. The nature of haemorrhoids. Br J Surg. 1975;62(7):542–52.

Anal Fissure

5

Eloy Espin

Abbreviations

BT	Botulinum toxin
GTN	Glyceryl trinitrate
IAS	Internal anal sphincter
ISDN	Isosorbide dinitrate
NO	Nitric oxide

5.1 Etiology

Anal fissure is a painful tear in the posterior or anterior epithelial lining of the anal canal distal to the dentate line. It is a highly distressing and common condition that affects different age groups, but most commonly in young adults (20-30 y.o.).

Although there are several theories about the origin of anal fissure, none of them is accepted as the unique cause; the etiology is probably multifactorial. For many years it was believed that trauma to the epithelium of the anal canal created by the passage of hard stools was the main cause. This initial trauma would be followed by pain and an increase in the internal sphincter tone, which in turn aggravated the pain during defecation—thus a vicious cycle was created. This theory, although simple and easy to understand, is not convincing because a history of hard stools is found in less than 25 % of patients with fissures; furthermore, almost 10 % of patients have diarrhea.

The two main factors associated with anal fissure are an increase in the internal sphincter tone and a decrease in blood flow in areas of anodermal epithelia. Manometric studies have demonstrated that patients with anal fissure have an increased resting anal pressure and a decrease of spontaneous relaxation of the internal anal sphincter (IAS) [1]. Similarly, some reports mention tissue ischemia as the initial mechanism of anal fissure. This theory is based on studies showing an important decrease of blood flow in the posterior part of the anal canal seen on Doppler laser flowmetry [2]. This low blood flow was also demonstrated in the anterior midline part, but not in the lateral quadrants, when compared with controls. These two theories are actually complementary and assist in the treatment of a chronic anal fissure. Decreasing the tone of the IAS significantly improves the irrigation of the ischemic area, causing the ulcer to heal gradually and symptoms to improve [3].

Recent studies also suggest a different pathophysiology for posterior and anterior anal fissures. Patients with an anterior anal fissure who

E. Espin, MD, PhD
Hospital Valle de Hebron.
Universitat Autonoma de Barcelona,
Pg Valle de Hebron 119-129, 4 planta Hospital General, Barcelona 08035, Spain
e-mail: eespin@vhebron.net

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_5

developed anal incontinence after sphincterotomy have been found to have an occult external anal sphincter injury and impaired external anal sphincter function compared with patients with posterior fissures [4]. These groups of patients are typically younger women, and their maximum squeeze pressure has been found to be significantly lower when compared with the posterior fissure group. More studies are needed to support these findings. Furthermore, postpartum fissures cause no increased anal tone and are probably caused by constipation and birth trauma.

Most fissures (90 %) arise in the posterior midline. An anal fissure occurs in the anterior midline in 10 % of affected men and up to 25 % of affected women. Accordingly, when there are multiple fissures or the fissure is located in the lateral position, other etiologies have to be investigated: anorectal trauma, Crohn's disease, infections (e.g., tuberculosis, HIV/AIDS, herpes, syphilis), anal or rectal cancer, and dermatologic diseases (e.g., psoriasis).

5.2 Incidence

Although multiple publications note that anal fissures are common, there are not many reliable estimates of the frequency of anal fissures among the general population. An overall incidence of 1.1 per 1,000 person-years has been recently published [5]. This incidence translates to an average lifetime risk of 7.8 %, which positions anal fissure as a real common health problem.

5.3 Epidemiology

Sex distribution shows almost no differences, although it is slightly more common in women. While anal fissure is a common cause of anal bleeding in children, the peak incidence occurs during adolescence and young adulthood in women, and during middle age among men. Constipation, hypothyroidism, obesity, pregnancy and weight loss have been associated with anal fissure [5].

5.4 Classification

An anal fissure can be classified in terms of its time of evolution (acute or chronic) or by the pathophysiologic cause (primary or secondary). Classification as primary or secondary is important because treatment is different and directed toward its cause. Primary anal fissures are treated with the objectives of decreasing anal sphincter tone and increasing blood flow. Secondary anal fissures are the result of several causes, including malignancy (anorectal cancer, leukemia), inflammation (Crohn's disease), infections (HIV/AIDS, herpes, tuberculosis, syphilis), anorectal trauma, or dermatologic conditions (psoriasis). The specific cause of secondary anal fissure must be accurately treated.

The treatment of anal fissure also follows multiple stages, from dietary modifications to medical therapy to surgical procedures. Nonoperative therapy is the first option; surgical treatment is reserved for failures or complications. If an acute fissure does not heal and lasts more than 6–8 weeks, it is then considered to be chronic. The grade of pain or bleeding does not distinguish between and acute or chronic fissure, but the duration of symptoms and clinical aspects do. Acute fissures are usually superficial, and the tear appears pink to red. Chronic fissures are deeper; the transverse fibers of the IAS are exposed and chronic granulated tissue is seen on its base. A sentinel pile and a hypertrophied anal papilla can be present (Fig. 5.1). Anal fissures are also classified as chronic if the secondary lesions mentioned above (e.g., deep scar, exposed internal sphincter, pile, and papilla) are present.

Coloproctologists will probably see more chronic than acute fissures because primary care physicians and emergency surgeons can treat and heal most acute anal fissures with conservative measures and nonsurgical interventions.

5.5 Diagnostics

Anal fissure is usually diagnosed through the history and a physical examination. Pain is the hallmark of anal fissure symptoms. Pain starts

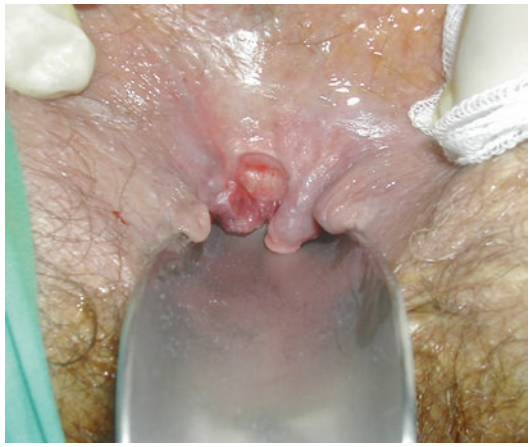


Fig. 5.1 Anal fissure. Internal anal sphincter at the base of the fissure (Courtesy of Dr. J.V. Roig)

during defecation or sometimes just after a bowel movement and can last from minutes to several hours. Patients frequently describe the pain as spasms or as if they were "passing glass"; the intensity of the pain while defecating enhances the fear of doing so, predisposing patients to constipation, harder and drier stools, and worse trauma. Rectal bleeding is frequent, minimal, bright red, and not related to the severity of the anal fissure.

Inspection with gentle traction of the buttocks often shows the fissure (Fig. 5.2). If a fissure is diagnosed during the initial consultation, other maneuvers (rectal examination or endoscopy) are not indicated in most patients at that time to avoid causing or increasing the existing pain. If a fissure is not observed, then an examination under anaesthesia should be advised to make the correct diagnosis and to rule out anorectal sepsis. Atypical fissures (lateral, nonhealing, painless, or multiple) are more appropriately managed with examination under anaesthesia, and a biopsy and culture should be evaluated.

Anoscopy, endoscopy, or rectal examination, if indicated, should be delayed if possible until symptoms resolve. Anal manometry is not recommended as a routine initial exploration because it can cause or aggravate the pain and is normal or low in 19 % of evaluated men and 42 % of affected women.

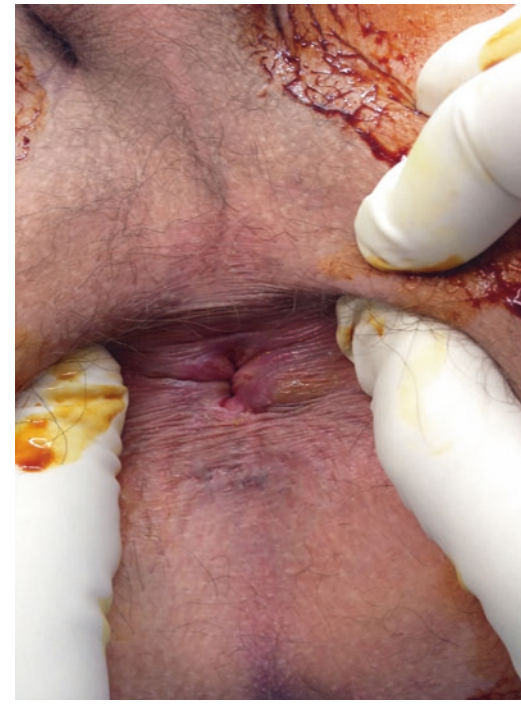


Fig. 5.2 Exposition of an anal fissure

5.6 Medical Treatment

Initial treatment of anal fissure includes dietary modifications, local measures, and pharmacological therapy. The first line of therapy is directed toward relaxing the IAS with the use of warm sitz baths. Also, modifying stool consistency to reduce trauma while passing stool can be achieved by increasing fluid and fiber intake both to avoid hard stools and to prevent diarrhea. Medical intervention should also be directed at relaxing the increased tone of the IAS and improving blood flow in the affected area. Surgery is indicated in cases of treatment failure or complications [6, 7]. The success of these general measures without accompanying drug treatment is 87 % in cases of acute anal fissure (but only 30 % in recurrences) and less than 50 % in cases of chronic anal fissure. The use of anaesthetic ointments does not improve the results of these conservative measures.

The main pharmacological treatments for anal fissure are nitric oxide (NO) donors, calcium

channel antagonists, and botulinum toxin (BT). The objectives of these measures are to reduce anal sphincter tone and to increase blood flow to the anal area.

5.6.1 Nitric Oxide Donors

Glyceryl trinitrate (GTN) and isosorbide dinitrate (ISDN) are the NO donors used to treat anal fissure. These are administered topically to the anal skin with the aims of relaxing the IAS and increasing local blood flow. GTN has been applied at two different concentrations: 0.2 % and 0.4 %. ISDN needs to be administered five times a day to achieve the same amount of nitrate that GTN provides with only two applications a day (although in published studies GTN is applied at a 1 % concentration three times a day) [8]. This is why ISDN is not routinely used in practice. GTN at a concentration of 0.4 % has been marketed in Europe. The topical application of GTN is associated with transient headache in 27–50 % of patients [8]. These may occur during the first 2 or 3 weeks of treatment and last between 10 and 30 min. The headaches usually respond to standard treatment with pain killers, but 10–20 % of patients abandon GTN treatment because of the headaches [6]. The pain caused by the anal fissure begins to improve between the fifth and seventh days, but the treatment must be maintained for minimum of 8 weeks to increase the chances of a cure. A meta-analysis of 75 studies showed that GTN has a better rate of healing of anal fissure than placebo (48.6 % vs. 37 %; $P = 0.004$) [8].

The figures published on recurrence are diverse and range between 17 % and 67 % [9–13]. A significant proportion of patients with long-term recurrence can be treated again with topical GTN or other topical medications, and surgery is not always necessary. In fact, the number of surgeries for anal fissure has decreased in recent years to between 60 % and 72 %.

Patients with a risk of hypotension and those taking sildenafil (Viagra) or another type of phosphodiesterase type 5 (tadalafil [Cialis], vardenafil [Levitra]) inhibitors should be treated with medications different from GTN because of such risk.

5.6.2 Calcium Channel Antagonists

Calcium channel antagonists such as nifedipine and diltiazem have been shown to relax the IAS and decrease resting pressure in the anal canal [14]. These drugs have been administered both orally and topically. Oral forms increase the risk of dizziness and episodes of significant hypotension in up to 5 % of patients and are not more effective than topical forms [15, 16]. Calcium channel antagonists are generally used as the first-line treatment or in patients resistant to treatment with GTN.

There is no commercial preparation available in Europe, so calcium channel antagonists must be compounded (custom-made) and prescribed as formulations: either diltiazem 2 % or nifedipine 0.2–0.5 %. Prescriptions are generally associated with lidocaine (a local anaesthetic) to help with the pain caused by the anal fissure. Their effectiveness is difficult to assess based on the literature because of the small number of publications and their short follow-up, but studies comparing nifedipine and diltiazem with GTN show that calcium channel antagonists are at least as effective as GTN (50–65 %), with a similar incidence of recurrence and fewer adverse effects (flushing, headache) [18, 19]. Headache occur in only 0–25 % of patients, that is, half of the prevalence when compared with GTN (33–50 %) [17].

A systematic review of studies comparing diltiazem and GTN included 481 patients. It concluded that their effectiveness and relapse rates are comparable, but the diltiazem group showed fewer adverse effects (Risk ratio (RR) = 0.48; 95 % CI = 0.27–0.86; $P < 0.01$) [20].

ISDN has also been compared to surgery; in a large study involving 207 patients with chronic anal fissures, success at 6 months was 77 % (ISDN) and 97 % (surgery). Recurrence at 12 months occurred in 4.8 % (ISDN) and 1 % (surgery). De novo fecal incontinence was diag-

nosed in 6 patients (3 %) of those treated with surgery and in none of the patients treated with ISDN [21].

5.6.3 Botulinum Toxin

BT is a protein synthesized by the bacterium *Clostridium botulinum* that has neuro-paralyzing effects. BT treatments are used to induce muscle paralysis through temporal local denervation of the treated muscles secondary to inhibition of the release of acetylcholine at the neuromuscular junction. There are various types of BT (A, B, C, D, E, F, and G); type A BT is currently used in the treatment of anal fissure.

There are several commercial presentations of BT. Those used in the treatment of anal fissure are botulinum toxin type A (Botox; 50 or 100 IU/vial), incobotulinumtoxinA (Xeomin; 50 and 100 IU/vial), and abobotulinumtoxinA (Dysport; 500 IU/vial). When Disport is used it should be remembered that dosing is on a ratio of approximately 1 to 3, meaning that 50 IU of Botox or Xeomin have the same effect as 150 IU of Disport [22]. Correct administration of BT is followed by local muscle relaxation that lasts around 2 to 4 months.

BT has been injected in different ways—unilateral or multilateral, at the base of the fissure or at one or both sides of the fissure, at the IAS, in the external anal sphincter, or both—and at different doses: from 5 to 50 IU (most commonly 50 IU) in single or multiple applications. This large variation in administration makes interpreting the results described so far difficult.

The first published results on the effectiveness of BT described a success rate over 80 % [22], but subsequent studies have shown that healing is accomplished in around 50 % of patients when follow-up is longer than 12 months [3, 23].

Local complications occur in less than 5 % of patients and include local hematoma or infection at the site of administration. General complications are toxin allergy or temporary incontinence (0–13 %), all of which are not frequent but dose dependent.

A meta-analysis including more than 270 patients demonstrated the superiority of surgery when compared with BT (RR = 1.31; 95 % CI = 1.50–1.57), a greater absolute benefit from surgery (23 %), and a higher recurrence with the toxin (RR = 5.83; 95 % CI = 2.96–11.49). Surgery was associated with increased rates of fecal incontinence (RR = 0.08; 95 % CI = 0.01–0.59) [24]. The benefits of BT treatment are ease of application, even in a doctor's office. The main disadvantage is the high cost.

Comparative results of BT against a combined treatment of GTN and BT in patients who did not respond to ISDN did not show the superiority of the combination. Although the association had a better cure rate after 6 weeks of treatment (66 % vs. 20 %), this superiority was not found at the 8th (73 % vs. 73 %) or at the 12th week of treatment (60 % vs. 66 %) [25].

NO donors have also been compared with BT in several studies. A recent study with a small number of patients compared BT (Dysport 60 IU) with ISDN. Toxin cure rates were higher and adverse effects were fewer than those observed with ISDN, although recurrence rates were high in both groups (50 % and 28 %, respectively) [26]. GTN and BT have also been compared in several studies. A meta-analysis of these studies concluded that the two treatments are equally effective, but incontinence after treatment is more common in patients treated with BT. BT is a more invasive treatment and also has a higher cost—these are reasons why many groups consider BT as a second-line treatment, for use in cases where topical treatment has not been effective [8].

Diltiazem was compared with BT in a randomized study with 143 patients. The two treatments were equally effective in the treatment of chronic anal fissure: a healing rate of 43 % was found for both treatments and a significant reduction in pain occurred in 78 % (diltiazem) and 82 % (BT) [27].

5.7 Surgical Treatment

Surgery is the definitive treatment of anal fissure. It is offered as a first treatment in patients without a risk of incontinence, although nowadays most

physicians propose it only to patients who do not respond to medical treatment or those who develop complications with medical therapy. Several surgical treatments have been described, but there is no doubt that the gold standard is still the lateral internal sphincterotomy, a section of the distal part of the internal sphincter.

5.7.1 Sphincterotomy

There are two different techniques described for a sphincterotomy: posterior and lateral, depending on the sectioned part of the internal sphincter. Posterior sphincterotomy, although used in the past, is not recommended today because it produces a keyhole deformity in the anus that is related to postoperative soiling. It is only performed in patients with a posterior anal fissure associated with intersphincteric abscess.

Lateral sphincterotomy is more effective than medical management; a greater than 90 % chance of cure and the patient satisfaction rate support this conclusion. It can be done under local anesthesia and is mostly performed as a same-day surgical procedure.

Sphincterotomy can be performed using an open or a closed technique. When both techniques were compared, no significative differences were found, although the open technique is related to superior healing rates but increased flatus incontinence [6].

Lateral sphincterotomy is more easily performed with the help of an anal retractor to correctly identify the intersphincteric groove. An incision is made at this level in the lateral quadrant of the anus (3 o'clock for right-handed or 9 o'clock for left-handed surgeons). The incision can be either circumferential or radial; there are no differences among the short- and long-term results when both have been compared [28]. Dissection of the internal sphincter from the anal mucosa and the external sphincter is followed by a partial section of the internal sphincter. No differences in healing or complications have been found when comparing suturing versus no suturing of the skin (Figs. 5.3, 5.4, 5.5, 5.6, and 5.7).

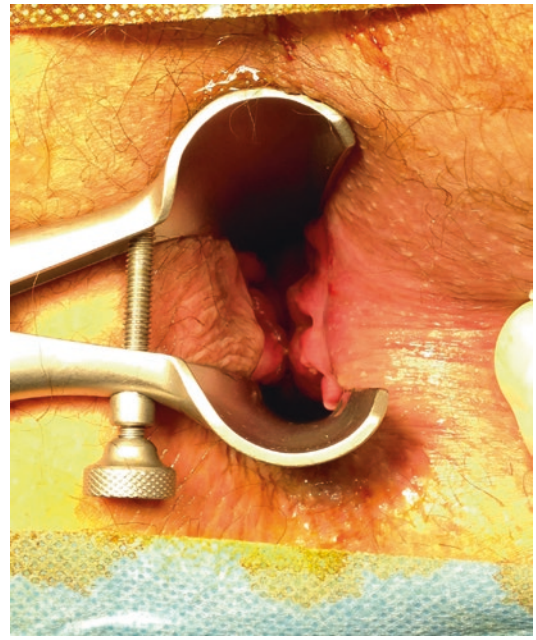


Fig. 5.3 Anal retractor to expose the intersphincteric groove

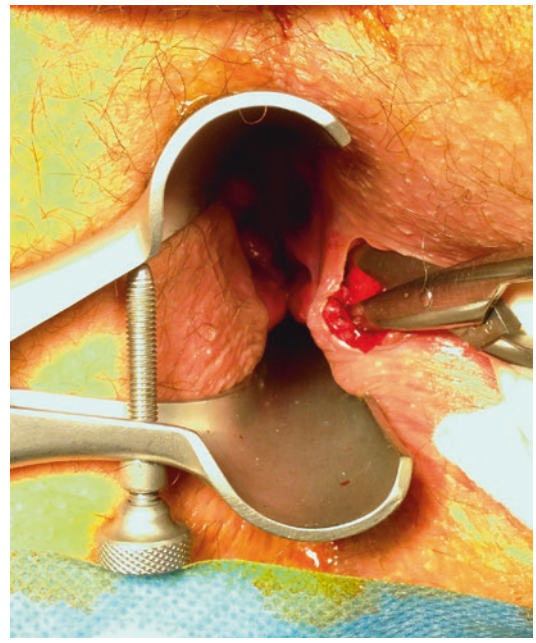


Fig. 5.4 Dissection of the internal sphincter from the anal mucosa

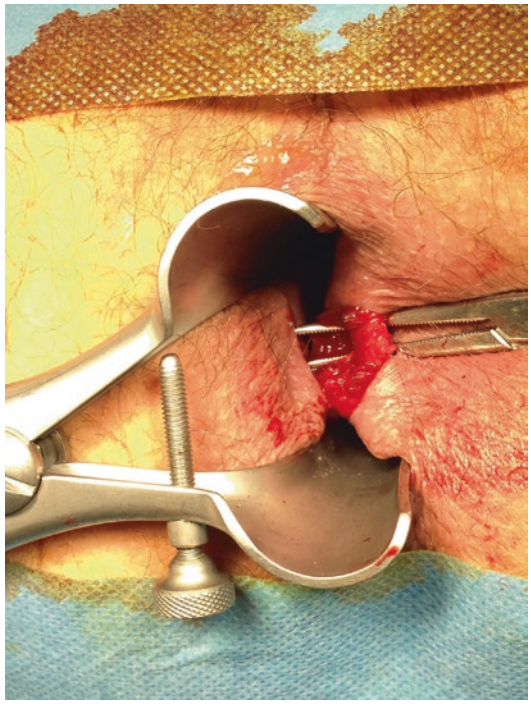


Fig. 5.5 Dissection of the internal anal sphincter

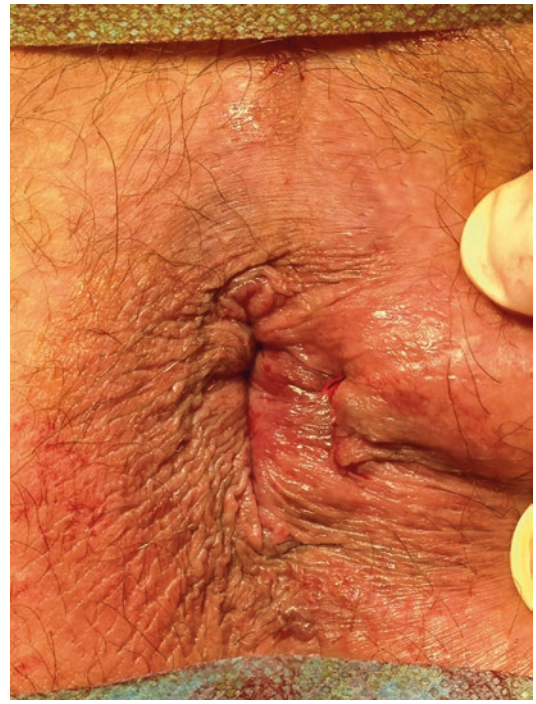


Fig. 5.7 Final aspect of the wound after lateral sphincterotomy

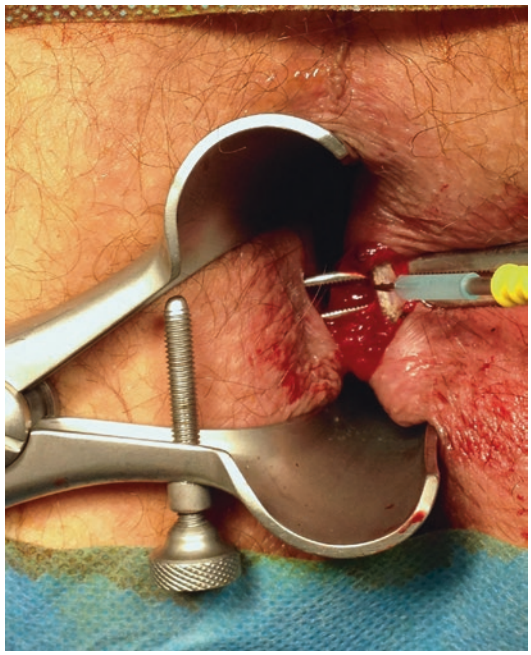


Fig. 5.6 Section of the internal anal sphincter

With respect to the internal sphincter section, limiting it to less than half the length of the sphincter does not increase the recurrence rate and diminishes postoperative fecal incontinence, although some groups recommend a more economical length of division at less than 25 % of its length, which in women corresponds to less than 1 cm [29].

When performing a lateral sphincterotomy, a tear produced while dissecting the anal sphincter from the anal mucosa is best solved by opening the entire involved mucosa, as in a lay-open technique, to avoid creating a postoperative fistula.

5.7.2 Fissurectomy

Fissurectomy includes excision of the fibrotic edge of the fissure, curettage of its base, and excision of the sentinel pile and/or anal papilla, if present. Some groups consider it to be a more conservative treatment for anal fissure. It can be combined with

the application of BT [30] in an effort to improve the results, which are poorer when fissurectomy is done alone [31]. Published healing rates when combined with BT are between 70 % [32] and 90 % [30], and de novo incontinence is usually temporal and minimal (occurring in <5 % of patients), or even absent in some other series [33].

5.7.3 Fissurotomy

Another novel procedure has recently been introduced in the surgical armamentarium for anal fissure: fissurotomy. It consists of unroofing the fissure, which significantly widens the distal anal canal, rendering internal sphincterotomy unnecessary [34]. Results have been promising, with less than a 2 % recurrence rate and no change in continence status. More studies and longer follow-up are needed to support these findings, which could also be influenced by the amount of anal dilatation involved in the procedure.

5.7.4 Anal Advancement Flap (Flap Anoplasty)

Advancement flap procedures have been reported in the treatment of anal fissures. These procedures involve fashioning a local flap to cover the fissure defect. Different flaps have been reported: island flap [35], house flap [36], V-Y flap, and a rotational flap [37]. These procedures are combined with fissurectomy and/or BT application. They do not involve disruption of the IAS and are mostly performed in patients with anal fissures and either a high risk of incontinence or low-pressure fissures to avoid compromising continence even more. Reported healing rates are between 80 % and 95 %, with 7 % flap disruption and a recurrence rate around 6 %. The postoperative incontinence rate is less than 5 % in the majority of reports [38, 39] (Fig. 5.8).

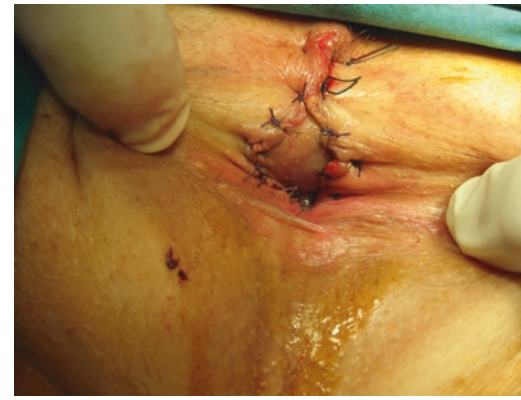


Fig. 5.8 Final aspect of the wound after a flap anoplasty for anal fissure (Courtesy of Dr. E. Garcia-Granero)

5.7.5 Anal Dilatation

Anal dilatation was one of the first surgical treatments for anal fissures. There are several ways to dilate the anus: manually, with progressive dilators, or with pneumatic balloons. Anal dilatation is not recommended as an outpatient treatment, neither under anesthesia nor under neuromuscular blockade. It does not show better results than other conservative treatments, is difficult and uncomfortable for the patient, and is related to an increase in incontinence (15–30 %) [8]. The incontinence is caused by multiple instances of (uncontrolled) damage to the IAS.

Treatment with progressive pneumatic balloons seems to provide good initial results [7], but there is a need for more prospective studies before this is recommended as a standard treatment.

Fecal incontinence is without a doubt the main reason why pharmacological treatments have recently been replacing surgery as the initial treatment for anal fissure. Surgery has been compared with GTN, BT, and nifedipine. Although these studies show healing rates of 60–70 % of patients treated with pharmacological and 95–97 % of those treated with surgical measures, they conclude that drug therapy should be the first treatment option, especially in groups with a high risk for fecal incontinence (e.g., multiparity, previous anal surgery, radiotherapy), given the higher number of serious complications with surgery among them [6, 40–42].

5.7.6 Other Innovative Treatments

Other therapies are being tested for the treatment of chronic anal fissures, such as posterior

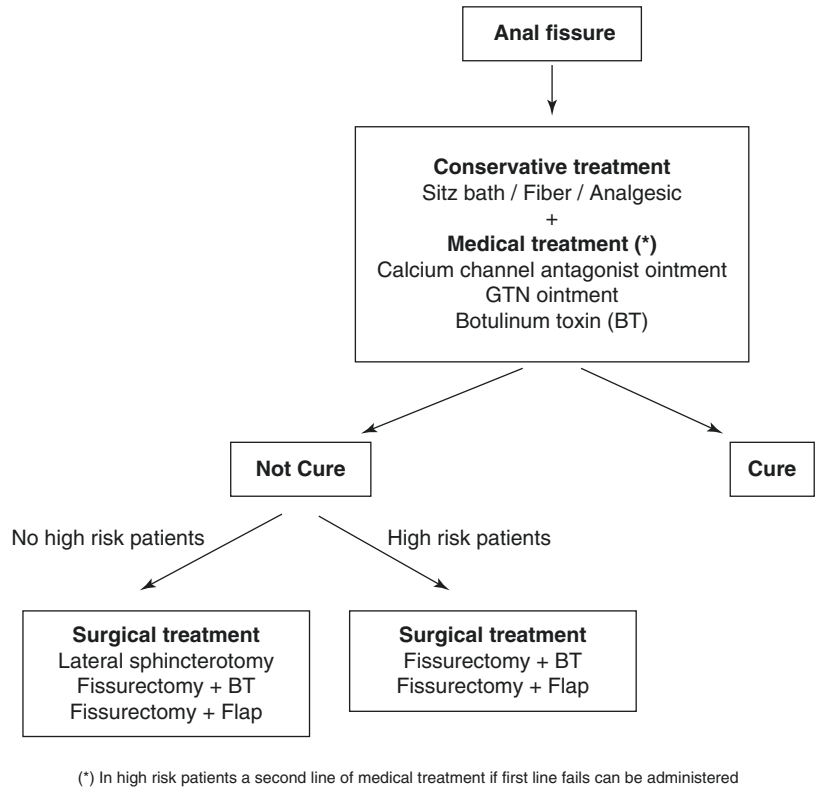


Fig. 5.9 Proposed algorithm for anal fissure treatment

perineal support devices [43], posterior tibial nerve stimulation [44], and sacral nerve stimulation [45]. More studies are needed to support the routine use, effectiveness, and cost analysis of these treatments in patients with anal fissure.

A basic algorithm for the treatment of anal fissure is proposed here (Fig. 5.9) according to the published evidence.

5.8 Complications

Complications of medical treatment of anal fissures are allergy to compounds, headache, and hypotension. These are usually dose dependent, easy to manage, and have minimal consequences for the patient.

The most important complication with all surgical techniques is the long-term consequence of permanently sectioning the sphincter: fecal incontinence. This condition can be temporary in up to 30 % of operated patients and permanent in 3–13 % of patients [40]. Among operated patients, permanent incontinence after lateral sphincterotomy can result in flatus incontinence (9 %), soiling/seepage (6 %), accidental defecation (0.91 %), incontinence to liquid stool (0.67 %), and incontinence to solid stool (0.83 %). These percentages are affected by the procedure, the patient's characteristics, and the surgeon's experience. High-risk factors for postoperative incontinence include age [46], female sex (shorter anal canal) [40], vaginal deliveries [47], radiotherapy, and previous anal trauma.

5.9 Special Considerations

5.9.1 Low Tone/Incontinence

Patients with anal fissure and anal hypotonicity or fecal incontinence should be treated conservatively. If the initial treatment fails there are reports of treatment with an advancement flap [48]. This procedure does not involve excising

the anal sphincter and has shown excellent results in these kinds of patients, with more than 90 % cure rates and no worsening of continence.

5.9.2 Recurrent Anal Fissure

A recurrent anal fissure can be a complex problem. Before starting treatment again, a complete evaluation of the symptoms and the aspect of the fissure, along with the patient's history and treatment preferences, is recommended [49].

Medical treatment should again be the first option, and a second line of treatment can be offered if the first fails. If this medical treatment does not cure the fissure, then surgery must be recommended (sphincterotomy, flap, fissurectomy with BT). If the patient already had a sphincterotomy, then a sphincter-saving procedure is encouraged (fissurectomy or flap).

5.9.3 Management of Concomitant Anal Lesions

Fibrous polyps and hypertrophied anal papillae are present in some chronic anal fissures and can be resected at the same time of sphincterotomy. However, adding a synchronous anal procedure (e.g., hemorrhoidectomy) at the time of sphincterotomy increases the risk of incontinence [47].

5.9.4 Crohn's Disease

Fissure in Crohn's disease is a common finding, although most of these fissures are related to the inflammatory disease and not to sphincter hypertonicity. Caution in treatment is mandatory. It is important to treat these patients accordingly, but it is also crucial to be as conservative as possible to avoid current or future complications. When medical treatment fails and there is no evidence of anorectal inflammation, a sphincterotomy has shown good results [50]. Multidisciplinary evaluation is highly recommended.

5.9.5 Anal Fissure in Children

Fissure in children should be treated with sitz baths and soft laxatives. If the fissure does not heal, then medical treatment should be tried: GTN or a calcium channel blocker ointments or BT administration are effective. Lateral sphincterotomy or fissurectomy are usually unnecessary and should be reserved only for those patients who do not heal with medical therapy alone.

Acknowledgements The author thanks Dr. Isaac Felemovicious for reviewing the grammatical aspects of the chapter.

References

1. Farouk R, Duthie G, MacGregor AB, Bartolo DCC. Sustained internal sphincter hypertonia in patients with chronic anal fissure. Dis Colon Rectum. 1994;37(5):424–9.
2. Schouten WR, Briel JW, Auwerda JJ. Ischaemic nature of anal fissure. Br J Surg. 1996;83(1):63–5.
3. Lund J, Nyström P-O, Herold A, Schouten WR, Arroyo A, Pescatori M. An evidence-based algotithm for anal fissure. Tech Coloproctol. 2006;10:177–80.
4. Jenkins JT, Urie A, Molloy RG. Anterior anal fissures are associated with occult sphincter injury and abnormal sphincter function. Colorectal Dis. 2008; 10(3):280–5.
5. Mapel DW, Schum M, Von Worley A. The epidemiology and treatment of anal fissures in a population-based cohort. BMC Gastroenterol. 2014;14:129.
6. RL Nelson, et al. Operative procedures for fissure in ano. Cochrane Database Syst Rev (Online). 2009;1–10.
7. Renzi A, Izzo D, DiSarno G. Clinical, manometric, and ultrasonographic results of pneumatic balloon dilatation vs. lateral internal sphincterotomy for chronic anal fissure: a prospective, randomized, controlled trial. Dis Colon Rectum. 2008;51(1):121–7.
8. Nelson RL, Thomas K, Morgan J, Jones A. Non surgical therapy for anal fissure. Cochrane Database Syst Rev (Online). 2012:CD003431.
9. Jonas M, Barrett DA, Shaw PN, Scholefield JH. Systemic levels of glyceryl trinitrate following topical application to the anoderm do not correlate with the measured reduction in anal pressure. Br J Surg. 2001;12:1613–6.
10. Lund J, Scholefield JH. Follow-up of patients with chronic anal fissure treated with topical glyceril trinitrate. Lancet. 1998;352:1681–2.
11. Jonas M, Lund J, Scholefield JH. Topical 0.2% glyceryl trinitrate ointment for anal fissures: long-term

efficacy in routine clinical practice. Colorectal Dis. 2002;4(5):317–20.
12. Graziano A, Svidler Lopez L, Lencinas S. Long term results of topical nitroglycerin in the treatmet of chronic anal fissures are disappointing. Tech Coloproctol. 2001;5:143–7.
13. Libertiny G, Knight JS, Farouk R. Randomised trial of topical 0,2% glyceryl trinitrate and lateral internal sphincterotomy for the treatment of patients with chronic anal fissure: long-term follow-up. Eur J Surg. 2002;168:418–21.
14. Carapeti EA, Kamm MA, Phillips RK. Topical diltiazem and bethanechol decrease anal sphincter pressure and heal anal fissures without side effects. Dis Colon Rectum. 2000;43(10):1359–62.
15. Jonas M, Neal KR, Abercrombie JF, Scholefield JH. A randomized trial of oral vs. topical diltiazem for chronic anal fissures. Dis Colon Rectum. 2001;44(8):1074–8.
16. Agrawal V, Kaushal G, Gupta R. Randomized controlled pilot trial of nifedipine as oral therapy vs. topical application in the treatment of fissure-in-ano. Am J Surg. 2013;5:748–51.
17. Nelson R. A systematic review of medical therapy for anal fissure. Dis Colon Rectum. 2004;47(4):422–31.
18. Ezri T, Susmallian S. Topical nifedipine vs. topical glyceryl trinitrate for treatment of chronic anal fissure. Dis Colon Rectum. 2003;46(6):805–8.
19. Ala S, Saeedi M, Hadianamrei R, Ghorbanian A. Topical diltiazem vs. topical glyceril trinitrate in the treatment of chronic anal fissure: a prospective, randomized, double-blind trial. Acta Gastroenterol Belg. 2012;4:438–42.
20. Sajid MS, Whitehouse PA, Sains P, Baig MK. Systematic review of the use of topical diltiazem compared with glyceryltrinitrate for the nonoperative management of chronic anal fissure. Colorectal Dis. 2012;15(1):19–26.
21. Arslan K, Erenoglu B, Dogru O, Turan E, Eryilmaz MA, Atay A, et al. Lateral internal sphincterotomy versus 0.25 % isosorbide dinitrate ointment for chronic anal fissures: a prospective randomized controlled trial. Surg Today. 2013;43(5):500–5.
22. Maria G, Brisinda G, Bentivoglio AR, Cassetta E, Gui D, Albanese A. Botulinum toxin injections in the internal anal sphincter for the treatment of chronic anal fissure: long-term results after two different dosage regimens. Ann Surg. 1998;228(5):664–9.
23. Arroyo A, Pérez-Vicente F, Serrano P, Candela F, Sánchez A, Pérez-Vázquez MT, et al. Treatment of chronic anal fissure. Cir Esp. 2005;78(2):68–74.
24. Shao W-J, Li G-C, Zhang Z-K. Systematic review and meta-analysis of randomized controlled trials comparing botulinum toxin injection with lateral internal sphincterotomy for chronic anal fissure. Int J Colorectal Dis. 2009;24(9):995–1000.
25. Lysy J, Israelit-Yatzkan Y, Sestiery-Ittah M, Weksler-Zangen S, Keret D, Goldin E. Topical nitrates potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure. Gut. 2001;48(2):221–4.
26. Berkel AEM, Rosman C, Koop R, van Duijvendijk P, van der Palen J, Klaase JM. Isosorbide dinitrate ointment versus botulinum toxin A (Dysport®) as primary treatment for chronic anal fissure: a randomized multicentre study. Colorectal Dis. 2014;16(10):360–66.
27. Samim M, Twigt B, Stoker L, Pronk A. Topical diltiazem cream versus botulinum toxin a for the treatment of chronic anal fissure: a double-blind randomized clinical trial. Ann Surg. 2012;1:18–22.
28. Kang WH, Lim CH, Choi DH, Shin HK, Lee YC, Jeong SK, et al. Comparison of skin incisions used for open lateral internal sphincterotomies – radial versus circumferential incisions: a retrospective cohort study. Int J Surg. 2014;12(11):1141–5.
29. Murad-Regadas SM, Fernandes GODS, Regadas FSP, Rodrigues LV, De Pereira JR J, Regadas Filho FSP, et al. How much of the internal sphincter may be divided during lateral sphincterotomy for chronic anal fissure in women? Morphol Funct Eval Sphincterotomy. 2013;56(5):645–51.
30. Lindsey I, Cunningham C, Jones OM, Francis C, Mortensen NJM. Fissurectomy-botulinum toxin: a novel sphincter-sparing procedure for medically resistant chronic anal fissure. Dis Colon Rectum. 2004; 47(11):1947–52.
31. Yurko Y, Crockett JA, Culumovic PJ. The efficacy and morbidity of different surgical treatment techniques for chronic anal fissure: an academic colorectal experience. Am Surg. 2014;80(3):241–4.
32. Scholz T, Hetzer FH, Dindo D, Demartines N, Clavien PA, Hahnloser D. Long-term follow-up after combined fissurectomy and Botox injection for chronic anal fissures. Int J Colorectal Dis. 2007;22(9): 1077–81.
33. Aivaz O, Rayhanabad J, Nguyen V, Haigh PI, Abbas M. Botulinum toxin A with fissurectomy is a viable alternative to lateral internal sphincterotomy for chronic anal fissure. Am Surg. 2009;75(10):925–8.
34. Pelta AE, Davis KG, Armstrong DN. Subcutaneous fissurotomy: a novel procedure for chronic fissure-in-ano. A review of 109 cases. Dis Colon Rectum. 2007;50(10):1662–7.
35. Nyam DC, Wilson RG, Stewart KJ, Farouk R, Bartolo DC. Island advancement flaps in the management of anal fissures. Br J Surg. 1995;82(3):326–8.
36. Alver O, Ersoy YE, Aydemir I, Erguney S, Teksoz S, Apaydin B, et al. Use of “house” advancement flap in anorectal diseases. World J Surg. 2008;32(10): 2281–6.
37. Singh M, Sharma A, Duthie G, Balasingh D, Kandasamy P. Early results of a rotation flap to treat chronic anal fissures. Asian J Surg. 2005;28(3): 189–91.
38. Halahakoon VC, Pitt JP. Anal advancement flap and botulinum toxin A (BT) for chronic anal fissure (CAF). Int J Colorectal Dis. 2014;29(9):1175–7.

39. Abramowitz L, Bouchard D, Souffran M, Devulder F, Ganansia R, Castinel A, et al. Sphincter-sparing anal-fissure surgery: a 1-year prospective, observational, multicentre study of fissurectomy with anoplasty. Colorectal Dis. 2013;15(3):359–67.
40. Garg P, Garg M, Menon GR. Long-term continence disturbance after lateral internal sphincterotomy for chronic anal fissure: a systematic review and meta-analysis. Colorectal Dis. 2013;15(3):e104–17.
41. Evans J, Luck A, Hewett P. Glyceryl trinitrate vs. lateral sphincterotomy for chronic anal fissure: prospective, randomized trial. Dis Colon Rectum. 2001;44(1):93–7.
42. Sajid MS, Hunte S, Hippolyte S, Kiri VA, Maringe C, Baig MK. Comparison of surgical vs chemical sphincterotomy using botulinum toxin for the treatment of chronic anal fissure: a meta-analysis. Colorectal Dis. 2008;10(6):547–52.
43. Tan K-Y, Seow-Choen F, Hai CH, Thye GK. Posterior perineal support as treatment for anal fissures – preliminary results with a new toilet seat device. Tech Coloproctol. 2009;13(1):11–5.
44. Altunrende B, Sengul N, Arisoy O, Yilmaz EE. Transcutaneous electrical posterior tibial nerve stimulation for chronic anal fissure: a preliminary study. Int J Colorectal Dis. 2013;28(11):1583–9.
45. Yakovlev A, Karasev SA, Dolgich OY. Sacral nerve stimulation: a novel treatment of chronic anal fissure. Dis Colon Rectum. 2011;54(3):324–7.
46. Arroyo A, Pérez F, Serrano P, Candela F, Lacueva J, Calpena R. Surgical versus chemical (botulinum toxin) sphincterotomy for chronic anal fissure: long-term results of a prospective randomized clinical and manometric study. Am J Surg. 2005;189(4):429–34.
47. Kement M, Karabulut M, Gezen FC, Demirbas S, Vural S, Oncel M. Mild and severe anal incontinence after lateral internal sphincterotomy: risk factors, postoperative anatomical findings and quality of life. Eur Surg Res. 2011;47(1):26–31.
48. Giordano P, Gravante G, Grondona P, Ruggiero B, Porrett T, Lunniss PJ. Simple cutaneous advancement flap anoplasty for resistant chronic anal fissure: a prospective study. World J Surg. 2009;33(5):1058–63.
49. Siproudhis L, Eléouet M, Abittan S. Treatment of recurrent anal fissures: what should be done? Gastroenterol Clin Biol. 2008;32(5 Pt 2):S215–20.
50. D'Ugo S, Franceschilli L, Cadeddu F, Leccesi L, Blanco GDV, Calabrese E, et al. Medical and surgical treatment of haemorrhoids and anal fissure in Crohn's disease: a critical appraisal. BMC Gastroenterol. 2013;13:47.

Anorectal Abscess and Fistula

6

Alexander Herold

6.1 Introduction

An anorectal abscess is a nonphysiological cavity filled with pus that develops as a result of acute inflammation. Anal fistulas are nonphysiological tract-like connections from the anal canal or the distal rectum to the perianal skin. They originate in the area of the rudimentary glands at the dentate line in the anal canal. Ninety percent of anal fistulas are of cryptoglandular origin [1].

Anal abscesses and anal fistulas are different stages in the course of the same basic disease. In most cases the abscess initiates the disease and represents its acute form, whereas the fistula usually is the second stage and represents chronic inflammation.

6.2 Etiology and Edidemiology

Anal fistula was first described in 380 B.C. by Hippocrates; he also mentioned a drainage seton. It is assumed that about 2 % of all people suffer from perianal abscesses or fistulas throughout the course of their lives. An annual incidence of 20 per 100,000 population makes fistula in ano a common proctological disease in Europe; this corresponds to around 15,000 patients with fistula per year in Germany. Although we do not speak of a life-threatening disease – at least in the case of fistulas – it is nevertheless stressful for patients since the recurrence rate is between 10 % and 50 %. Anorectal abscesses and fistulas are three times more frequent among men than women. Abscesses occur most frequently between the ages of 20 and 40 years, and fistulas between the ages of 20 and 50. Presumably, the cause of an abscess is a bacterial infection, which subsequently occludes drainage from the crypts. This primary abscess often does not appear clinically and can either heal spontaneously or drain via the crypt into the anal canal. If, however, the infection channels its way along preexisting paths intersphincterically, submucosally, subanodermally, transsphincterically, or even suprasphincterically, it may result in clinically impressive secondary abscesses. With a classical perianal abscess, spontaneous remission is not possible, and without treatment it can perforate into the rectum, into the anal canal, or to the outside of the body, depending on the location where it originates.

6.3 Classification

Anal abscesses are classified based on their relation to the surrounding anatomic structures (Fig. 6.1).

A. Herold, MD
1End- und Dickdarmzentrum Mannheim, Consultant
Medical University Mannheim,
Bismarckplatz, 168165 Mannheim, Germany
e-mail: a.herold@enddarm-zentrum.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_6

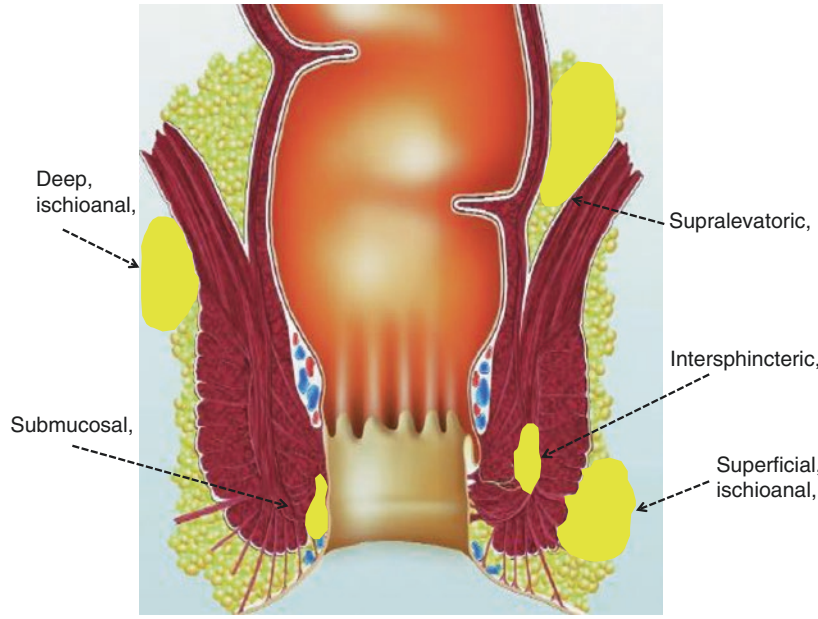


Fig. 6.1 Abscess classification

- Ischioanal: Abscesses located in ischioanal fat are bordered by the sphincter muscles medially by the levator ani in the cranial aspect, and by the ischial bone laterally. They can occur on one or both sides. Depending on the location, sometimes these can be differentiated into superficial and deep.
- Intersphincteric: Acute abscesses located between the internal and external sphincter are very painful and not easy to detect. Chronic cavities often remain as incomplete internal fistulas. Since they usually drain through the tracts of the infected anal glands, pus may be suddenly purged during examination; others perforate distally. Also, these abscesses can rise to the supralevator level and lead to suprasphincteric fistulas.
- Subanodermal/submucosal: This kind of abscess is located superficially between the sphincter and the anoderm (subanodermal) or rectal mucosa (submucosal). For this reason we distinguish between subanodermal and submucosal abscesses. These terms are also often used as synonyms.
- Supralevatoric: This abscess is located in the retroperitoneal fat outside the rectal wall and above the levator muscle. Another synonym for abscesses of this kind is *retrorectal abscess*. These often extend on both sides and are therefore called "horseshoe" abscesses.

Anal fistulas are classified using the same system as abscesses: according to their anatomic relation to the anal sphincter (Fig. 6.2). In nearly all (except extrasphincteric fistulas) the origin is cryptoglandular and therefore the internal opening lies at the dentate line.

- Submucosal (synonym: *subanodermal*): run under the anoderm or the rectal mucosa
- Intersphincteric: cross the internal sphincter and reach the skin, mostly near the anus
- Transsphincteric: cross the internal and external sphincters, protrude from the ischioanal fossa, and reach the external skin, mostly a few centimeters from the anus. we should distinguish A distal (low) or proximal (high) position should be distinguished, depending on their height. Some authors describe the location of a fistula depending on the affected third of the anal sphincter.

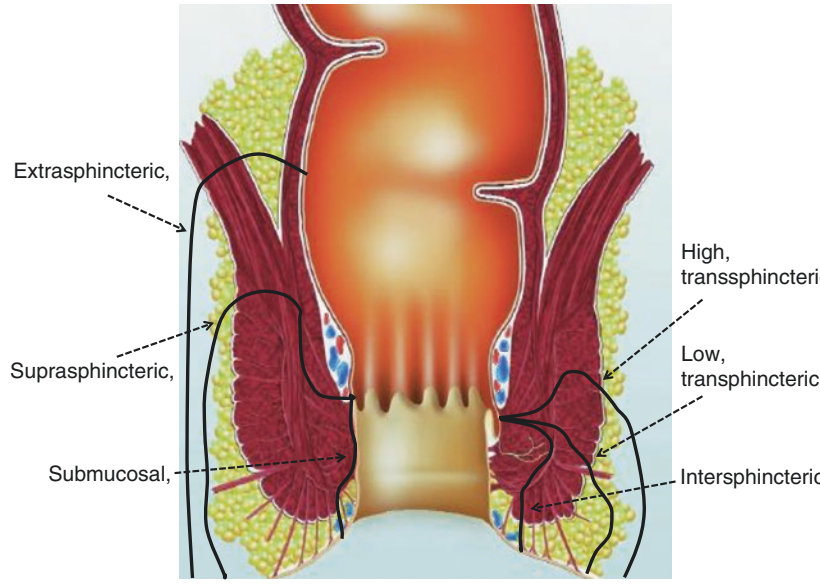


Fig. 6.2 Fistula classification

- Suprasphincteric: cross the internal sphincter, run proximally in the intersphincteric plane, curve around the complete external sphincter, and reach the skin.
- Extrasphincteric: originate in the distal rectum, pass through the rectrorectal space and the pelvic floor from a proximal direction, protrude from the ischioanal fossa, and reach the skin

There is a distinction between primary and recurrent fistulas, and between straight and curved tracts. Surgeons often differentiate into simple and complex fistulas (e.g., a complex fistula occurs when more than one-third of the sphincter is affected). Two special forms are anorectovaginal fistulas and horseshoe fistulas [2–5].

6.4 Symptoms

In most cases patients experience intense, somewhat pulsating pain, sometimes with fever and a distinct sensation of being ill. Here also the pathology is dependent on the exact location of the abscess. This typical presentation is mostly seen with distal (perianal, low intersphincteric, transsphincteric) locations. If the abscess develps in a proximal direction (high intersphincteric, pelvirectal, supralevatoric), the symptoms are not distinct at first. Pain will decline considerably in the case of spontaneous perforation, but it does not resolve completely. Such perforation can occur toward the outside, into the anal canal, or into the rectum, depending on the initial location. After perforation, spontaneous drainage can cause persistent drainage or might heal at the dermal surface, which causes retention of fluids and thereby a recurrence of symptoms. After the spontaneous perforation of (or a deficient operative incision into) an abscess, an anorectal fistula may remain or develop. Complete healing without a persisting fistula in up to 40 % of cases is described by some authors, but no convincing figures are available. Fistula healing without complications can only be expected when the abscess is opened operatively and the corresponding fistula is removed completely.

Contrary to abscesses, the clinical pathology of perianal fistulas is characterized by chronic complaints and discomfort. Secretion predominates; its intensity varies and is often accompanied by anal eczemas. If the external fistula opening will be epithelialized,“sham healing” sometimes

occurs. In this case the external opening is temporarily closed with a thin layer of epithelium, but the fistula itself does not heal completely. Then it is only a matter of time until the fistula reopens, with secretion occurring again. In the case of anorectal fistulas, spontaneous remission rarely occurs; in general, healing cannot be expected. Recurrent and variably strong secretion is the expression of a chronic inflammatory infiltrate. Without treatment this can lead to an extension of the disease, with the potential to develop new abscesses and more fistulas. In the long run this leads to impairment and disorders of continence. In the case of immunological dysfunctions, phlegmons with septic and therefore life-threatening conditions can occur. Also, fistula carcinomas have been described over the course of many years with long-lasting diseases [6].

6.5 Diagnostics

It is easy to diagnose an acute abscess through its typical history, clinical pathology, and symptoms and using inspection and palpation. Ischioanal abscesses, when located superficially, mostly show a reddish livid discoloration with an explicitly visible prominence. Extended abscesses can lead to a dislocation of the rima ani and occasionally show fluctuation at palpation. Initially it can be difficult to reliably objectify a pelvirectal or deep ischiorectal abscess. A bidigital rectal examination, with palpable swelling and pain at pressure/touch, is a help in such cases. Only in selected cases are high-tech diagnostic methods necessary (e.g., transanal endosonography, transcutaneous sonography, or pelvic floor magnetic resonance imaging [MRI]; Figs. 6.3 and 6.4).

Most fistulas are easy to diagnose: you see the external opening, you feel the internal opening, and you can find the tract by probing. During digital examination, the course of a fistula often can be palpated as a stringlike structure. Only with a complicated courses might there be difficulties in diagnosing an anorectal fistula. The external opening of an anal fistula is usually easily perceptible, but locating the internal opening may be difficult sometimes. In the case of cryptoglandular fistulas, the internal opening is generally found at the dentate line. The clinical experience of the therapist is crucial in the diagnostic investigation of anal fistulas. While dorsal anal fistulas take a curved course, ventral fistulas generally proceed straight (Goodsall's rule). According to this, fistulas with an external opening dorsal to a line between 3 and 9 o'clock in the lithotomy position (the "anal horizon") run predominantly curved, and those with an opening ventral to this line are straight (there are, of course, exceptions to this old rule). In the case of restrained inflammation, the fistula's course can be followed easily with a small metal probeWith pronounced inflammation, however, probing can be problematic; there might be a danger of causing a via falsa, which often leads to complicated

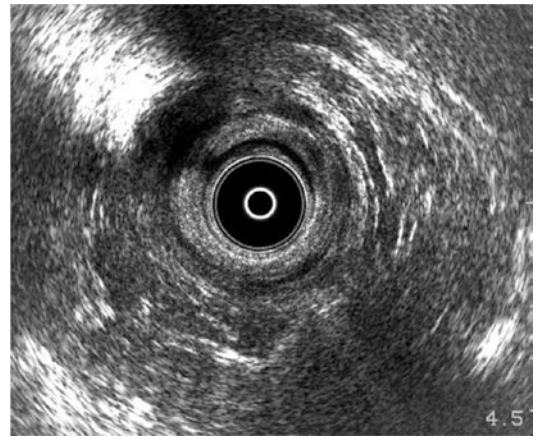


Fig. 6.3 Right anterior ischioanal abscess (11 o'clock in the lithotomy position)

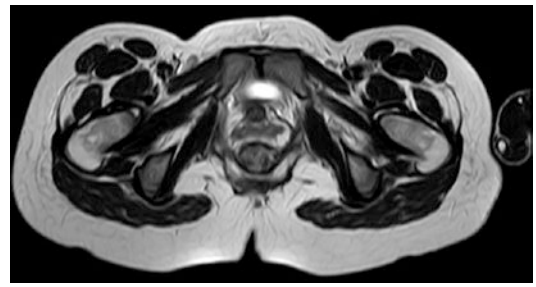


Fig. 6.4 Retrorectal, supralevatoric, horseshoe abscess

fistulas. This ought to be considered, especially in the case of fistula courses with secondary tracts. Thus, probing should never be mandated and whenever possible should be done by an experienced physician.

The clinical examination may be performed under anesthesia since the probing of fistulas is painful and often fails. Operations are almost always necessary, and thus can be performed while the patient is still anesthetized.

As a primary instrumental examination, anal endosonography is simple, inexpensive, and immediately available. Endosonography or MRI should be considered but are only necessary for complex or recurrent fistulas. Both of these largely depend on the examiner but are otherwise comparable; endosonography is considerably cheaper and can be conducted intraoperatively. In the case of complex fistulas that have larger cavities and run far away from the midline, MRI of the pelvic floor and the small pelvis might be indicated and superior to ultrasound (Fig. 6.5). A radiographic examination of fistulas (fistulography) is now obsolete because it just shows the fistula and does not sufficiently visualize its three-dimensional course.

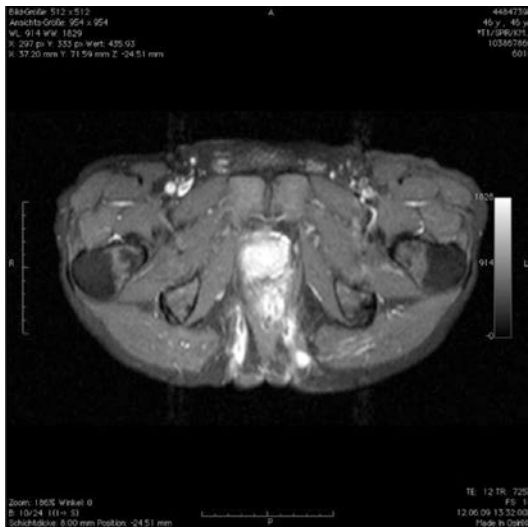


Fig. 6.5 Chronic fistulas on both sides in a patient with Crohn's disease

6.6 Differential Diagnosis

Differential diagnosis of a dorsal sinus pilonidalis in the rima ani usually is not difficult. Perianal acne inversa (synonym: *hidradentitis suppurativa*) may be a problem in the differential diagnosis, especially with regard to the differentiation of perianal Crohn's disease. The most frequent differential diagnosis is a fistula caused by Crohn's disease (this is strictly defined; it is not really a differential but an additional diagnosis). Perianal fistulas caused by tuberculosis are rare (1–3 %) in Europe, but in India, for example, this is the most common cause of fistulas.

Without any therapy, fistula in ano can lead to an expansion of inflammation with the potential to develop new abscesses and fistulas. This primarily results in permanent impairment and disorders of anal continence. In the case of long-lasting chronic inflammation, fistular carcinomas are reported in singular cases; on the whole these are extremely rare.

6.7 Abscess Treatment

Surgical interventions are the first-line treatment for anorectal abscesses [6–8]. An anorectal abscess is an emergent indication for surgery because of the dangers of progression into the surrounding structures and –rarely – life-threatening systemic sepsis. Therefore, incision and adequate drainage should follow directly after diagnosis. Unsuitable measures, such as waiting until fluctuation occurs, providing a therapy with any ointment, or administering only antibiotics, can cause a delay. A supplementary therapy with antibiotics should be exceptional (e.g., diffuse pararectal extension, immunosupression, or septic systemic reactions). The insertion of only a draining catheter is indicated in a few special cases but is insufficient even for an uncomplicated abscess.

During operations to repair anorectal abscesses, the surgeon should simultaneously search for the cause. If they find a connection to the anal canal or distal rectum, they should either primarily dissect it or initially place a drainage seton to provide

a later final therapy. Rough manipulation should be avoided because of the danger of a causing a via falsa.

- **Perianal excision**: Smaller perianal abscesses can often be incised and drained in the outpatient department as an initial measure; however, sufficient drainage and complete unroofing, respectively, must be achieved; subsequently the wound heals with secondary intention (Fig. 6.6a–d).
- **Drainage into the anal canal**: An intersphincteric abscess is often diagnosed too late because the typical redness and swelling in the perianal region are missed. Many times it can only be recognized by acute, fierce, regional pain in the anal canal. When in doubt, an examination while the patient is anesthetized and subsequent complete unroofing of the abscess – in most cases dissecting the distal parts of the internal sphincter – are recommended. If the abscess is in the upper part of the anal canal, internal drainage into the anal canal is indicated. When an intersphincteric abscess extends toward the retrorectal region, the drainage must be directed into the distal rectum. Here a wide excision of the rectal wall is often inevitable. This should be carried out in a way that leaves no cavities with insufficient drainage; also, a partial dissection – in this case of a proximal part of the internal sphincter – might be necessary.
- **Treatment of deep ischioanal or retrorectal abscesses** (Fig. 6.1): If the abscess is large and/or is in the deep postanal space, reaching the distal aspect of the levator ani or even crossing the pelvic floor muscles and reaching the supralevatoric retrorectal space, a deep and wide excision is necessary to achieve acceptable drainage. Cautious dissection is mandatory because of blood vessels (e.g., obturatoric vessels) and nerves (e.g., the pudendal nerve) in this area. Preparation often is restricted and

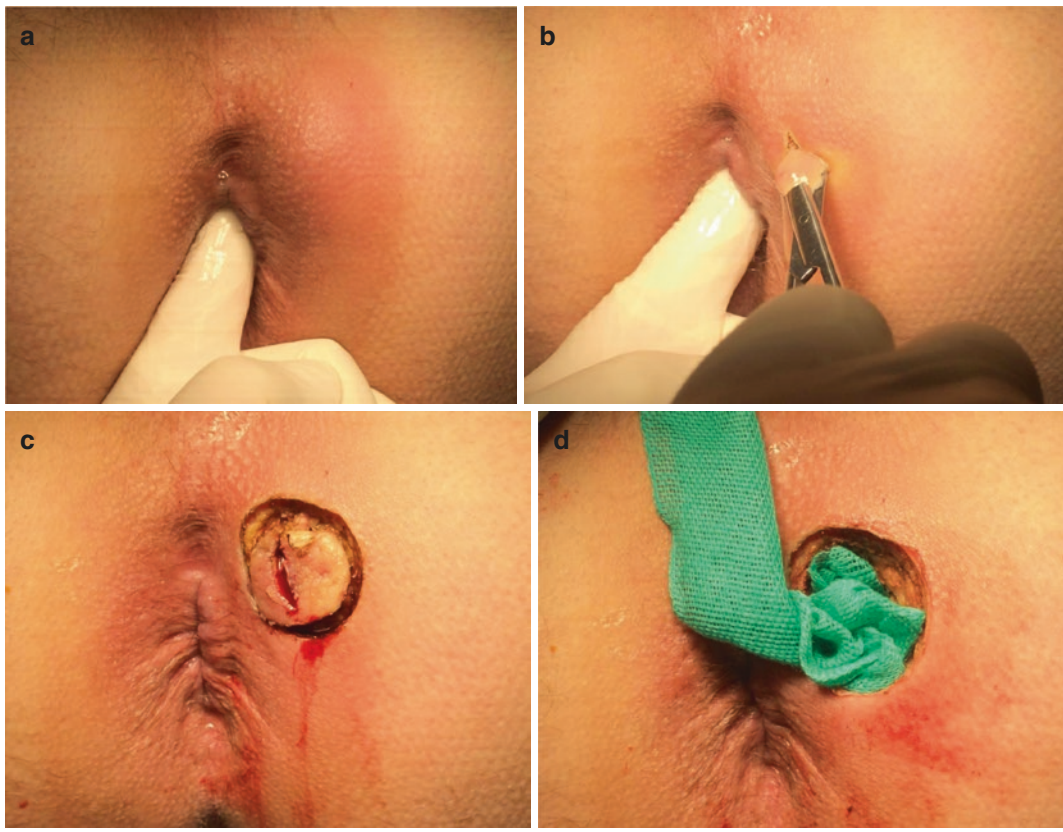


Fig. 6.6 (**a**–**d**) Treatment of an acute anal abscess with wide drainage

limited because of the narrow field between the rectum/anal canal and the lateral ischial bone, especially in men. For supralevatoric cavities, a narrow funnel at the pelvic floor muscles is a problem in achieving sufficient drainage to the perianal outside. For selected cases, placing a mushroom catheter or a vacuum-assisted closure system might be helpful.

6.8 Fistula Treatment

Fistula in ano is a principal indication for surgery. Spontaneous healing is extremely rare, and waiting risks an increase in inflammation, and in rare cases pelvic sepsis. The aim of surgery is healing of the fistula without disturbing continence. Operative measures must be based on the location and the course of the fistula, and therefore on its relation to the sphincter muscle [8]. The planning of treatment poses a problem: the operation should remove the fistula as completely as possible yet not compromise continence. On the other hand, an inflammatory reaction may also impair continence. Therefore every fistula operation requires balancing the risk of recurrence and continence dysfunction; however, there is no ideal method that optimally satisfies both requirements with regard to all fistula manifestations. This situation is rendered even more difficult by the impossibility of preoperatively evaluating the continence that is to be expected postoperatively; it cannot be measured and depends on many different variable factors. The surgeon thus has to adjust the operative technique to the particular fistula in ano. This decision considers as many risk factors for the development of postoperative incontinence as possible, for example, female sex, previous childbirth, traumata, previous fistula operations, or preexisting restraints on function or comorbidities. These are two almost contradicting demands, which is why different operations are applied, depending on the type of fistula. Here is a principle we recommend:

- Distal, simple fistulas should be layed open but as little sphincter as possible should be sacrificed.
- Proximal, complex fistulas usually are treated by extirpating the entire fistula and closing the internal opening.

But this strategy is based on the theoretical idea that fistulas are straightforward: they are simply small, narrow tubes. But in reality, in daily practice we have to realize that cannulas enlarge to create cavities of different sizes, affecting the choice of treatment (Fig. 6.7). Before definitve elimination of the fistula, cavities ought to be removed.

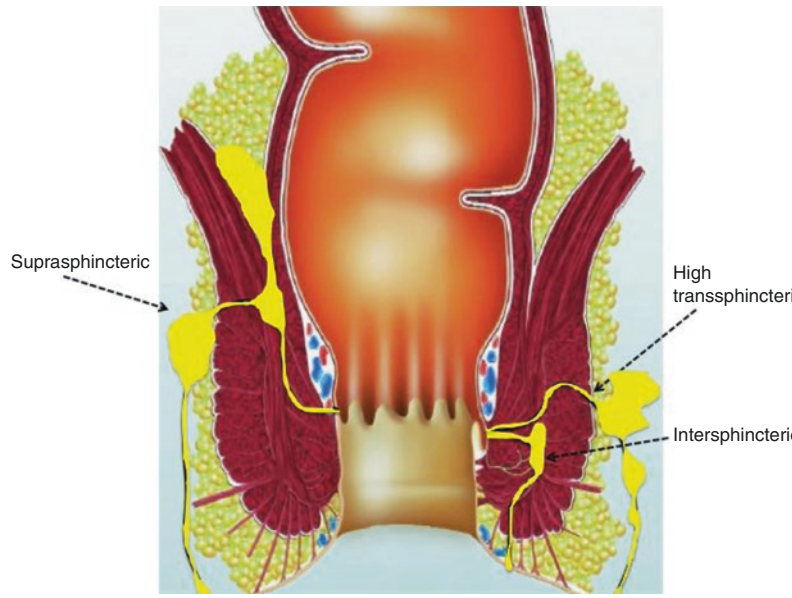


Fig. 6.7 Examples of different fistula extensions with additional cavities

6.9 Standard Treatment

6.9.1 Laying Open Fistulas (Fistulectomy, Fistulotomy)

Subanodermal, submucosal, subcutaneous, intersphincteric, and distal transsphincteric fistulas that comprise only a small part of the sphincter muscle can be split completely without affecting continence. This means that the fistula and its covering tissue, including the sphincter muscles, are cut through lengthwise to lay open the entire fistula (fistulotomy). With a fistulectomy, the fistular tissue at the back wall (dorsal part of the fistula´s canal) is also completely removed. The decision of how much of the sphincter can be cut through is influenced by the following factors: patient sex, previous operations, patient age, location of the fistula, preoperative sphincter function, and additional diseases of the intestinal tract. In general, the lesion requires 6–12 weeks to heal, depending on the size of the wound. The recurrence rate is less than 10%, whereas continence dysfunction depends on the degree of involvement of the sphincter. Previously up to two-thirds of the muscle mass was disected and accordingly up to 50% continence dysfunction was seen. Today, legal considerations generate a notably more reserved attitude toward the use of this technique.

6.9.2 Flap Procedures

Fistulas that run around essential parts of the sphincter (proximal transsphincteric, suprasphincteric, and extrasphincteric) can be extirpated and the internal opening closed using a flap procedure (Fig. 6.8a–d).

Technique:

- After total extirpation of the fistula tract, especially the cryptoglandular region, the sphincter muscle is sutured directly to close the internal opening. In this case no muscles are dissected. Sometimes sphincter defects originating from a prior inflammatory reaction could be reaired with this suture, too.
- To additionally stabilize this muscular suture, it is secured with a second layer of tissue, a *U*-shaped and proximally based advancement flap. In the majority of cases this flap consists of mucosa and a thin layer of internal sphincter. In other variations only mucosa or the full wall is used. Thus the internal fistula opening is closed with a double layer of sutured tissue.
- For these operations it is mandatory that local conditions are without inflammation – otherwise the chances of the fistula healing are reduced. That is why, in the acute state of inflammation, one would usually primarily drain with a seton and then close the fistula during a second session several weeks later.
- The skin lesion is left wide open to ensure secretion.

With flap procedures healing rates between 50% and 70% are achieved. In up to 40% of cases only minor continence disorders are reported, which hardly compromise quality of life (QoL) the patient.

6.10 Treatment Alternatives

6.10.1 Fistulectomy with Primary Sphincter Reconstruction

Fistulas are being dissected followed by immediate muscle reconstruction with increasing frequency [9–12] (Fig. 6.9a–d).

Technique:

- Several weeks after resolving acute inflammation by placing a seton, the whole length of the fistula tract is dissected and the distal parts of the sphincter muscle are separated. All granulation tissue within the tract is meticulously removed.
- The anoderm and sphincter may be mobilized laterally 2–3 mm.
- Afterward the sphincter muscle is directly readapted with single, full-size stitches.
- Finally, the anoderm is closed with single sutures and the para-anal incision is left open

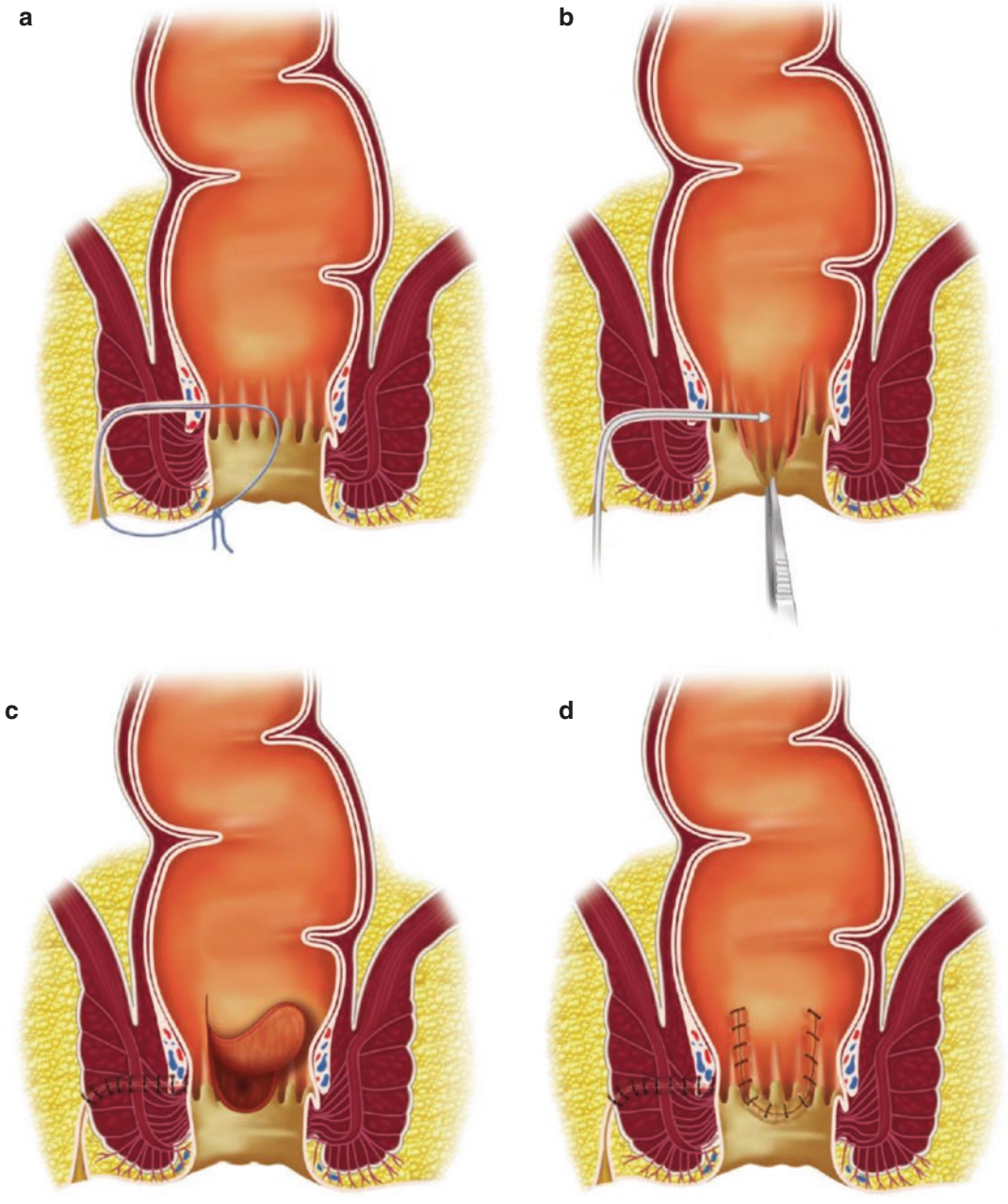


Fig. 6.8 (**a**–**d**) Flap procedure to close a transsphincteric fistula

for drainage. In the end the entire sphincter complex is anatomically restored.

Using these techniques, experiences to date report a healing rate of 80–95 %, but also a rate of muscle suture dehiscence of 5–10 %. A second operation resolves this muscle suture dehiscence in almost all cases. Apparently the healing rates are always somewhat higher when compared with other methods, and therefore this technique seems to have become an accepted standard, but further evaluation is necessary.

6.10.2 Fistula Plug

Originating in the USA, the anal fistula plug was introduced in Europe in 2006. With the help of a small cylinder made of pig collagen, the fistula canal is closed from the inside (similar to a cork closing a wine bottle). Contrary to other operative techniques, this is mostly done without extensive removal of fistula tissue, which makes the operation easier and results only in small postoperative external wounds. After euphoric initial successes reporting

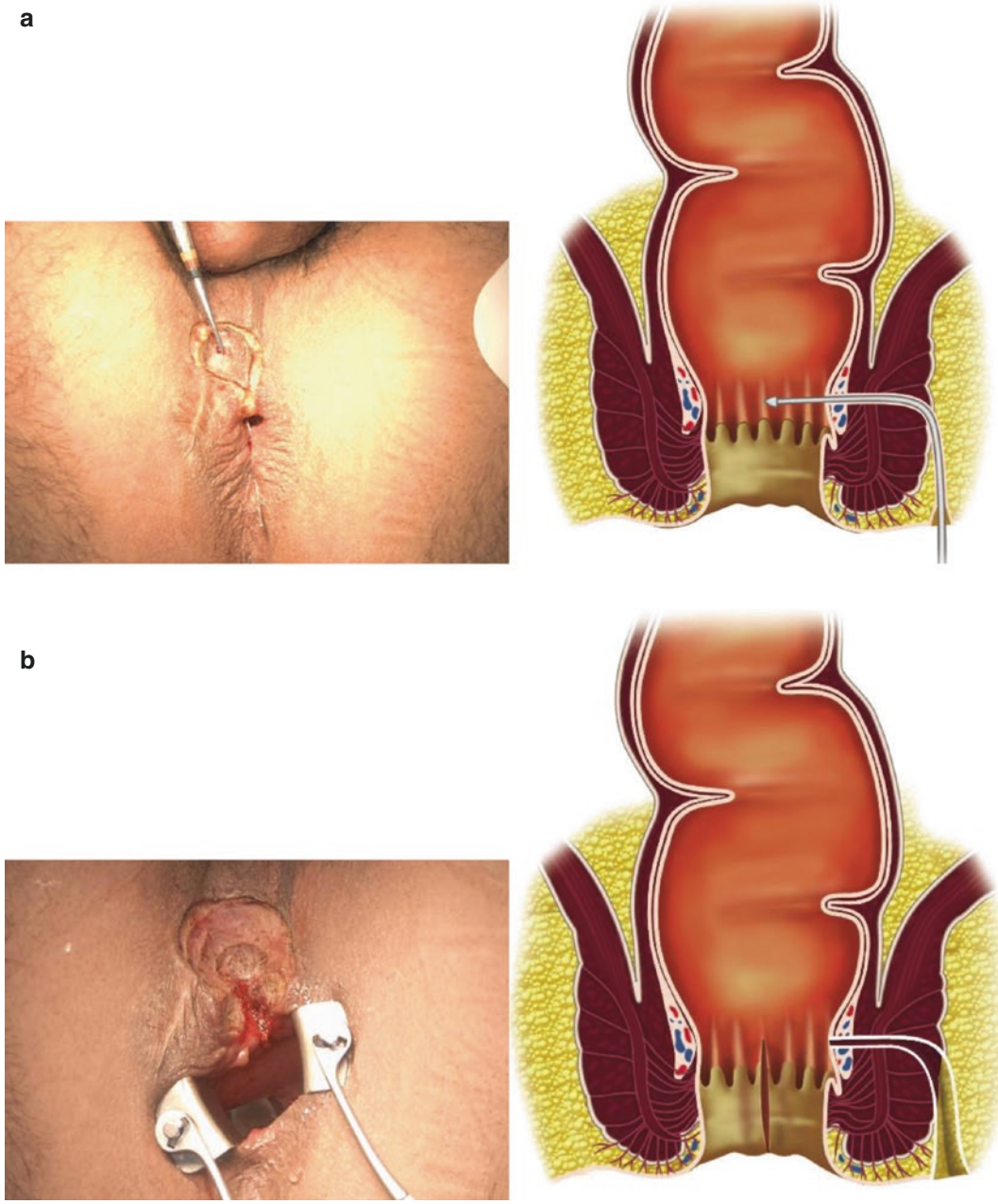


Fig. 6.9 (**a**–**d**) Fistulectomy with primary sphincter reconstruction (original and schematic drawing)

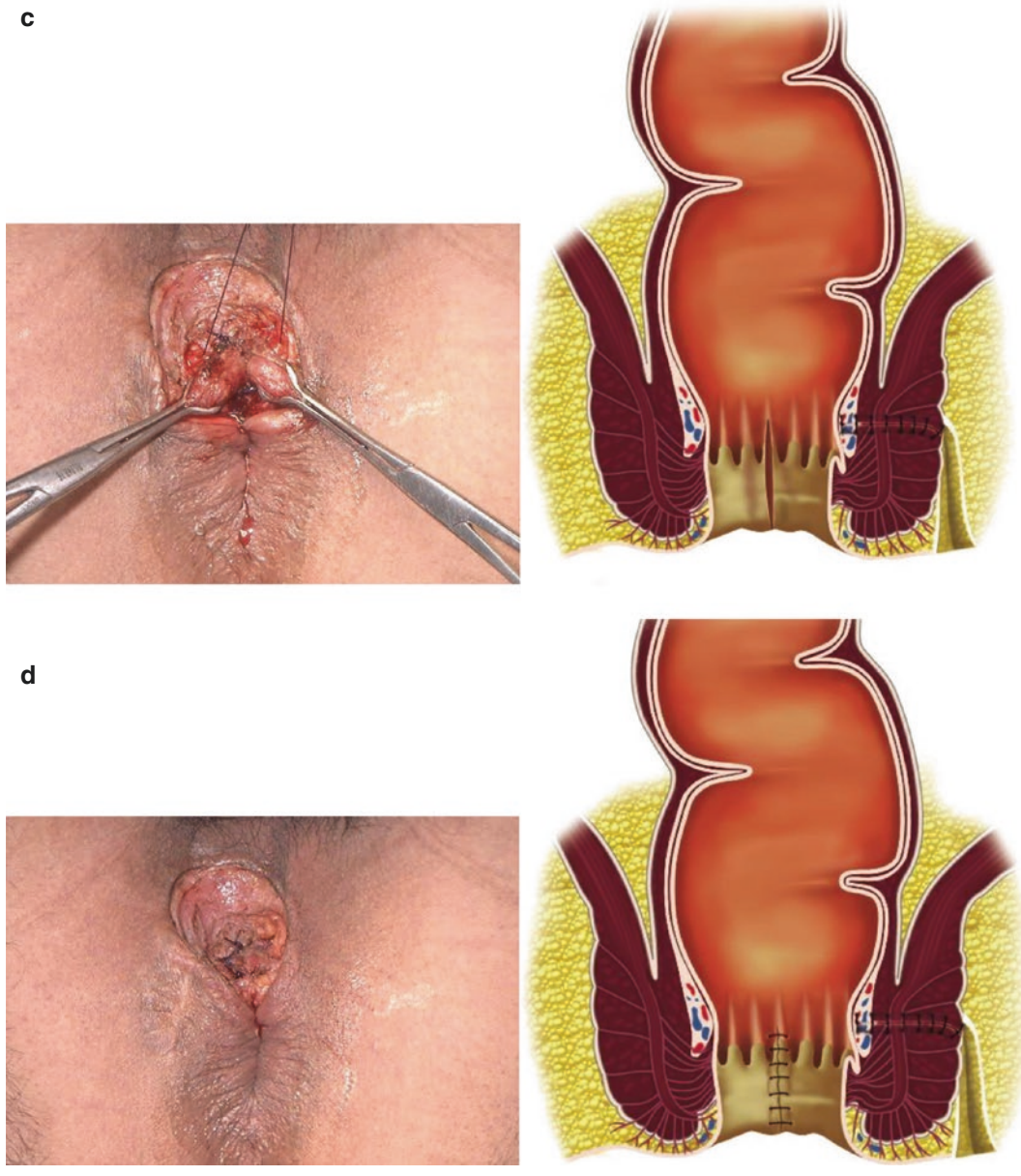


Fig. 6.9 (continued)

healing rates of more than 85 %, more recent publications report healing rates between 30 % and 70 % [13, 14]. Two prospective randomized studies of transsphincteric fistulas showed highly significantly worse results compared to the flap procedure: 87 % versus 20 % healing [15, 16].

Another plug is available. It is made of polyglycolic acid, similar to modern mesh and suture material, and it is fully resorbable within several weeks (Fig. 6.10a–e). However, studies of this plug are lacking, and therefore it is not possible to give a conclusive evaluation or treatment suggestion at this point [17–20].

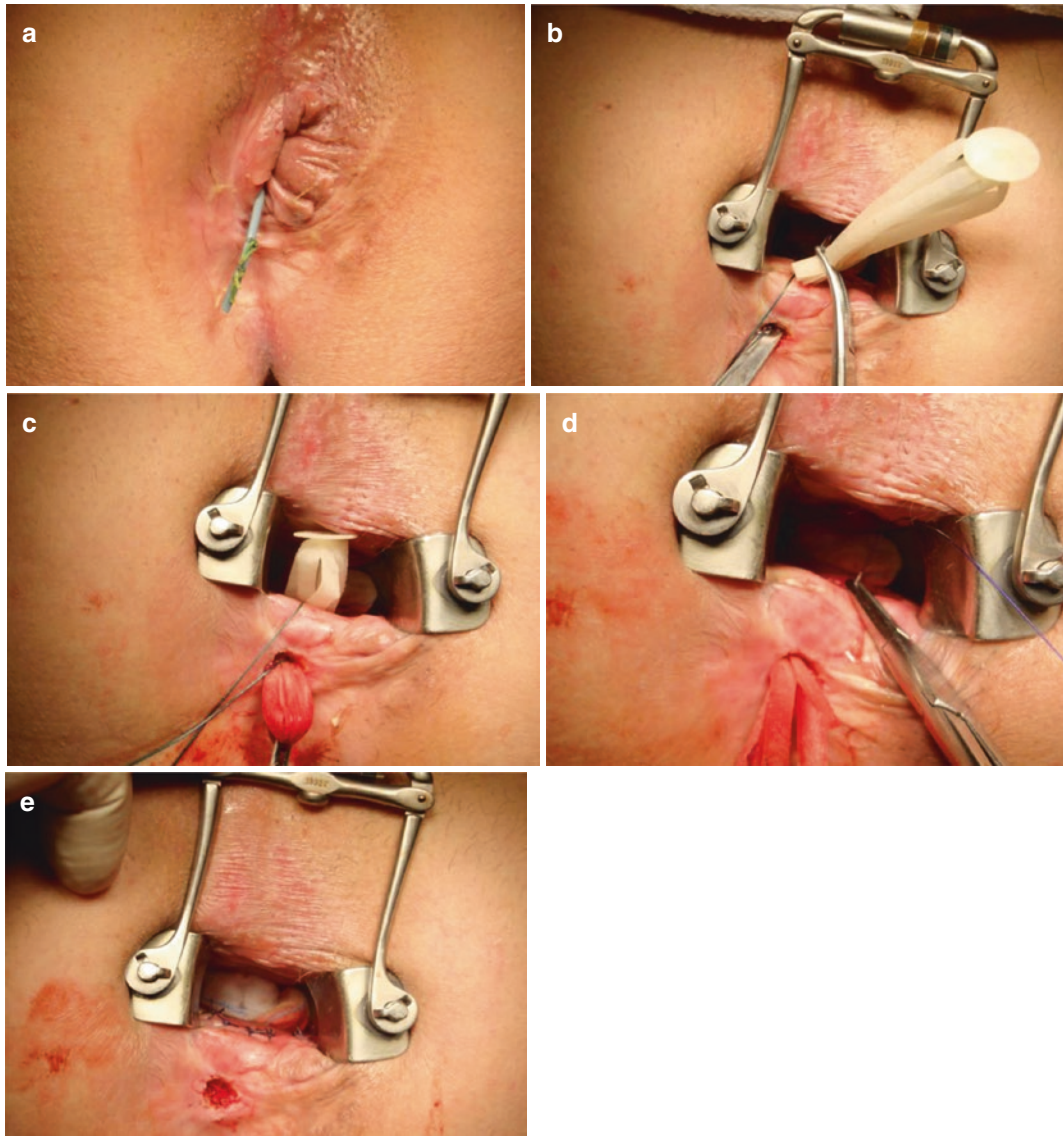


Fig. 6.10 (**a–e**) BIO-a plug procedure

6.10.3 LIFT Technique

A completely new operative technique that uses a new access route was recently introduced: ligation of the intersphincteric fistula tract (LIFT).

Technique:

- With a small incision at the intersphincteric groove, the intersphincteric plane is exposed and the fistula tract is located.
- The tract is encircled and cut through.
- Finally, the tract is closed on both sides with direct sutures or ligated (LIFT).

Experience has shown healing rates between 60 % and 80 %. There are no comparative studies, though, and therefore we might assume that there was a strong selection bias [21, 22]. Especially in the case of high fistulas, because they are often connected to larger cavities, there will be objections and the indication will be questioned.

6.10.4 Fistula Clip

A clip was recently developed for endoscopic use; using an endoscope it could be placed onto a perforation and a bleed (an "over-the-scope clip"). It was redesigned for use in the anal region as a fistula closure so that it can be placed with an applicator and without an endoscope. First experiences are positive, although they are reported in only very small cohorts [23].

6.10.5 Fibrin Glue

For 30 years the advise to treat perianal fistulas with fibrin glue has been given again and again. Whenever a new industrial preparation is on the market, new studies are published. Although some of them report success rates up to 90 %, this method has not yet been established– no doubt because at the same time there are reports with healing rates under 20 % [24]. The more recent autologous fibrin glues (autologous fibrin tissue adhesives) stand out for their particularly good tissue adhesion when compared with other glues that were previously used. Still, no convincing data are available.

6.10.6 Stem Cell Injection

As in nearly all fields of medicine, studies of the use of autologous stem cells have been carried out regarding anal fistulas. Stem cells are obtained from fat or muscle tissue, bred in vitro, and injected into and/or around the fistula. This is tedious, labor-intensive, and therefore extremely expensive. Healing rates have not been sufficiently evaluated.

6.11 Special Situations and Considerations

6.11.1 Long-Term Seton Drainage

Contrary to the above-mentioned short seton drainage for the treatment of acute inflammation of abscesses or fistulas, long-term seton drainage

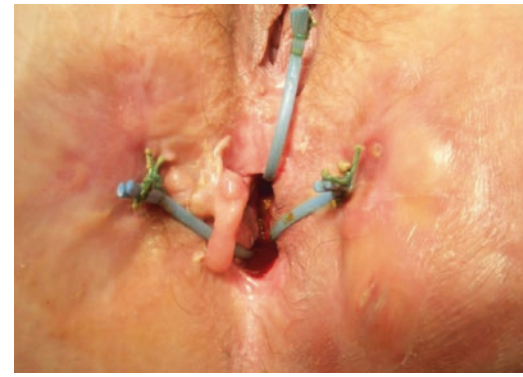


Fig. 6.11 Long-term seton in a patient with Crohn's disease

is an option for select perianal fistulas (Fig. 6.11). It is especially suitable when other techniques are declined by the patient or when previous operations render complete restoration impossible, which is often the case in Crohn's fistulas. Long-term seton drainage aims at achieving sufficient drainage of the complete fistula tract and cavities within several weeks or months. Therefore the fistula tracts – several, if necessary – are provided with nylon or silicone setons and the ends are fastened by or to a loose loop. This way the fistula can be permanently kept open, preventing an accumulation of secretion. Thereby a reduction in symptoms can be expected, even in the case of previously operated fistulas, without affecting the sphincter organ. The aim of this therapy is a preferably dry fistula tract without or with only minimal symptoms. Several authors define this achievement as "healed" because there are no symptoms – but the fistula is still there! This procedure is also recommended by health care systems that cannot offer all of the previously mentioned extensive operations to their patients.

6.11.2 Vaginal Fistula

Rectovaginal and anovaginal fistulas are special types of anorectal fistulas and are diagnosed and managed according to the principles above. The majority originate at the dentate line, running proximally and encircling the complete ventral sphincter. Because of their high transsphincteric

or suprasphincteric location, flap procedures are necessary for most. Because in this area the surrounding connective and muscular tissue of the septum rectovaginale is missing, success rates are not as good as for other anorectal fistulas.

In addition to the above techniques, other methods are applied in individual cases: closing the internal opening with sutures and additionally interpositioning muscles (e.g., musculus gracilis or musculus rectus abdominis) or fat tissue (bulbocavernosus-plasty).

6.11.3 Fistulas with Crohn's Disease

Among Crohn's-related anal fistulas, 75 % are, like other fistulas, of cryptoglandular origin and follow the course described above. By contrast, 25 % do not follow the anatomic structures and distructively pervade the tissue. Those fistulas are managed according to the above-mentioned strategies. Since repeat operations are necessary in many cases because of the high recurrence rate of the underlying disease, protecting the sphincter muscles is of particular interest. Before any fistula restoration/reconstruction, the systemic abdominal disease must be under control and the local conditions must be without infection. In the case of complex fistulas with recurrent episodes of inflammation, loose long-term seton drainage over months or years is usually tolerated well by patients and avoids or at least delays the necessity of a temporary or permanent stoma.

The following options – mainly no longer used –cannot be recommended for different reasons or are graded as being obsolete:

- Removal of the drainage seton after regression of inflammation without further measures. In this case healing almost never occurs and an oligosymptomatic tract usually remains, which in some studies is reported as "healing."
- Complete dissection of the fistula after primary insertion of a drainage seton, with the objective of fibrosing the fistula tract. Through this fibrosing, the sphincter muscle separation should be reduced after the second operation. Studies show that results after a straight transection (only one operation) are the same.
- Applying a cutting seton that dissects the sphincter step by step: a seton is placed around the fistula and then slowly pulled tighter at regular intervals until the seton cuts completely throught the sphincter (Hippocrates's technique). This method is tedious, painful, and equates to total transection. Consequently, severe continence problems are reported in over 50 % of cases.

Suggested Reading

1. Gordon P. Anorectal abscesses and fistula-in-ano. In: Gordon PH, Nivatvong S, editors. Principles and practice of surgery for the colon, rectum and anus. St. Louis: Quality Medical Publishing; 1999. p. 241–86.
2. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg. 1976;63:1–12.
3. Williams JG, Farrands PA, Williams AB, et al. The treatment of anal fistula: ACPGBI position statement. Colorectal Dis. 2007;9 Suppl 4:18–50.
4. Stelzner F. Die anorectalen fisteln. 3.Aufl, Coloproctology 23. Berlin: Springer; 2001. Coloproctology 23, 17–21, 2001.
5. Buchmann P, Alexander-Williams J. Classification of perianal Crohn's disease. Clin Gastroenterol. 1980;9:323–30.
6. Joos AK, Bussen D, Herold A. Abszess, Analfistel, Analfissur. Allg Viszeralchirurgie up2date 2009; 3(4):221–36.
7. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. Cochrane Database Syst Rev (Online). 2010:CD006319.
8. Ommer A, Herold A, Berg A, et al. S3-leitlinie: Kryptoglanduläre Analfistel. Coloproctology. 2011;33:295–324.
9. Christiansen J, Ronholt C. Treatment of recurrent high anal fistula by total excision and primary sphincter reconstruction. Int J Colorectal Dis. 1995;10:207–9.
10. Perez F, Arroyo A, Serrano P, Candela F, Perez MT, Calpena R. Prospective clinical and manometric study of fistulotomy with primary sphincter reconstruction in the management of recurrent complex fistula-in-ano. Colorectal Dis. 2006;21:522–6.
11. Ratto C, Litta F, Parello C, Zaccone F, Donisi L, De Simone V. Fistulotomy with end-to-end primary sphincteroplasty for anal fistula: results from a prospective study. Dis Colon Rectum. 2013;56:226–33.
12. Hirschburger M, Schwandner T, Hecker A, Kierer W, Weinel R, Padberg W. Fistulectomy with primary sphincter reconstruction in the treatment of high

transsphincteric anal fistulas. Int J Colorectal Dis. 2014;29:247–52.
13. Johnson E, Gaw J, Amstrong D, et al. Efficacy of anal fistula plug vs fibrin glue in closure of anorectal fistulas. Dis Colon Rectum. 2006;49:371–6.
14. Adamina M, Hoch JS, Burnstein MJ. To plug or not to plug: a cost-effectiveness analysis for complex anal fistula. Surgery. 2010;147:72–8.
15. Ortiz H, Marzo J, Ciga F, et al. Randomized clinical trial of anal fistula plug versus endorectal advancement flap for the treatment of high cryptoglandular fistula in ano. Br J Surg. 2009;96:608–12.
16. Van Koperen P, Hoore A, Wolthuis A, et al. Anal fistula plug for closure of difficult anorectal fistula: a prospective study. Dis Colon Rectum. 2007;50:2168–72.
17. Buchberg B, Masoomi H, Choi J, Bergman H, Mills S, Stamos M. A tale of two (Anal Fistula) plugs: is there a difference in short-term outcomes? Am Surg. 2010;76:1150–3.
18. Ommer A, Herold A, Joos A, Schmidt C, Weyand G, Bussen D. Gore BioA fistula plug in the treatment of high anal fistulas – initial results from a German multicenter-study. Ger Med Sci: GMS e-J. 2012;10:Doc13.
19. Heydari A, Maria Attinà G, Merolla E, Piccoli M, Fazlalizadeh R, Melotti G. Bioabsorbable synthetic plug in the treatment of anal fistulas. Dis Colon Rectum. 2013;56:774–9.
20. O'Riordan JM, Datta I, Johnston C, Baxter NN. A systematic review of the anal fistula plug for patients with Crohn's and non-Crohn's related fistula-in-Ano. Dis Colon Rectum. 2012;55:351–8.
21. Rojanasakul A. LIFT procedure: a simplified technique for Fistula-in-Ano. Tech Coloproctol. 2009;13:237–40.
22. Hong K, Kang S, Kalaskar S, Wexner S. Ligation of intersphincteric fistula tract (LIFT) to treat anal fistula: systematic review and meta-analysis. Tech Coloproctol. 2014;18:685–91.
23. Prosst RL, Joos AK, Ehni W, Bussen D, Herold A. Prospective pilot study of anorectal fistula closure with the OTSC proctology. Colorectal Dis. 2014;17:81–9.
24. Cintron J, Park J, Orsay C, et al. Repair of fistulas-in-ano using autologous fibrin tissue adhesive. Dis Colon Rectum. 1999;42:607–13.

Perianal Skin Conditions

7

Brian Kirby

Numerous dermatoses can affect the perianal skin. It is the author's opinion that these conditions are best managed by a dermatologist in conjunction with a colorectal surgeon/gastroenterologist. Pruritus is the predominant symptom of perianal dermatoses and is itself a nonspecific symptom [1, 2]. A full dermatological history is required, including the duration of symptoms, the severity of pruritus if present, the history of skin disease, and a history of colonic/rectal disease. Detailed knowledge of the treatment used for the condition is needed, including perianal hygiene habits. A complete medical and surgical history is required, with appropriate questioning about medications, foreign travel, and sexual history. A full skin examination is also necessary. This allows the detection of inflammatory dermatoses that may also affect the perianal skin. The majority of perianal skin conditions can be diagnosed clinically; a skin biopsy is rarely helpful. Inflammatory dermatoses often require a clinicopathological correlation. There is an old adage in dermatology: if a clinician does not have any idea of the diagnosis, then a histopathologist rarely will be able to help.

B. Kirby, MD, FRCPI
Department of Dermatology, St Vincent's University Hospital, Elm Park, Dublin, Ireland
e-mail: b.kirby@svuh.ie

7.1 Inflammatory Dermatoses

7.1.1 Perianal Dermatitis

This is the most common perianal dermatosis seen by dermatologists. It presents with perianal pruritus, which may be severe and occasionally painful. Sleep disturbance is common [1, 2]. Perianal dermatitis may be exacerbated by fecal leakage [1–3]. Patients may have a history of atopic dermatitis or contact dermatitis [4]. Clinical examination often reveals a diffuse erythema of the perianal skin with lichenification and often excoriations.

Internal hemorrhoids can exacerbate perianal dermatitis, but perianal pruritus has rarely been reported in conjunction with rectal polyps and carcinoma [5]. It is therefore recommended that all patients have a sigmoidoscopy, that internal hemorrhoids be appropriately treated, and any concurrent rectal pathology be reviewed.

All patients should be educated about appropriate hygiene. Most patients overclean the area with soaps, baby wipes, and/or excessive water. Soaps are an irritant that may exacerbate pruritus and inflammation. Patients with perianal dermatitis are at high risk for contact dermatitis from ingredients in soap, such as fragrances [4]. Wet wipes often contain preservatives such as methylisothiazolinone, which are potent contact sensitizers [4] and should be avoided. Patients should

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_7

be advised to clean the area once daily with only water and to dab the area dry avoiding excessive friction.

There is no evidence that dietary measures improve perianal dermatitis. Although it has been postulated that caffeine can reduce anal tone and perhaps increase anal leakage [7], there is no evidence that avoiding caffeine improves symptoms. This lack of evidence also applies to avoiding spicy foods, alcohol, and any other dietary manipulation. Given this lack of evidence, there seems to be little logic in recommending such interventions. Topical anesthetic preparations such as lidocaine or cinchocaine are ineffective for pruritus and should be avoided because there is a significant risk for contact sensitization [8].

There is evidence that chronic pruritus can result in reduced anal sphincter tone with microscopic leakage of fecal material after defecation [3]. Feces are highly irritant to the skin and may exacerbate skin that is already inflamed. The use of a barrier cream such as zinc oxide after a bowel movement may prevent fecal material from irritating the perianal skin. Mild-potency topical steroids such as 1 % hydrocortisone ointment may be effective, especially when applied at night before sleep. One percent hydrocortisone does not cause skin thinning, unlike more potent topical steroids.

It is recommended that all patients undergo contact allergy testing or patch testing. Up to 30 % of patients with perianal dermatitis have a relevant contact allergy [9]. Patients should be tested for several allergen series according to local protocols. In our centre, patients are tested to the British standard series, the fragrance series, the medicament series, the textile series, and their own leave-on products. The patches are applied on the back on Monday and read on Wednesday and Friday of the same week. Patch testing should only be done by medical and nursing staff who have appropriate training [4]. The most common allergens in patients with perianal dermatitis are fragrances, preservatives such as methylisothiazolinone [6], and sodium metabisulfite [10], which are used in wet wipes and medicaments such as cinchocaine [2, 8]. Contact allergens may include nail varnish [11], topical steroids [4], and textile dyes [12]. The majority of patients who are investigated and treated according to the above protocol achieve remission of their pruritus. Patients with more refractory disease may require more potent topical steroids, topical tacrolimus, and/or systemic antipruritic therapies.

7.2 Perianal Psoriasis

Psoriasis often affects the perianal skin. It can present with pruritus, bleeding, and/or perianal pain from fissuring. In these cases it is usually present in other areas, especially flexural areas including the genital region [13]. This psoriasis is treated with mild-potency topical steroids or topical tacrolimus 0.1 % ointment. Severe perianal psoriasis may require treatment with systemic antipsoriatic agents such as methotrexate, fumaric acid esters, or tumor necrosis factor (TNF)-α inhibitors [13].

7.3 Lichen Sclerosus

Lichen sclerosus is an immune-mediated skin condition that results in skin atrophy and genital scarring [14]. It is more common among women than men. It can affect the perianal skin, with resultant pruritus and pain, but is often asymptomatic. Upon clinical examination there are well-demarcated white/ivory plaques. Genital involvement is a given when the perianal skin is involved. Vulval lichen sclerosus can result in resorption of the clitoris, fusion of the labia minora, and urethral strictures. Long-standing lichen sclerosus can result in squamous cell carcinoma of the vulva and (rarely) perianal squamous cell carcinoma [9]. Skin histology reveals characteristic findings of epidermal atrophy, homogenization of collagen with the formation of a cell poor Grentz zone in the upper dermis, and dermal fibrosis. Lichen sclerosus is treated with superpotent topical steroids such as clobetasol propionate ointment. This is highly effective in managing pruritus and in improving the histological features of the disease [14].

7.4 Hidradenitis Suppurativa

Hidradenitis suppurativa is a disease characterized by the development of painful nodules and abscesses commonly affecting the axillae, submammary area, inguinal folds, perineum, and perianal area [15]. It is more common among women than men (3:1), smokers, and obese patients. There seems to be a genetic component in some patients; mutations of gamma secretase in familial hidradenitis suppurativa have been described [16]. This disease significantly disturbs quality of life. Follicular occlusion seems to be the earliest abnormality in the pathogenesis of hidradenitis suppurativa, with subsequent abscess formation leading to sinuses and scarring. Perianal hidradenitis may present in isolation with recurrent nodules, abscesses that may develop into painful sinuses, fistulae, and scarring. The abscesses tend to be sterile. There is an association with Crohn's disease [15]. Skin histology may be of benefit in cases of diagnostic doubt.

The treatment of hidradenitis suppurativa involves both medical and surgical input. Medical treatments include the combination of oral clindamycin and rifampicin at a dosage of 300 mg of each drug twice daily for 10 weeks. In one series, up to 80 % of patients achieved remission with this combination [15]. The main side effects of treatment are diarrhea and abnormal liver function test results. Oral tetracycline monotherapy and penicillins such as flucloxacillin seem to be ineffective. Topical clindamycin may be effective in some patients with mild disease. Intralesional triamcinolone has been reported as effective. Oral metformin and dapsone are used as second-line agents with moderate success. Inhibition of TNF-α with adalimumab has been demonstrated to be effective with 160 mg as a loading dose and 40 mg weekly. Over 40 % of patients achieve 50 % improvement [17]. Infliximab has also been reported as an effective therapy for hidradenitis at a dosage of 5 mg/kg every 4 or 8 weeks. [18].

The best long-term results have been reported with surgery. Incision and drainage of recurrent abscesses do not result in improvement, and almost 100 % recur [19]. Extensive excision of sinus tracts and fistulae offers the best hope for long-term remission. Excising sinus tracts with a Seton suture insertion delivers some success in patients with sinus tract disease.

The perianal skin is rarely affected in Crohn's disease. It may present with perianal abscesses, similar to hidradenitis suppurativa. It may be contiguous with lower-bowel Crohn's disease or associated with perineal fistulae, or be separate (so-called metastatic Crohn's disease). The treatment of cutaneous Crohn's disease is difficult. The best results have been achieved with topical superpotent and/or intralesional steroids in combination with TNF-α inhibition with adalimumab or infliximab [20]. Surgical excision is ineffective.

7.5 Infectious Processes

Pinworm infection in adults is rare and should be obvious to the patient. Dermatophyte infection affecting the perianal area alone is rare in immunocompetent patients. Patients usually have concomitant involvement of the crural folds (tinea cruris) and usually the feet (tinea pedis). Skin scrapings and fungal culture are useful in cases of diagnostic doubt. Treatment with topical steroids can alter the morphology of perianal dermatophyte infection (so-called tinea incognito). Micropustules often form, and diagnosis may be difficult for a nondermatologist. Dermatophyte infection is treated with topical antifungals such as terbinafine or miconazole. Oral antifungal treatments are rarely necessary.

Candida infections are common on perianal skin but usually involve other flexural areas such as the inguinal folds. Candidal infection is common in patients with diabetes, obese patients, and the immunocompromised. This infection is treated with topical anticandidal agents such as miconazole 2 % cream. Oral anticandidal agents may be needed in severe cases in immunocompromised patients.

Bacterial infection with streptococcus group D is usually a disease of childhood. It presents with perianal cellulitis and systemic upset [21].

Diagnostic is not difficult in the majority of cases, and the infection is treated with appropriate antibiotics according to local protocols.

7.6 Condylomata Acuminate (Anal Warts)

Human papillomavirus (HPV) infection has a predilection for skin in the genital and perianal areas and can cause condylomata acuminata [22]. Condylomata acuminata is usually a sexually transmitted disease that occurs especially in men who have sex with men (MSM), but skin-to-skin contact without sexual activity may also result in condylomata. Perianal HPV infection is common in smokers, the immunocompromised, patients with multiple sexual partners, and HIV-positive patients [22]. The incidence of perianal HPV infection is common, affecting 57 % of MSM who are HIV negative, and it is considerably higher in HIV-positive men. It is recommended that all patients with perianal condylomata have a full screen for sexually transmitted diseases [22]. In addition, women with perianal condylomata should be screened for vulval and cervical HPV infection. Perianal condylomata are difficult to treat. All treatment methods are only partially effective.

Topical podophyllin reduces mitotic activity in keratinocytes, resulting in cell death. Podophyllin 0.15 % is applied once daily for 3 consecutive days and then stopped for 4 days. This is continued for 4 weeks. Series have reported the efficacy of this approach in up to 62 % of patients. Recurrence rates are high and have been reported in up to 55 % of patients [22]. Podophyllin can cause significant skin irritation, and patients need to be instructed carefully in its use.

Imiquimod (Aldara) is approved for the treatment of genital warts and is effective for perianal condylomata. Imiquimod activates Toll-like receptors 7 and 8 in the skin. These receptors form part of the innate immune system. When activated they cause local immune upregulation, with increased activity of antigen-presenting cells and hence the activation of specific immunity, with local interferon release and increased cytotoxic T-cell activity against virally infected cells. Imiquimod 5 % cream applied three times weekly for up to 16 weeks is effective in up to 56 % of patients, with recurrence rates as low as 13 % reported [22]. Imiquimod 5 % cream can cause marked local irritation and pain. Systemic side effects caused by enhanced systemic inflammation are rare but have been reported. Cryotherapy is a cost-effective therapy for condylomata. Response rates up to 81 % have been reported. As with other modalities, relapse rates up to 30 % are common [22]. Surgical excision is painful and requires local, regional, or even general anesthesia. Response rates are similar to those for other modalities. Because HPV has a predilection for scarred or injured sites, surgical excision itself may promote HPV infection. This may explain relapse rates up to 50 % [22].

Vaccination against HPV offers hope that, in the future, HPV infection and therefore perianal warts and anal carcinoma will be significantly reduced or even eradicated. Gardasil is the first vaccine approved for the prevention of HPV infection. The majority of perianal warts are caused by HPV 6 and 11. Gardasil is a highly effective quadrivalent vaccine that protects against infection with HPV 6, 11, 16, and 18. In one study of more than 4,000 young men, Gardasil was effective in preventing perianal warts in over 90 % of cases [23]. HPV 16 and 18 cause cervical carcinoma and most anal cancers. The widespread use of this vaccine among young men and women seems to be the best strategy to eradicate perianal HPV infection.

7.7 Anal Intraepithelial Carcinoma and Anal Carcinoma

Anal carcinoma is rare and accounts for 2 % of all gastrointestinal cancers, but the incidence is increasing. It is more common among women than men. There is a clear association with HPV infection. Anal carcinoma is common in women with genital HPV pathology such as cervical intraepithelial neoplasia, patients with HIV,

patients receiving chronic immunosuppression, smokers, and MSM. The detailed treatment of anal carcinoma is reviewed in Chap. 27.

Extramammary Paget's disease may affect the perianal area and present as pruritus ani [24]. Paget's disease is an intraepithelial carcinoma that rarely becomes invasive. Paget's disease is diagnosed based on skin histology, where typical pagetoid cells are seen. Extramammary Paget's disease may be a marker of internal malignancy of the anal canal, colon, or prostate and even of breast carcinoma. The prevalence of an internal malignancy in extramammary Paget's disease is unclear, but associated rates of up to 12 % have been reported [24]. Extramammary Paget's disease is treated with excision of the affected area, with clear margins. Local recurrence is high. Mohs' micrographic surgery has been used with some success. Topical photodynamic therapy has been reported as successful in cases where surgery would result in a significant loss of function or unacceptable scarring [24].

7.8 Perianal Drug Eruptions

The perianal skin may be preferentially affected by drug eruptions. Systemic drug-related intertriginous and flexural exanthema (SDRIFE) is preferred to the term *baboon syndrome* for a constellation of symptoms and signs related to certain medications. Patients are affected in the flexural areas, and systemic upset is common. The most common drugs implicated in SDRIFE are β-lactam antibiotics, but numerous drugs have been reported [25].

7.9 Perianal Ulceration

Perianal ulceration is rare. The causes of perianal ulceration include inflammatory conditions such as pyoderma gangrenosum [26], drug-induced causes such as nicorandil-induced perianal ulceration [27], factitious causes such as dermatitis artefacta, neoplastic causes such as squamous cell carcinoma, and infectious causes. The majority of infectious causes occur in immunocompromised patients and include atypical fungal and mycobacterial infections and cytomegalovirus [28]. Perianal ulceration requires specialist dermatological input in conjunction with colorectal surgical expertise.

In summary, perianal skin problems are common. A logical approach to management offers the best possibility for treatment success. The long list of dermatological conditions that can cause pruritus ani mandates a multidisciplinary approach to the management of this condition.

References

1. Markell KW, Billingham RP. Pruritus ani: etiology and management. Surg Clin N Am. 2010;90:125–35.
2. Siddiqi S, Vijay V, Ward M, Mahendran R, Warren S. Pruritus ani. Ann R Coll Surg Engl. 2008;90:457–63.
3. Farouk R, Duthie GS, Pryde A, Bartolo DC. Abnormal transient internal sphincter relaxation in idiopathic pruritus ani: physiological evidence from ambulatory monitoring. Br J Surg. 1994;81:603–6.
4. Beck MH, Wilkinson SM. Contact dermatitis. In: Burns, Breathnach, Cox, Griffiths, editors. Rook textbook of dermatology. New Jersey: Wiley Blackwell; 2010. p. 1–106. Chp 26.
5. Zuccati G, Lotti T, Mastrolorenzo A, Rapaccini A, Tiradritti L. Pruritus ani. Dermatol Ther. 2005;18:355–62.
6. Higgins E, Kirby B, Rogers S, Collins P. Methylchloroisothiazolinone and methylisothiazolinone allergic contact dermatitis and the effect of patch test concentration. Dermatitis. 2013;24:73–6.
7. Smith LE, Henrichs D, McCullah RD. Prospective studies on the etiology and treatment of pruritus ani. Dis Colon Rectum. 1982;25:358–63.
8. Ramirez P, Sendagorta E, Floristan U, Feltes RA, Vidaurrazaga C. Allergic contact dermatitis from antihemorrhoidal ointments: concomitant sensitization to both amide and ester local anesthetics. Dermatitis. 2010;21:176–7.
9. González-Pérez R, Sánchez-Martínez L, Piqueres Zubiaurrre T, Urtaran Ibarzábal A, Soloeta Arechavala R. Patch testing in patients with perianal eczema. Actas Dermosifiliogr. 2014;105:694–8.
10. Ralph N, Verma S, Merry S, Lally A, Kirby B, Collins P. What is the relevance of contact allergy to sodium metabisulfite and which concentration of the allergen should we use? Dermatitis. 2015;26:162–5.
11. Lazarov A. Perianal contact dermatitis caused by nail lacquer allergy. Am J Contact Dermat. 1999;10:43–4.
12. Wentworth AB, Richardson DM, Davis MD. Patch testing with textile allergens: the mayo clinic experience. Dermatitis. 2012;23:269–74.

13. Omland SH, Gniadecki R. Psoriasis inversa: a separate identity or a variant of psoriasis vulgaris? Clin Dermatol. 2015;33:456–61.
14. Fistarol SK, Itin PH. Diagnosis and treatment of lichen sclerosus: an update. Am J Clin Dermatol. 2013;14:27–47.
15. Hughes R, Kelly G, Sweeny C, Lally A, Kirby B. The medical and laser management of hidradenitis suppurativa. Am J Clin Dermatol. 2015;16:111–23.
16. Pink AE, Simpson MA, Desai N, Trembath RC, Barker JN. γ-secretase mutations in hidradenitis suppurativa: new insights into disease pathogenesis. J Invest Dermatol. 2013;133:601–7.
17. Kimball AB, Kerdel F, Adams D, et al. Adalimumab for the treatment of moderate to severe hidradenitis suppurativa: a parallel randomized trial. Ann Intern Med. 2012;157:846–55.
18. Moriarty B, Jiyad Z, Creamer D. Four-weekly Infliximab in the treatment of severe hidradenitis suppurativa. Br J Dermatol. 2014;170:986–7.
19. Blok JL, Boersma M, Terra JB, et al. Surgery under general anaesthesia in severe hidradenitis suppurativa: a study of 363 primary operations in 113 patients. J Eur Acad Dermatol Venereol. 2015;29:1590–7.
20. Hagen JW, Swoger JM, Grandinetti LM. Cutaneous manifestations of Crohn disease. Dermatol Clin. 2015;33:417–31.
21. Block SL. Perianal dermatitis: much more than just a diaper rash. Pediatr Ann. 2013;42:12–4.
22. Leszczyszyn J, Łebski I, Łysenko L, Hirnle L, Gerber H. Anal warts (condylomata acuminata) – current issues and treatment modalities. Adv Clin Exp Med. 2014;23:307–11.
23. McCormack PL. Quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine (gardasil(®)): a review of its use in the prevention of premalignant anogenital lesions, cervical and anal cancers, and genital warts. Drugs. 2014;74:1253–83.
24. Mengjun B, Zheng-Qiang W, Tasleem MM. Extramammary Paget's disease of the perianal region: a review of the literature emphasizing management. Dermatol Surg. 2013;39:69–75.
25. Tan SC, Tan JW. Symmetrical drug-related intertriginous and flexural exanthema. Curr Opin Allergy Clin Immunol. 2011;11:313–8.
26. Burgess NA, Lari JL. Pyoderma gangrenosum with large circumferential perianal skin loss in a child. Br J Clin Pract. 1991;45:223–4.
27. Claeys A, Weber-Muller F, Trechot P, et al. Cutaneous, perivulvar and perianal ulcerations induced by Nicorandil. Br J Dermatol. 2006;155:494–6.
28. Ryan C, De Gascun CF, Powell C, et al. Cytomegalovirus-induced cutaneous vasculopathy and perianal ulceration. J Am Acad Dermatol. 2011;64:1216–8.

Pilonidal Disease

8

Peter Dawson

8.1 Introduction

In 1990 T.G. Allen Mersh wrote a seminal review in the *British Journal of Surgery* entitled "Pilonidal Sinus: Finding the Right Track for Treatment" [1]. Little has changed since that time, nor has knowledge significantly advanced in the understanding or treatment of this common condition, which affects 26 per 100,000 population [2]. This chapter presents an update and suggests where the future may lie in achieving a simple, effective strategy/algorithm for clinicians to follow in the treatment of this disease.

8.2 Etiology

The etiology of pilonidal disease (PD) (*pilus* = hair, *nidus* = nest) (Fig. 8.1) is unclear, although it is probably an acquired disease originating within a natal cleft follicle that becomes distended with keratin. The distended follicle becomes inflamed and obstructed as a result of edema, eventually rupturing into the subcutaneous fat. In addition to the midline pits, the characteristics of the early stages of PD are a result of marked hyperkeratosis of the enlarged hair follicle ostium. These features, together with moisture – especially in this area – make the skin susceptible to the penetration of shed hair shafts.

Work by Karydakis [3] with 6,000 patients suggests that loose hairs "impale" normal tissue inducing, a foreign body reaction. He devised a pathogenic formula involving three variables, namely, loose hair (*H*), force (*F*), and the vulnerability (*V*) of local skin and tissues. In this model the primary sinuses represent hair entry sites and secondary sinuses represent exit points, such that Pilonidal disease = $H \times F \times V^2$.

The most common site of occurrence is the sacrococcygeal region. Rarer sites include the interdigital cleft, the breast, and the umbilicus [4]. Not uncommonly (20 %), PD occurs with hidradenitis suppurativa (acne inversa) [5], sharing the same pathological process, that is, an occluding follicular hyperkeratosis followed by a dissecting cellulitis and the formation of draining sinuses (Fig. 8.2). In addition, friction between the buttocks may be responsible for sucking or sticking hairs into the pits. The stiffness of body hair and hair scales functioning as microbarbs facilitate the penetration of hair shafts deeper into the skin. Hair acts as a potent foreign body, causing a prolonged inflammatory reaction and the development of sinus tracts filled with granulated tissue and often

P. Dawson, MS, FRCS
West Middlesex and Chelsea and Westminster Hospitals, London, UK

Honorary Senior Lecturer Imperial College, London, UK
e-mail: peter.dawson@chelwest.nhs.uk

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_8

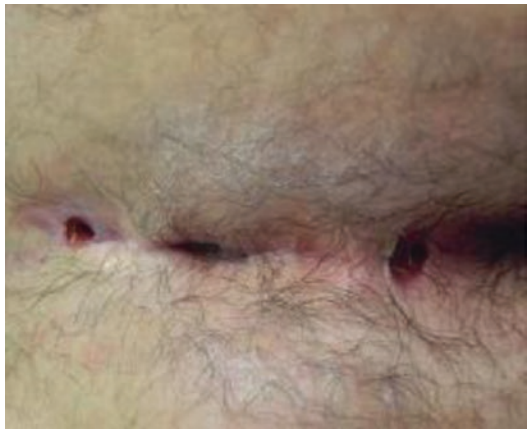


Fig. 8.1 Uncomplicated pilonidal sinus disease with multiple midline pits

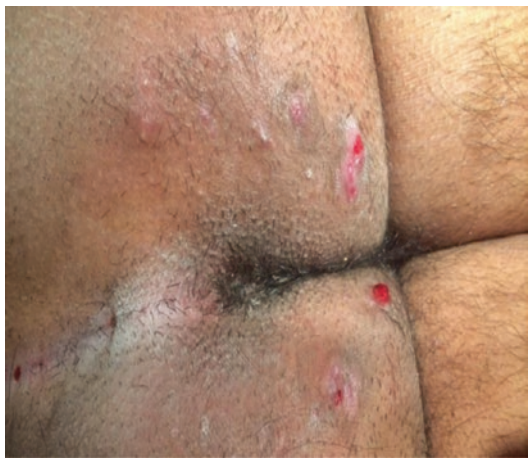


Fig. 8.2 Pilonidal sinus and hidradenitis suppurativa (acne inversa)

with masses of hair shafts. By this time these tracts are always at least partially lined by epithelium.

The risk factors for the development of symptomatic PD are listed in Table 8.1.

Table 8.1 Risk factors for pilonidal disease

A deep natal cleft [6]
Family history
Hirsute individuals
Young individuals
Obesity
Long-standing pressure or friction
Inadequate personal hygiene
Occupation ("Jeep disease") [7]

8.3 Incidence

PD most commonly occurs in the second and third decades of life, and it is twice as common among men than women. The incidence is highest among Caucasians. An estimated 1.1 % of male students and 0.11 % of female students suffer from PD [8]. PD is rare after the age of 40 years, suggesting an association with sex hormones, which can affect pilosebaceous glands.

8.4 Clinical Presentation and Diagnosis

PD is clinically diagnosed by visible single or a series of midline pits in the natal cleft that have the microscopic appearance of enlarged hair openings. Often these pits are minute, whereas others may contain a tuft of hairs. The clinical picture of a developing acute abscess maybe inconspicuous, presenting as a slight bulging of the skin in the natal cleft. Recurrent painful indurations in this area with purulent secretion followed by silent periods are characteristic of PD. These often settle down with antibiotic treatment but almost always recur later.

Chronic PD may reveal a lateral track in the upper parts of the buttocks filled with granulation tissue resembling pyogenic granuloma. The differential diagnosis may include fistula in ano, hidradenitis, and, rarely, perforating diverticular disease [9].

In selected cases computed tomography or magnetic resonance imaging (MRI) may be indicated. The latter is particularly useful to exclude fistula in ano or to clarify obscure presentations [10] (Fig. 8.3).

8.5 Therapy

The management of PD is variable, debateable, and occasionally difficult. The principles of treatment are eradication of the sinus tract and complete healing of the epidermis with no recurrence. Ideal treatment should be quick, allowing these

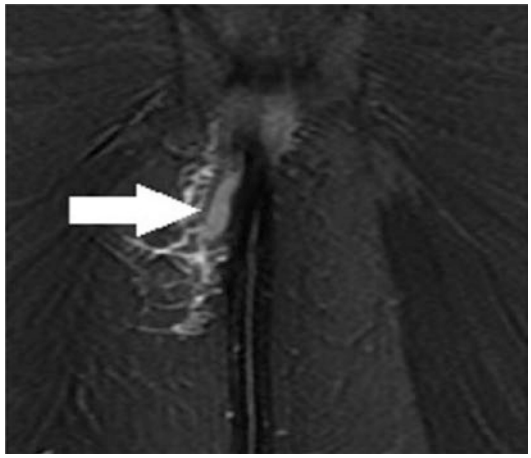


Fig. 8.3 Magnetic resonance imaging of a pilonidal sinus and track (*arrow*) (Courtesy of Dr. D. Blunt)

young patients to return early to normal activity and work, with minimal complication.

8.6 Nonoperative Treatment

Asymptomatic PD may be treated conservatively by meticulous hair control (shaving the natal cleft), improved hygiene, and mechanical removal of shed hairs [11]. Laser removal of hair in the natal cleft is increasingly popular [12]. Evidence that conservative treatment of symptomatic PD is effective is limited; therefore the mainstay of treatment is surgical. Antibiotics may be indicated in purulent stages of PD before surgery or in rare cases of systemic infection. Prophylactic use of antibiotics in the surgical treatment of PD remains unproven [13].

8.7 Surgical Treatment

Several techniques are described. Recurrence rates are variable with all procedures and may reach 20% or more. Postoperative professional wound care and hair control are important for optimal wound healing and are likely to play an important role in avoiding complications and recurrences. The main therapeutic goals are set out in Table 8.2.

Table 8.2 Therapeutic goals

Flatten the natal grove
Low rate of complications and recurrences
Minimal discomfort for the patient
Short healing and little time off work
Good cosmetic results
Suitable for a day-case operation

8.8 Pilonidal Abscess

Pilonidal abscess (which occurs in half of all cases of PD) should be drained or deroofed to provide optimal drainage. This rapidly alleviates symptoms and can control PD in the outpatient setting. General anesthesia allows curettage of the sinus in the same session and, together with removal of the pits, occasionally may heal PD, but recurrences often occur [1, 14].

8.9 Chronic Pilonidal Disease

8.9.1 Minimal Surgery

Brushing or phenolization of the track produces similar results to laying the track open [15]. While this technique may be useful, the lack of randomized studies results in weak evidence. Expert nursing, dressing, and careful shaving of the area are required and are often not freely available.

8.9.2 Open Surgery

Wide excision of all involved skin with shallow resection margins and open granulation remains a common surgical treatment for the majority of patients (Fig. 8.4). Short hospitalizations (approximately 2 days) often are unavoidable. Leaving the wound open results in longer healing periods and requires repeated visits by a community nurse with the associated costs of time and dressing. While the longer healing time is not an obstacle to patients' early return to work and social activities, it is a great inconvenience. Some wounds may take up to a year to heal and yet still recur. Shorter healing times can be achieved using the lay-open technique, modified with marsupialization [16]. The

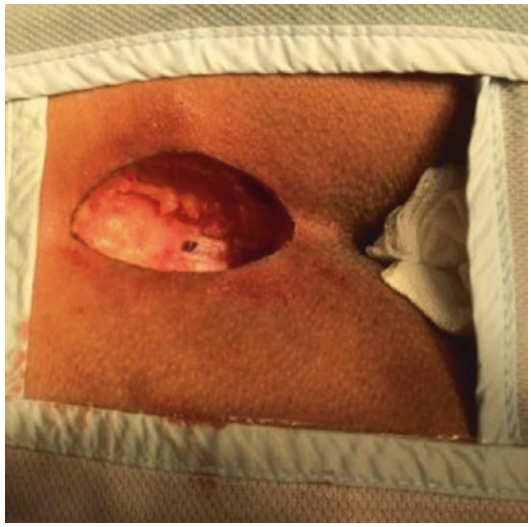


Fig. 8.4 Wide local excision

use of mobile vacuum-assisted closure therapy may facilitate healing by secondary intention.

8.9.3 Wound Closure Procedures

Wound closure methods offer the potential advantages of shorter stays, day-case procedures, quicker healing, and less time off work. The disadvantages are a higher rate of complications and recurrences with inferior cosmetic results when wound closure is achieved using flaps [17].

The following methods of wound closure are most used:

- Simple excision of the sinus complex with primary closure in the midline. This procedure is frequently complicated by wound breakdown caused by hematoma formation.
- Better results are reported for oblique and asymmetric excisions and closure techniques to minimize or to avoid midline sutures. The latter procedures can be combined with an advancement flap to facilitate wound closure and to create a flattened anal cleft [5].
- The Bascom I technique conservatively excises midline pits with hair and debris. The infected epithelialized pits are removed while the extent of the midline wound is minimized. Senapati et al. [18] reviewed 200 patients with a 90 % success rate at 1 year.

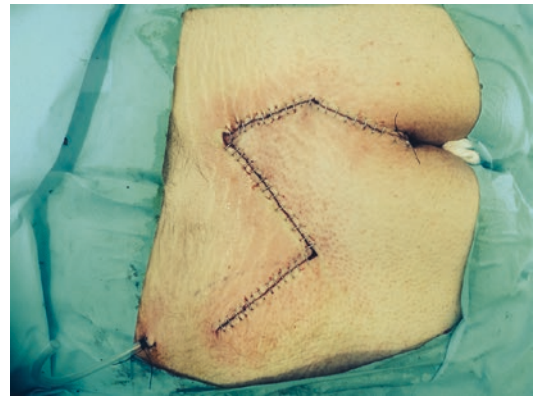


Fig. 8.5 Final appearance of a rhomboid excision and Limberg flap procedure (Kieninger G et al.)

- The Karyadakis technique is an advancing flap operation where a "semilateral" incision is made around the sinus down to the presacral fascia. The subcutaneous flap is mobilized and sutured to the opposite side, effectively placing the suture line away from the midline [5].
- A tension-free wound closure can be achieved by plastic flaps such as the Limberg flap (Fig. 8.5; also rotational, rhomboid advancement flaps and Z-plasty), but the goal to attenuate the natal groove is fulfilled only in the upper part; the lower part of the cleft remains deep, sometimes bulging under the flap, and recurrences are possible [19]. Flap techniques have a higher complication rate and the cosmetic results are often poor compared with the other techniques. Their use in female patients should be considered carefully. Further research is needed to compare flaps with off-midline repairs [20]. Therefore plastic flaps should be reserved for complicated cases, such as in the malignant transformation of PD or recurrent/extensive disease.
- Fibrin glue techniques are being increasingly used, although the recurrence rate remains at 20 % [21].

8.9.4 Complications of Surgery

Early bridging is not an uncommon complication in an open wound with secondary healing and is a result of inadequate wound packing. Wounds may fail to heal for unknown reasons, even under

optimal wound care conditions; however, many recurrences may be prevented by assiduous wound management.

Conclusions

Primary closure techniques provide for quicker healing but have higher recurrence rates compared with laying the wound open [17]. There are no differences in surgical site infection rates between the two methods. Off-midline closure has better healing rates compared with midline closure, whereas fewer recurrences occur with open healing compared with midline closure.

Systematic reviews of each surgical treatment of PD are prone to bias because blinding patients, surgeons, and assessors is not possible. Many minor small variations in technique occur, adding to the great divergence of published results and in the understanding of the pathogenesis of PD. In addition, many trials of treatment are small and at risk of failing to detect clinically relevant differences. Standardizing each method, which should be done only by well-trained operators, will further optimize results. Meanwhile, the literature suggests a trend away from wide excision and leaving wounds to heal by secondary intention toward less invasive procedures [22].

References

1. Allen MT. Pilonidal sinus: finding the right track for treatment. Br J Surg. 1990;77:123–32.
2. Sondenaa K, Andersen E, Nesvik I, Soreide JA. Patient characteristics and symptoms in chronic pilonidal sinus disease. Int J Colorectal Dis. 1995;10:39–42.
3. Karydakis GE. Easy and successful treatment of pilonidal sinus after explanation of its causative process. Aust N Z J Surg. 1992;62:285–9.
4. Ballas K, Psarras K, Rafailidis S, Konstantinidis H, Sakadamis A. Interdigital pilonidal sinus in a hairdresser. J Hand Surg. 2006;31:290–1.
5. Nelson JM, Billingham RP. Pilonidal disease and hidradenitis suppurativa. In: Wolff BC, Fleshman JW, Beck DE, Pemberton JH, Wexner SD, editors. The ASCRS textbook of colon and rectal surgery. New York: Springer; 2007. p. 228–39.
6. Akinci OF, Kurt M, Terzi A, Subasi IE, Akbilgic O. Natal cleft deeper in patients with pilonidal disease: implications for choice of surgical procedure. Dis Colon Rectum. 2009;52:1000–2.
7. Buie L. Jeep disease. South Med J. 1944;37:103–9.
8. Dwight RW, Maloy JK. Pilonidal sinus – experience with 449 cases. N Engl J Med. 1953;249:926–30.
9. Evans J, Lake B, Harris P. No hair? Beware. An unusual presentation of fistulating diverticular disease. Colorectal Dis. 2012;14:206–7.
10. Taylor SA, Halligan S, Bartram CI. Pilonidal sinus disease: MRI imaging distinction from fistula in ano. Radiology. 2003;226:662–7.
11. Armstrong JH, Barcia PJ. Pilonidal sinus disease. The conservative approach. Arch Surg. 1994;129:914–7.
12. Odili J, Gault D. Laser depilation of the natal cleft – an aid to healing the pilonidal sinus. Ann R Coll Surg Engl. 2002;84:29–32.
13. Khanna A, Rombeau JL. Pilonidal disease. Clin Colon Rectal Surg. 2011;24:46–53.
14. McClaren CA. Partial closure and other techniques in pilonidal surgery: an assessment of 157 cases. Br J Surg. 1984;71:561–2.
15. Kayaalp C, Aydin C. Review of phenol treatment in sacrococcygeal pilonidal disease. Tech Coloproctol. 2009;13:189–93.
16. Karakayali F, Karagulle E, Karabulut Z, Oksuz E, Moray G, Haberal M. Unroofing and marsupialization vs rhomboid excision and Limberg flap in pilonidal disease: a prospective, randomized, clinical trial. Dis Colon Rectum. 2009;52:496–502.
17. McCallam IJ, King PM, Bruce J. Healing by primary closure versus open healing after surgery for pilonidal sinus: systematic review and meta-analysis. BMJ. 2008;336:868–71.
18. Senapati A, Cripps NP, Thompson MR. Bascoms operation in the day – surgical management of symptomatic pilonidal sinus. Br J Surg. 2000; 87:1067–70.
19. Mentes O, Bagci M, Bilgin T, Ozgul O. Limberg flap procedure for pilonidal sinus disease; results of 353 patients. Langenbecks Arch Surg. 2008;393:185–9.
20. Horwood J, Hanratty D, Chandran P, Billings P. Primary closure or rhomboid excision and Limberg flap for the management of primary sacrococcygeal pilonidal disease? A meta-analysis of randomized controlled trials. Colorectal Dis. 2012;14:143–51.
21. Handmer M. Sticking to the facts: a systematic review of fibrin glue for pilonidal disease. ANZ J Surg. 2012;82:221–4.
22. Enriquez-Navascues JM, Emparanza JI, Alkorta M, Placer C. Meta-analysis of randomized controlled trials comparing different techniques with primary closure for chronic pilonidal sinus. Tech Coloproctol. 2014;18:863–72. Epub ahead of print.

Fecal Incontinence

9

Klaus E. Matzel

9.1 Introduction

Fecal incontinence (FI) – also called bowel or anal incontinence – is the inability to control bowel movements, resulting in involuntary loss of solid or liquid stool. It can range from occasional leakage while passing gas to complete loss of bowel control. It is a symptom, and its causes are manifold: FI can be directly related to the anorectal continence organ itself or can be secondary to various pathological conditions. It is debilitating both physically and psychosocially [1]. The majority of affected individuals, many of whom prefer the term "accidental bowel leakage" [2], hesitate to seek help [1, 3], and thus FI remains largely undiagnosed.

9.2 Etiology

In brief, FI is the result of the integrated functioning of various organs and their peripheral and central nerve supplies. It is maintained by coordinated, synergistic, organic functioning of the reservoir system of the rectum (the colon in part), the outlet resistance of the sphincteric complex, and the sensory lining of the anal canal. Their interaction is attained by a convergence of somatomotor, somatosensory, and autonomic innervation. A functional deficit resulting in FI can be caused by trauma, deficiency, or pathological alterations of any of the components of the organ system or organic and functional factors that ensure adequate bowel control: stool consistency, colonic motility, rectal capacity and compliance, intact neural pathways, anal sphincter and pelvic floor function, and anorectal sensation. Frequently, however, a functional deficit of a single component of this complex system is compensated for by other components. Because FI is often caused by multiple factors, the relative contribution of a single morphological aspect or function may be impossible to ascertain. This adds to the complexity of management.

When FI occurs secondary to an underlying disease or disorder, treatment should be directed to the primary disease. This chapter focuses on incontinence owing to disorders primarily related to the anorectal continence organ.

9.3 Incidence

The true prevalence of FI is unknown. Approximately 2 % of the general population suffers from the inability to control bowel emptying [4]. The problem increases with age: up to 11 % of men and 26 % of women report incontinence after age 50 [5], reaching 40 % in nursing home

K.E. Matzel, MD, PhD
Chirurgische Klinik, Universität Erlangen,
Krankenhausstr.12., 91054 Erlangen, Germany
e-mail: Klaus.Matzel@uk-erlangen.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_9

patients, in whom urinary incontinence is frequently concomitant [6]. The latter patient population is mostly treated by conservative means.

With better diagnostic methods, the understanding of the physiology and pathophysiology of the various components of the anorectal continence organ has recently improved. Now not only the sphincter complex is considered a potential cause of fecal incontinence; reservoir function can be altered by various factors such as operative intervention, Crohn's disease, ulcerative colitis, radiation, irritable bowel syndrome, and internal rectal prolapse [7]. These can be addressed therapeutically with surgical replacement after resection or refixation in cases of rectal prolapse, but most surgical procedures for FI aim to improve, augment, or substitute sphincter function. Trauma to the sphincter complex remains the most common cause of uncontrollable loss of bowel content.

9.4 Classification

Continence is defined as the ability to control bowel content, to discriminate feces from gas, and to empty the bowel at will. The simplest, most often used, rather pragmatic classification distinguishes three grades of FI:

- Incontinence 1: inability to retain gas
- Incontinence 2: inability to retain liquid stool
- Incontinence 3: inability to retain solid stool

This numeric grading system may seem to suggest that the severity of FI can be quantified, but this is not the case. Patients report FI of liquid stool to be more bothersome than FI of solid stool.

Another classification describes the clinical presentation of FI and distinguishes between the inability to actively postpone the urge to empty stool (urge incontinence) and the unconscious loss of stool (passive incontinence). Both can be due to various underlying pathologies such as urge incontinence to external anal sphincter weakness, proctitis, or rectal carcinoma; passive incontinence can be caused by internal anal sphincter disorders, loss of sensory function, and keyhole deformation after anal surgery. Overlap of both classifications can occur.

Because FI is usually acquired, determining the underlying cause is often used to classify FI and to decide on further diagnostic examination and the therapeutic pathway.

9.4.1 Overflow Incontinence

Fecal impaction is a major cause of overflow FI among the elderly frail population. Diagnosis is easy using digital examination. Treatment aims to clear the bowel and avoid recurrence.

9.4.2 Anal Sphincter Lesion

The most common cause of FI in women is obstetric trauma. After vaginal delivery, up to 10 % of primiparous women have a clinically recognized sphincter disruption; the incidence of occult injuries that do not cause immediate postpartum incontinence and are diagnosed sonographically can be as high as 35 % [8]. Episiotomy is not consistently protective against sphincter injury. The incidence is higher among multiparous women and after instrument-assisted delivery [9, 10]. Anorectal surgical procedures such as hemorrhoidectomy and fistulotomy can cause direct trauma to the anal sphincters. The subsequent FI can be due to a loss of the normal anal cushions, resulting in sensory impairment in the anal canal, or due to muscular or neural trauma. Risk factors for FI after fistula-in-ano surgery include high or complex fistulae. An rate of FI up to 20 % has rendered obsolete manual anal dilatation for the treatment of anal fissure.

Sphincter trauma can also arise after major resections, such as low anterior resection with coloanal anastomosis. Under these circumstances, FI is often associated with evacuation disorders, fecal urgency, and pain, representing the so-called low anterior resection syndrome [11]. The reduction in reservoir capacity and the disruption of intramural neural pathways contribute. Function is also frequently adversely affected by chemotherapy or radiation. Further traumatic causes of FI include trauma to the perineum or

pelvis, such as pelvic fractures after traffic accidents, impalement injuries, or sexual assault.

9.4.3 Neurogenic Fecal Incontinence

Systemic and localized neurologic dysfunction, as in multiple sclerosis, muscular dystrophy, and congenital myelomeningocele (spina bifida), can cause incontinence that is frequently combined with constipation/evacuation problems [1].

9.4.4 Idiopathic Fecal Incontinence

The term *idiopathic incontinence* is commonly used if the precise etiology of FI remains unclear. This condition often presents with signs of pudendal neuropathy [12], low squeeze pressures, decreased anal canal sensation, and perineal descent, indicating a potentially underlying neurogenic cause.

9.5 Diagnosis

The diagnosis of FI is based on a standard anorectal examination (which excludes pathologic conditions that may result in secondary FI) and a focused history that includes stool frequency, urge symptoms, incontinence for gas, liquid stool, or solid stool, difficulties passing stool, which requires digital help, and day- and time-dependence of symptoms. Bowel habit diaries, standardized questionnaires, and general and disease-specific quality-of-life scores help to document symptoms in detail and to quantify the extent and severity of the disorder and its impact on quality of life (the last of which also affects decision making). The same instruments are used to monitor the clinical efficacy of interventions.

9.5.1 History

Clinical assessment starts with a detailed history, which can be complex since the causes of FI are manifold. A structured approach is advisable. In women, an obstetric history is mandatory (including the number of pregnancies, mode of delivery, type of presentation and birth weight), as is querying about urinary incontinence. Hormonal status can also be of interest. In men, a history of anal surgery is particularly important: in up to 25 % iatrogenic sphincter injury can be the cause of FI [13].

The simple clincial distinction between urge and passive incontinence may be helpful to suggest an underlying functional deficit and to guide further diagnosis. However, a simple correlation of either presentation with a single physiological function (external vs. internal sphincter weakness) is an oversimplification because of the complex interaction of various organs and their functions. Indeed, symptoms may overlap. FI may not even be the only clinical symptom. It can present in combination with obstructed defecation, representing the clinical sequelae of posterior compartment prolapse syndrome [7].

Standardized scoring systems are useful to quantify the frequency and severity of incontinence episodes and can provide a semiobjective assessment before and during treatment. The Cleveland Clinic incontinence score [14] and the St. Marks incontinence score [15] have the broadest acceptance. Bristol stool charts can be helpful to assess stool consistency on a seven-point scale from hard to liquid.

The perception of FI varies enormously among individuals; the correlation between symptom severity and quality of life is not linear. Assessment of quality of life is therefore essential, and both disease-specific and unspecific (e.g., 36-item Short Form) scores are commonly used. The disease-specific Fecal Incontinence Quality of Life instrument attempts to measure impairment in four different domains (lifestyle, coping and behavior, depression, and embarrassment) related to “accidental bowel leakage” [16].

9.5.2 Inspection and Palpation

The anal sphincter should be examined in a dynamic way: at rest, during voluntary contraction, and while pushing (Valsalva maneuver). Simple inspection can detect distinct alterations such as deformities, muscular defects, scars, and altered

skin appearance (skin excoriation can suggest long-term seepage of stool). Inspection of the pelvic floor during squeeze and push provides signs of a descending perineum, perineocele, less obvious muscle defects, and possible coexisting urological or gynecological disorders.

Digital examination of the pelvic floor and sphincters at rest and during active contraction and the Valsalva maneuver provides a first impression of resting and squeeze pressure, sphincter defects, length of the anal canal, rectocele, intussusception, and scarring.

The skin-prick test (touching/scratching the anal and perianal skin) and subsequent reflex contraction of the anal sphincter (anocutaneous reflex) can serve as a basic neurological investigation to check cutaneous sensibility, motor function, and afferent and efferent innervation.

In some patients, history, inspection, and palpation provide sufficient diagnostic information to dictate therapy; for example, postpartum incontinence caused by a clearly visible defect consequent to sphincter laceration may be treated by surgery, with a limited need for further diagnostics.

9.5.3 Proctoscopy and Rigid Sigmoidoscopy (Rectoscopy)

The visual evaluation of the internal aspects of the anal canal and the rectum by proctoscopy and rigid sigmoidoscopy (rectoscopy) serves to identify causes of primary incontinence and to exclude potential causes of secondary incontinence, such as inflammatory diseases, tumors, intussusception, internal mucosal prolapses, and limited rectal extension after air inflation.

9.5.4 Endoanal Ultrasound/ Magnetic Resonance Imaging

Endoanal ultrasound (EAUS) is the procedure of choice in patients with suspected sphincter injury. It is relatively easy to perform and, with experience, approaches 100 % sensitivity and specificity in identifying internal and external sphincter defects [17]. Morphologic findings do not necessarily correlate with clinical presentation: in a study of 335 patients with FI, 115 continent patients, and 18 asymptomatic female volunteers, sphincter defects were detected by EAUS in 65 %, 43 %, and 22 %, respectively [18].

EAUS assesses the thickness and structural integrity of the external and internal sphincter muscles (Fig. 9.1), rectal mucosa, rectal wall, puborectalis muscle, and adjacent anatomic structures such as the prostate, vagina, and bladder. The internal and external anal sphincters and puborectalis sling can be demonstrated in the longitudinal and horizontal planes. Also,

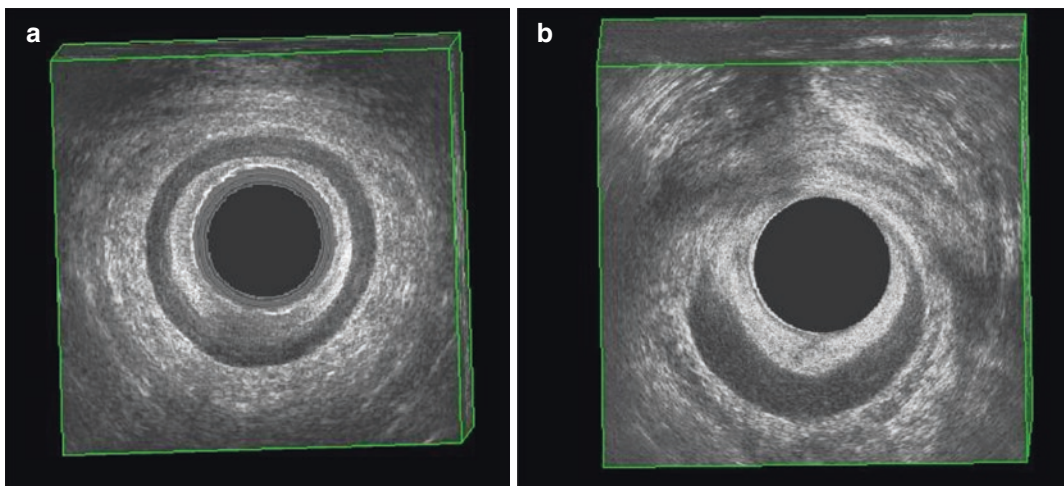


Fig. 9.1 Endoanal ultrasound showing intact internal and external sphincters (**a**) and lesions of the internal and external sphincters (**b**) (Courtesy G. Santoro; Treviso)

potential causes of secondary incontinence disorders (e.g., fistula tracts) and concomitant disorders (e.g., small abscesses) can be detected. Comparative examinations have confirmed the excellent correlation of EAUS with intraoperative findings.

The anatomy and its potential defects can also be explored by magnetic resonance imaging (MRI). Whereas EAUS is widely available, relatively easy to perform, and considered an essential part of the initial diagnostic workup, MRI has limited availability and is considered part of an advanced diagnostic workup. Both imaging techniques help to differentiate muscular lesions from other causes.

9.5.5 Anorectal Physiology

Anorectal physiology studies may help to better define the dysfunctional component of the continence-maintaining function. They are essential to provide an objective assessment of anal sphincter pressures, rectal sensation, rectoanal reflexes, and rectal compliance, some of which may guide management [19]. However some of the procedures are operator-dependent, the findings do not consistently correlate with symptom severity, and their value in decision making is limited and increasingly debated, although findings may help to monitor functional changes.

9.5.6 Anorectal Manometry

Anorectal manometry can assess and quantify muscular function of the smooth-muscle internal anal sphincter (resting pressure, length of the pressure zone) and the striated-muscle external anal sphincter (squeeze pressure), perception of rectal filling and distension (first sensation, urge to pass stool, maximal tolerable volume), compliance of the rectal reservoir, and the reflexive interaction of the rectum and anal sphincter (rectoanal inhibitory reflex). Even though the method is simple, techniques vary (water-perfused catheters, solid-state catheters, stationary pull-through, mechanical pull-through), and thus findings in different settings should be compared with caution. The normal values used by the particular lab must be considered.

9.5.7 Neurological Examination

Electromyographic recording of the striated muscles of the external anal sphincter and the pelvic floor differentiates muscular from neurogenic deficits and estimates the extent of reinnervation and denervation. It is rarely used for sphincter mapping because EAUS offers excellent access and painless imaging of sphincter morphology.

Pudendal nerve terminal motor latency (PNTML), which measures the conductance of the peripheral nerves by stimulating and recording evoked muscular contractions, helps to identify peripheral lesions of the pudendal nerve. Unilateral lesions can be distinguished from bilateral ones. Although normal values for conduction velocity are defined, their relation to clinical findings is weak, the technique is operator-dependent, and patient discomfort is noteworthy. Thus the role of PNTML in the assessment of FI remains controversial, and questions of the relevance of its findings have recently caused it to be used less.

9.5.8 Sensibility Testing

Anorectal sensitivity is often disturbed in neurogenic FI, and a clinical examination of the sensible anoderm with a needle and brush is part of the basic workup. Electrosensitivity and temperature sensitivity are complementary investigations of anal sensitivity. Rectal sensibility with balloon distension is part of anorectal manometry.

9.5.9 Defecography

The defecation process can be imaged with dynamic standard imaging or MRI. Although it is not routine, defecography can be helpful if a patient who presents with FI has signs of an evacuation disorder (e.g., intussusception, enterocele, rectocele).

9.5.10 Continence Testing

General global continence tests are more of historical interest and have been widely replaced by the examinations described above. However, a first impression of anorectal continence function may be obtained by the simple application of a suppository or – more advanced – the instillation of porridge or mashed potato, which the patient holds for 15 min while walking around before defecating normally.

Adding to the above, FI can also coexist with other pelvic floor pathologies, such as rectal intussusception; patients can present with varying combinations and severity of urge and passive FI or leakage after defecation. Indeed, a high percentage of patients with rectal intussusception have FI, with up to 56 % presenting with this symptom alone [7]. Although the exact mechanism remains unclear, it is postulated that rectal intussusception stretches the internal anal sphincter and also triggers the rectoanal inhibitory reflex, leading to a temporary reversal of the pressure gradient in the anal canal and soiling. The accompanying incomplete rectal emptying can also contribute to leakage after defecation.

9.6 Treatment

Only when all potential secondary causes are excluded should incontinence as such be addressed. Therapy should be adapted to the patient's individual needs and expectations. The following general principles should be observed:

- From conservative to invasive, surgical treatment is indicated if conservative means do not result in adequate symptom relief [20]
- From less to more invasive

Conservative therapy is pragmatic, often based on a trial-and-error approach, and is adapted to the patient's acceptance of, compliance with, and ability to handle the treatment. Conservative modes can also be adjuvant after operative therapy.

9.6.1 Conservative Therapy

Conservative therapy is considered first-line treatment unless it becomes evident during diagnosis that the cause, extent, and severity of the disease render it inappropriate. Conservative treatment aims to affect stool consistency, colonic transit, bowel emptying, sphincter function and its perception, and rectal filling. Various treatment options are available. They have evolved empirically, and limited data exist to prove their efficacy [20]. A combination has been demonstrated to be clinically more effective than a single treatment [21].

Local measures:

- *Skin care* (fastidious anal hygiene, skin care lotions or ointments, soft napkins, diapers)
- *Anal plugs*: poorly accepted in general; only 10–20 % of patients use continence plugs regularly. They may be better tolerated in patients with reduced anal sensation owing to neurological impairment (spina bifida) [22]. Recent results of a newly designed, flexible silicone plug indicate better acceptance and good improvement of FI [23].

Regulation of bowel emptying: laxative suppositories or retrograde lavage. The purpose of retrograde irrigation is twofold: to cleanse the distal bowel mechanically and to improve rectal reservoir function by distension and improved perception through a defined stimulus. Thus a rhythm of sufficient bowel emptying and time intervals free of fecal loss is established.

Regulation of stool consistency: low-fiber diet, meals that do not cause bloating, and constipating medication (e.g., psyllium, plantago ovata, loperamide, codeine). A paradoxical reaction may occur, and individual testing is advisable. In general, the aim should be behavioral training by a regular daily routine and regular defecation.

Pelvic floor muscle exercise: indicated in patients with reduced voluntary sphincter function. These exercises are recommended as an early intervention based on their low cost, the absence of morbidity, and evidence (although

weak) suggesting efficacy. They should be taught under the guidance of a physiotherapist.

Biofeedback: based on the concept of operant conditioning. Visual or acoustic signals are used to teach the patient to be aware of and use specific physiologic functions and thus to recruit residual function. Both motor and sensory function can be addressed. The therapeutic effect is based on an increase in the strength and duration of contraction, an improvement in coordination and sensory perception, and the suppression of internal relaxation. Training should follow a strict protocol: after instruction the patient must train at home for some months. Success varies widely, and data are inconsistent. A recent randomized controlled trial failed to demonstrate the superiority of biofeedback over general conservative measures and good clinical management, despite a large body of uncontrolled studies supporting its efficacy. Thus the current consensus is that biofeedback is possibly effective but unproven [24]. Because it is painless and risk-free, it can be recommended after other behavioral and medical management has failed to result in adequate symptom relief.

Anal electrostimulation: The periodic application of anal electrostimulation to strengthen the sphincter muscles passively remains controversial. Few, mostly anecdotal, experiences report variable improvements in heterogeneous patient groups. Neither recent nor randomized results from trials are available.

9.6.2 Operative/Interventional Therapy

The choice of surgical treatment is mainly guided by symptom severity and etiology and the structural integrity of the sphincter muscles.

9.6.2.1 Anal Sphincteroplasty

Direct sphincter reconstruction aims to reestablish function by closing a morphologic defect by coapting the dehiscent muscle. The term *anal sphincter repair* is used to describe primary repair of the anal sphincter immediately after direct trauma; *anal sphincteroplasty* describes a secondary or delayed reconstruction of the anal sphincter musculature when lesions were initially either unrecognized or functionally irrelevant, or when the outcome of primary repair was unsatisfactory. Only anal sphincteroplasty is discussed here.

Overlapping sphincteroplasty is the standard of care for disruption postpartum, postoperatively, or after trauma. Anterior sphincteroplasty after obstetric injury is the most common.

- The patient is placed in either the prone jackknife or lithotomy position.
- Through a transverse incision on the perineum the dehiscent muscles are identified and mobilized. (Adequate mobilization is essential for tension-free approximation and adaptation.)
- Suturing can either be overlapping or applied by direct adaptation [25] (Fig. 9.2).
- Separate identification and repair of the internal anal sphincter is technically challenging and has an unproven therapeutic effect.
- A levatorplasty can be added, but vaginal narrowing needs to be avoided beause of the risk of dyspareunia.
- A biological implant may be advantageous to reinforce the anal muscles [26].

Reported short- and mid-term success ranges from 43 to 89 %. Continence deteriorates with long-term follow-up [27]. Patient satisfaction after 5–10 years is 40–45 %.

- Predictors of poorer outcome are age ≥50 years, deep wound infection, and isolated external anal sphincter defects.
- Coexisting neurogenic damage has repeatedly been discussed as a predictor of lower success, but this remains controversial and is not contraindicative.
- Preoperative manometric variables do not predict outcome [28].
- Adjuvant biofeedback therapy after surgery may improve quality of life and help sustain symptomatic improvement over time.

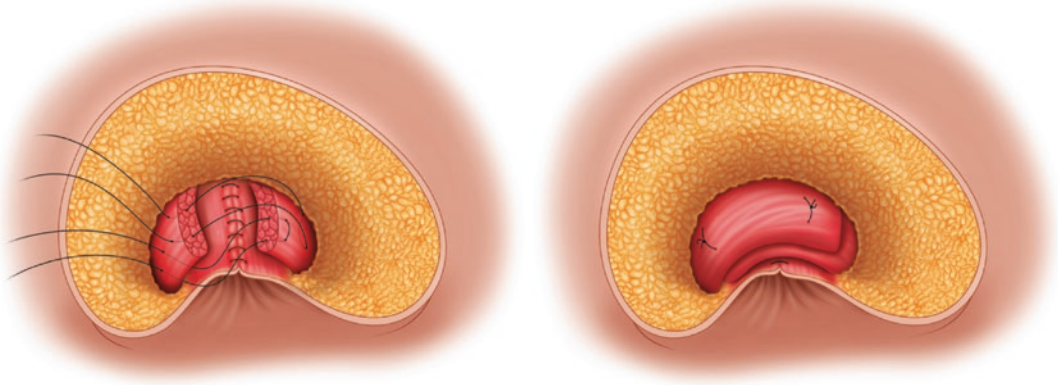


Fig. 9.2 Sphincteroplasty by muscular overlap

Sphincteroplasty can be repeated if initial repair fails. Outcomes seemed to be similar for patients with or without a previous sphincteroplasty, but recent findings raise doubts [29]. Resphincteroplasty should be the choice once other modalities have been explored [30].

9.6.2.2 Pelvic Floor Repair

The aim of postanal repair is to increase the length of the anal canal and its high-pressure zone and to restore the anorectal angle, thus re-creating the flap-valve mechanism thought to contribute to continence. This concept was the treatment of choice in the 1970s and 1980s for patients presenting with incontinence owing to a generalized weakness of the pelvic floor and external anal sphincter without disruption. Initial symptomatic improvement did not last. Given the better surgical options available today, postanal or total pelvic floor repair cannot be recommended [30].

9.6.2.3 Sphincter Replacement/ Substitution

Autologous and heterologous sphincter replacement procedures have been used in patients with failed sphincteroplasty, extensive soft-tissue damage, congenital abnormalities (such as anal atresia), or neurogenic damage. Nonstimulated muscle transpositions (such as uni- or bilateral gluteoplasty or graciloplasty) and stimulated transpositions (stimulated dynamic graciloplasty) have been used to create a neosphincter, or artificial neosphincters have been implanted. Only dynamic graciloplasty (DGP) and artificial bowel sphincters have gained broader clinical acceptance.

9.6.2.4 Dynamic Graciloplasty

In adults the simple transposition of the gracilis muscle around the anus failed to achieve sufficient clinical effect because of fibrosis and the inability for proper activation and durable contraction. The addition [31] of continuous low-frequency electrical stimulation of the supplying nerve with an implantable stimulator consisting of electrodes, an impulse generator, and a remote control device shows various results:

- The phenotype of the transposed muscle is transformed from fast-twitch, fatigable type II fibers to the slow-twitch, fatigue-resistant type I fibers, which are capable of sustained contraction and mimic the physiological characteristics of continuous anal canal closure.
- Increased anal canal closure pressure results from this continous contraction.
- The neoanal sphincter opens when the stimulator is switched off – a voluntary act similar to voluntary bowel emptying.

The longevity of an impulse-generator battery is limited; thus operative replacement is mandatory. The procedure of dynamic graciloplasty (DGP) is complex and associated with high morbidity, and the most frequent complication is infection that ultimately mandates removal of the implanted foreign material and the need for operative reintervention [38]. Outcomes are best in specialized centers.

Depending on the underlying etiology, success rates of DGP in cohort studies range from 55 to 83 % and are best with pathophysiological conditions that are not associated with impaired sensory function. Multicentee trials have shown a poorer functional outcome [32].

DGP has also been used for total anorectal reconstruction after abdominalperineal excision for low rectal or recurrent anal cancers. Its relevance is now considerably reduced.

9.6.2.5 Artificial Bowel Sphincter

Artificial sphincters are designed to reinforce or replace the anal sphincter. Three models – prosthetic bowel sphincter, the soft anal band system from the Agency for Medical Innovations, and the Acticon Neosphincter (American Medical Systems, Minnetonka, MN) – are available on the market. Artificial bowel sphincter (ABS) results have been reported only for the Acticon Neosphincter [33]. Its use is supported in the current recommendations of both the National Institute for Health and Clinical Excellence and the American Society of Colon and Rectal Surgeons [1, 30].

- An ABS is a silicone device that restores anal canal closure by means of an inflatable cuff placed around the lower rectum or upper anal canal and connected to a pressure-regulating balloon implanted in the retropubic space. The patient controls the balloon via a pump placed for convenient accessibility in the labia majora or scrotum [34].
- The deflation of the cuff is limited to several minutes. Refilling allows a pressure gradient between the pressure balloon and the cuff.

Reported success rates range from 50 to 75 %. Continence for liquid and solid stool can be achieved, but the complication rate is high. In up to 30–50 %, infection and technical failure have resulted in device removal [35]. The revision rate increases with the duration of follow-up. The system can be reimplanted, with success rates comparable to those of the first implantation.

Despite their high complication rates, DGP and the ABS remain alternatives to the creation of a stoma in severe end-stage FI. Certain conditions influence the preference of one over the other; for example, the success of DGP depends on intact innervation of the gracilis muscle. Trophic alterations of the perineal or perianal area carry an increased risk of infection if foreign material is implanted.

Exclusion criteria for these procedures include morbid obesity, insulin-dependent diabetes mellitus, Crohn's disease, pelvic sepsis, radiation proctitis, and the practice of anoreceptive intercourse. It is also vital that all patients be adequately motivated and have sufficient manual dexterity to operate the devices independently.

9.6.2.6 Sacral Nerve Stimulation/Sacral Neuromodulation

Sacral nerve stimulation (SNS) aims to recruit residual function of the anorectal continence organ [36]. Prerequisites are residual sphincter function and an existing neuromuscular connection to the sphincter, which is tested by observing the voluntary squeeze or reflex activity after a pin prick.

The system consists of a fully implantable electrode placed close to a target nerve at the level of the sacral spinal nerves, most commonly S3 or S4, and connected to an impulse generator placed in a subcutaneous pocket (Fig. 9.3), which can be programmed and activated via telemetry. The mechanism of action is complex and multifactorial; the effect of SNS is not limited to the anorectal continence organ and the large bowel, affecting the somatomotor, somatosensory, and autonomic nervous systems; it also seems to

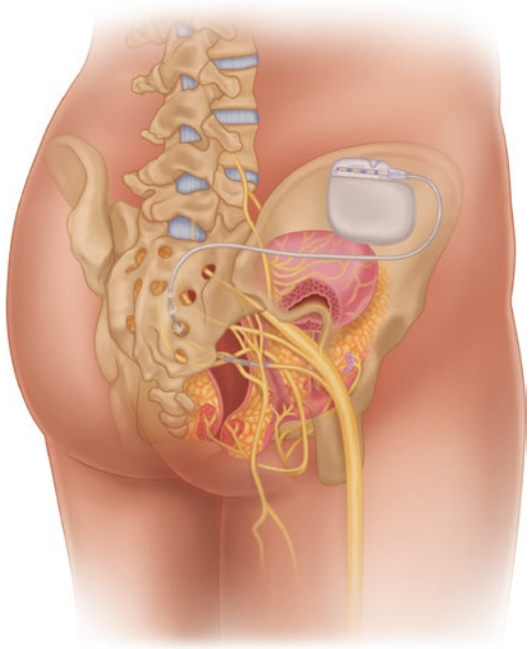


Fig. 9.3 Sacral spinal nerve stimulation

affect the central nervous system, which controls bowel and sphincter activity.

Patients are selected for permanent SNS with the help of a limited period of test stimulation with an external impulse generator:

- A 3-week screening phase of peripheral nerve evaluation, during which patients document bowel habits in standardized bowel diaries, permits evaluation of the clinical effect of SNS.
- Two techniques are available for testing: temporary electrodes to be removed after test stimulation and electrodes that can remain for chronic stimulation if testing is successful. These quadripolar, so-called tined lead electrodes are placed under fluoroscopic guidance. Both types of electrodes are connected to an external pulse generator for the duration of the test period.
- If at least 50 % improvement occurs during testing, it is followed by the second phase – permanent neurostimulator implantation. In approximately 25 % of patients, peripheral nerve evaluation fails to achieve adequate symptom relief.
- If tined leads are used for testing, only the implantable pulse generator (IPG) is added; it is usually placed in a subcutaneous pocket in the gluteal area. If temporary electrodes are used, a complete neurostimulation system – an electrode and IPG – needs to be implanted for therapeutic stimulation.
- The IPG is activated and stimulation parameters are set by telemetry. The chronic stimulation pattern, which is set arbitarily (15 Hz, 210 μs, a continuous or on/off cycle: 5 s/1 s, and voltage adapted to pthe atient's perception in the anal and perineal regions), can be deactivated with a small, hand-held device, the so-called patient programmer.

SNS has been effectively applied in a wide spectrum of pathophysiological conditions, including anal sphincter disruption. Based on patient selection by test stimulation, a success rate of around 80 % for permanent SNS is achieved and efficacy is sustained long term; a median of 36 % (21–96) patients with chronic SNS experiences 100 % symptom improvement, 78 % (21–96) experiencce a 50 % improvement at a median of 85 months [37].

Severe morbidity is low; device removal is unavoidable in around 3 % [38]. The overall complication rate is 15 % in patients with permanent implants. However, the therapy requires maintenence; not only does the IPG need to be exchanged once the battery is depleted, but a substantial proportion of patients require repeated adjustment of the stimulation parameters.

The minimally invasive nature of SNS, its reversibility, and the fact that its clinical effect can be tested before chronic therapy have led to broad acceptance. Test stimulation is not indicated based on a specific underlying physiologic condition, and thus SNS is used on a pragmatic trial-and-error basis. Candidates have an existing anal sphincter with reduced or absent voluntary squeeze function but existing reflex activity indicating an intact nerve-muscle connection.

Contraindications to SNS include pathological conditions of the sacrum that prevent adequate electrode placement, skin disease at the area of implantation, severe anal sphincter damage, trauma sequelae with micturition disorders or low bladder capacity, pregnancy, risk for bleeding, psychological instability, low mental

capacity, the presence of a cardiac pacemaker or implantable defibrillator, and the need for MRI (other than a head coil).

9.6.2.7 Posterior Tibial Nerve Stimulation

Electrical tibial nerve stimulation, either percutaneous with needle electrodes [39] or transcutaneous [40] with adhesive surface electrodes, has been adapted from urology. The mechanism of action is currently unknown. Analogies with findings of physiological changes with SNS have not been explored systematically. Posterior tibial nerve stimulation (PTNS) has recently gained increasing interest as a minimally invasive outpatient procedure with a relatively low cost. Inclusion criteria range from idiopathic FI and FI owing to inflammatory bowel disease or partial spinal injury to FI with internal or external sphincter lesions or a combination, some after obstetric trauma. PTNS has been applied for passive, urge, and mixed incontinence [41] and seems to be more effective in urge FI. As yet there is no agreement regarding the most effective stimulation protocol and parameters.

- The treatment is ambulatory, with one or two 30-min courses per week and subsequent declining periodicity.
- Adequate electrode placement is confirmed by inducing digital plantar flexion, and the ground pad is placed in the proximity.
- Both systems are powered by a portable pulse generator. The stimulation parameters are set arbitrarily, usually to 0.2 ms, a current below the threshold for motor response, and a frequency of 10–20 Hz.

Experience with PTNS is growing. Positive outcomes reported by single-center cohort studies indicate a short success rate of 59–71 % [42], but these data have recently been challanged by a multicenter randomized controlled trial indicating that PTNS is not superior to sham treatment [43].

9.6.2.8 Injectables

The technique of injection of so-called bulking agents or injectables into the anal sphincter for FI relies on the bulking effect of the injected materials with subsequent fibrosis/collagen deposition, but the mechanism of action remains controversial; enlargement of the hemorrhoidal cushions and filling of sphincter gaps have been proposed. The route of application and the location of the deposits vary; depending on the substance, deposits are placed submucosally or intersphincterically by a transanal or transsphincteric approach (Fig. 9.4). In silicone-based injectables,

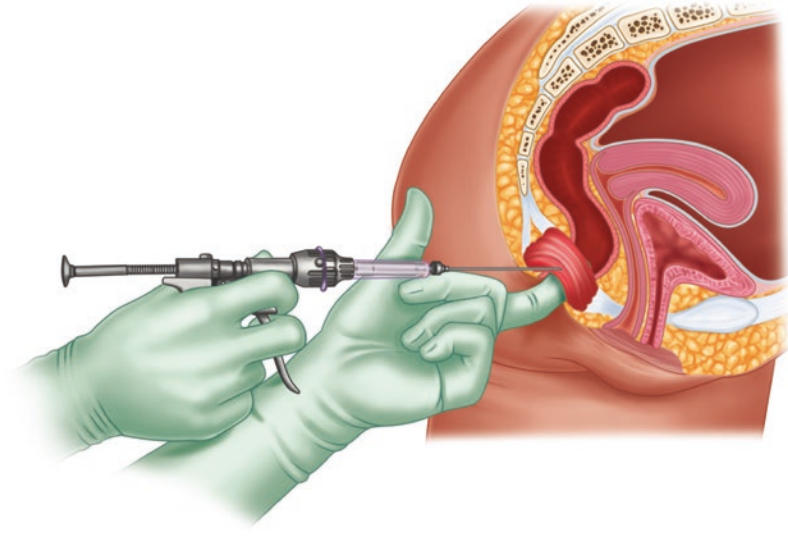


Fig. 9.4 Injectables

EAUS-guided application resulted in a better clinical outcome than digitally guided application for a silicone-based substance [44]. Various substances such as autologous fat, glutaraldehyde cross-linked collagen (Contigen), pyrolytic carbon beads (Durasphere), and silicone biomaterial or injectable silicone biomaterial (PTQ, Bioplastique) have been used, but only a few have gained broad acceptance.

- Internal anal sphincter gaps and internal sphincter degeneration are the most frequent indications.
- Risk is low with most substances.
- Application can be repeated if efficacy diminishes.

Reported success, limited to the short term, ranges between 52 and 70% (various outcome measures are used). The most recently available injectable, dextranomer in stabilised hyaluronic acid (NASHA Dx, Solesta), was shown to be more effective than sham treatment in a double-blind, randomized, controlled trial, and clinical improvement persisted over 3 years of follow-up [45, 46].

Injection has recently been used to deliver a self-expanding device of polyacrylonitrile (Gatekeeper), which enlarges its diameter of 1.2 mm seven times once it comes in contact with human tissue. Sustained improvement in FI and quality-of-life scores over a mean follow-up of 33 months has been shown [47], but this has yet to be confirmed by other studies.

The ease of use, especially transanal submucosal application, and its low risk has sparked an increasing interest in injectables to treat anal sphincter insufficency, but there is little evidence of their effectiveness in passive FI. Existing data indicate that the clinical effects of bulking agents seem to be limited and short-term; they are to be recommended only for selected cases of mild passive FI related to internal sphincter dysfunction and soiling.

9.6.2.9 Magnetic Sphincter

The use of a magnetic ring (FENIX) placed around the anal sphincter like a dynamic Thiersch wire aims to augment the native anal sphincter. To adapt to cirumferential differences, the ring consists of a variable number of connected magnetic beans (14–20) that separate with the passage of bowel content (Fig. 9.5) [48].

The advantages of this technique are its relative simplicity – it is simpler than the ABS – and its immediate efficacy without the need for further manipulation by the patient or surgeon. Short-term data are good and are comparable to

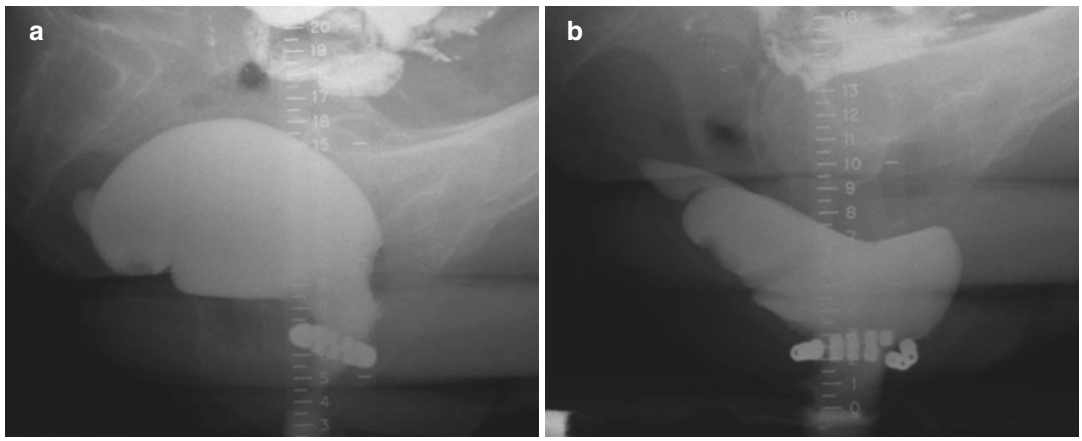


Fig. 9.5 Magnetic sphincter (15 beans): standard defecography in lateral views (**a**) closed (**b**) open at straining (Courtesy P.A. Lehur; Nantes)

ABS or SNS. The spectrum of indications has not yet been clearly defined. The risk profile and comorbidity are moderate, but the long-term complication profile needs to be identified.

9.6.2.10 Sphincter Modulatory Therapy

Sphincter muscle remodeling by transanal delivery of radiofrequency energy (Secca), a minimally invasive procedure, has regained interest. Animal research suggests an alteration in smooth muscle, connective tissue, and collage distribution as well as a change of interstitial cells of Cajal with treatment [49]. The clinical effect in humans is modest and experience is limited. It is currently not clear which patient group is the most suitable, whether the effect is sustained, and how the technique is positioned in the therapeutic algorithm.

9.6.2.11 Anterograde Irrigation

Anterograde irrigation seeks to avoid FI by regularly cleansing the large bowel via an artificial opening at the cecum, thus preventing leakage from a functionally impaired continence organ. Various procedures are currently applied:

- A continent stoma, an "appendicostomy" (Malone procedure), created by tunnelling the tip of the appendix into the cecum to create a one-way valve
- A transcutaneous cecal catheter, placed either endoscopically (CHAIT Trapdoor) or by surgery, or an ileostomy

Good results can be achieved; for example, after 4 years' follow-up up to 91 % of patients were still performing antegrade enemas with significant reduction in incontinence scores. However, wound infection and leakage from the mini stoma and psychological distress may be burdens of this treatment.

9.6.2.12 Stoma

If other treatments have failed or are inapplicable or unacceptable to the patient, stoma creation remains an option, although it is often associated with psychosocial issues and stoma-related complications.

For FI, an end sigmoid colostomy without proctectomy is usually recommended. Diversion colitis of the Hartmann's stump and mucous leakage sometimes present problems and may prompt secondary proctectomy. However, because it offers definitive avoidance of FI with a consequent improvement in quality of life, a high percentage of patients thus treated report they would consider this option again.

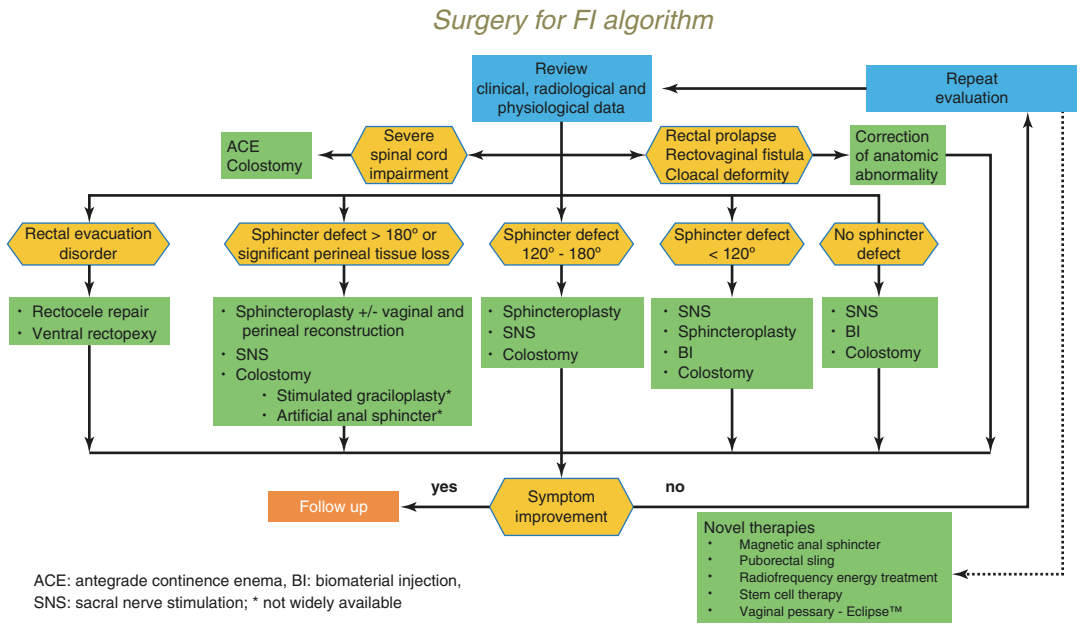
9.6.3 Treatment Algorithms/ Conclusion

As a general rule, conservative treatment should be attempted first. Surgery is only indicated if conservative therapy does not result in adequate symptom relief or is meaningless. Surgical intervention should be based on the findings of clinical and physiological evaluation and aimed either to reconstruct anatomy and thus restore function or to recruit residual function of the continence organ.

Comparison of different techniques is challenging, follow-ups are variable, and comparative studies are rare. Outcome measures have their limitations and are heterogenous. Both symptom improvement and quality of life need to be considered.

Evidence for some aspects of assessment and treatment methods is still low, but guidelines and recommendations are increasing [19, 30, 50]. Decision making often relies on expert opinion and personal experience. It should be personalized and tailored to the cause and severity of the FI and adapted to the needs of the individual patient. There is growing acceptance that in some patients no single treatment mode will be sufficient and a combination – both conservative and operative – may be necessary for an optimal outcome.

Surgical treatment algorithm from the International Consultation on Incontinence [50]



Cleveland Clinic incontinence score [14]

	Frequency				
Type of incontinence	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alternation	0	1	2	3	4
Never: 0 Rarely: <1/month Sometimes: <1/week, ≥1/month Usually: <1/day, ≥1/week Always: ≥1/day			0: Perfect 20: Complete incontinence		

St. Marks incontinence score [15]

	Never	Rarely	Sometimes	Weekly	Daily
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4
				Yes	*No*
Need to wear a pad or plug				0	2
Taking constipating medicines				0	2
Lack of ability to defer defecation for 15 min				0	4
Never: no episodes in the past 4 weeks Rarely: 1 episode in the past 4 weeks Sometimes: >1 episode in the past 4 weeks but <1 a week Weekly: 1 or more episodes a week but <1 a day Daily: 1 or more episodes a day			*Add one score from each row:* Minimum score = 0 = perfect continence Maximum score = 24 = totally incontinent		

References

1. National Institute for Health and Clinical Excellence (NICE) Clinical Guideline 49. Faecal incontinence: the management of faecal incontinence in adults. June 2007. http://www.nice.org.uk/nicemedia/pdf/. CG49 NICE Guidance. Accessed Jan 2012.
2. Brown HW, Wexner SD, Segall MM, et al. Accidental bowel leakage in the mature women's health study: prevalence and predictors. Int J Clin Pract. 2012;66:1101–8.
3. Johanson JF, Mafferty J. Epidemiology of fecal incontinence; the silent affliction. Am J Gastroenterol. 1996;91:33–6.
4. Nelson R, Norton N, Cautley E, et al. Community based prevalence of anal incontinence. JAMA. 1995;274:559–61.
5. Roberts RO, Jacobsen SJ, Reilly WT, et al. Prevalence of combined fecal and urinary incontinence: a community-based study. J Am Geriatr Soc. 1999;47:837–41.
6. Chiang L, Ouslander J, Schnelle J, et al. Dually incontinent nursing home residents: clinical characteristics and treatment differences. J Am Geriatr Soc. 2000;48:673–6.
7. Wijffels NA, Jones OM, Cunningham C, et al. What are the symptoms of internal rectal prolapse? Colorectal Dis. 2013;15:368–73.
8. Johnson JK, Lindow SW, Duthie GS. The prevalence of occult obstetric anal sphincter injury following childbirth-literature review. J Matern Fetal Neonatal Med. 2007;20:547–54.
9. Bharucha AE, Fletcher JG, Melton LJ, Zinsmeister AR. Obstetric trauma, pelvic floor injury and fecal incontinence: a population-based case-control study. Am J Gastroenterol. 2012;107:902–11.
10. Rao SS, American College of Gastroenterology Practice Parameters Committee. Diagnosis and management of fecal incontinence. American College of Gastroenterology Practice Parameters Committee. Am J Gastroenterol. 2004;99:1585–604.
11. Bryant CL, Lunniss PJ, Knowles CH, et al. Anterior resection syndrome. Lancet Oncol. 2012;13:e403–8.
12. Kiff ES, Swash M. Slowed conduction in the pudendal nerves in idiopathic (neurogenic) faecal incontinence. Br J Surg. 1984;71:614–6.
13. Qureshi MS, Rao MM, Sasapu KK, et al. Male faecal incontinence presents as two separate entities with implications for management. Int J Colorectal Dis. 2011;26:1589–94.
14. Oliviera L, Pfeifer J, Wexner S. Physiological and clinical outcome of anterior sphincteroplasty. Radiology. 1996;199:529–32.
15. Vaizey CJ, Carapeti E, Cahill JA, et al. Prospective comparison of faecal incontinence grading systems. Gut. 1999;44:77–80.
16. Rockwood TH, Church JM, Fleshman JW, et al. Fecal incontinence quality of life scale: quality of life instrument for patients with fecal incontinence. Dis Colon Rectum. 2000;43:9–16.
17. Berger N, Tjandra JJ, Solomon M. Endoanal and endorectal ultrasound: applications in colorectal surgery. Aust NZ J Surg. 2004;74:71–5.
18. Karoui S, Savoye-Collet C, Koning E, et al. Prevalence of anal sphincter defects revealed by sonography in 335 incontinent patients and 115 continent patients. Am J Roentgenol. 1999;173:389–92.
19. Madoff R, Laurberg S, Lehur PA, et al. Surgery for fecal incontinence. In Abrams P, Cardozo L, Khoury S, Wein AJ, editors. Incontinence: 5th International Consultation on Incontinence. Paris: ICUD-EAU; 2013.
20. Norton C, Whithead W, Bliss DZ, et al. Conservative and medical managment of fecal incontinence in adults. In Abrams P, Cardozo L, Khoury S, Wein AJ, editors. Incontinence: 5th International Consultation on Incontinence. Paris: ICUD-EAU; 2013.
21. Sjödahl J, Walter SA, Johansson E, et al. Combination therapy with biofeedback, loperamide, and stool-bulking agents is effective for the treatment of fecal incontinence in women – a randomized controlled trial. Scand J Gastroenterol. 2015;50:965–74.
22. Deutekom M, Dobben AC. Plugs for containing faecal incontinence.Cochrane Database Syst Rev. 2015;(7):CD005086. doi: 10.1002/14651858.
23. Lukacz ES, Segall MM, Wexner SD. Evaluation of an anal insert device for the conservative management of fecal incontinence. Dis Colon Rectum. 2015;58:892–8.
24. Norton C1, Cody JD. Biofeedback and/or sphincter exercises for the treatment of faecal incontinence in adults. Cochrane Database Syst Rev. 2012;(7):CD002111. doi: 10.1002/14651858.
25. Tjandra JJ, Han WR, Goh J, et al. Direct repair vs. overlapping sphincter repair: a randomized, controlled trial. Dis Colon Rectum. 2003;46:937–42.
26. Zutshi M, Ferreira P, Hull T, et al. Biological implants in sphincter augmentation offer good short-term outcomes after a sphincter repair. Colorectal Dis. 2012;14:866–71.
27. Glasgow SC, Lowry AC. Long-term outcomes of anal sphincter repair for fecal incontinence: a systematic review. Dis Colon Rectum. 2012;55:482–90.
28. Gearhart S, Hull T, Floruta C, et al. Anal manometric parameters: predictorsof outcome following anal sphincter repair? J Gastrointest Surg. 2005;9:115–20.
29. Hong K, Dasilva G, Dollerschell JT, et al. Redo sphincteroplasty: are the results sustainable? SD. Gastroenterol Rep (Oxf). 2015. Epub Jun 29.
30. Paquette IM, Varma MG, Kaiser AM, et al. The American Society of Colon and Rectal Surgeons' clinical practice guideline for the treatment of fecal incontinence. Dis Colon Rectum. 2015;58:623–36.
31. Baeten CG, Bailey HR, Bakka A, et al. Safety and efficacy of dynamic graciloplasty for fecal incontinence: report of a prospective, multicenter trial. Dynamic Graciloplasty Therapy Study Group. Dis Colon Rectum. 2000;43:743–51.
32. Chapmann AE, Geerdes B, Hewett P, et al. Systematic review of dynamic graciloplasty in the treatment of faecal incontinence. Br J Surg. 2002;89:138–53.

33. Wong WD, Congliosi SM, Spencer MP, et al. The safety and efficacy of the artificial bowel sphincter for fecal incontinence: results from a multicenter cohort study. Dis Colon Rectum. 2002;45:1139–53.
34. Lehur PA, Roig J, Duinslaeger M. Artificial anal sphincter: prospective clinical and manometric evaluation. Dis Colon Rectum. 2000;43:1213–6.
35. Mundy L, Merlin TL, Maddern GJ, Hiller JE. Systematic review of safety and effectiveness of an artificial bowel sphincter for faecal incontinence. Br J Surg. 2004;91:665–72.
36. Matzel KE, Stadelmaier U, Hohenfellner M, et al. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. Lancet. 1995;28(346): 1124–7.
37. Altomare DF, Giuratrabocchetta S, Knowles CH, et al. Long-term outcomes of sacral nerve stimulation for faecal incontinence. Br J Surg. 2015;102:407–15.
38. Tan E, Ngo NT, Darzi A, et al. Meta-analysis: sacral nerve stimulation versus conservative therapy in the treatment of faecal incontinence. Int J Colorectal Dis. 2011;26:275–94.
39. Stoller ML. Afferent nerve stimulation for pelvic floor dysfunction (abstract). Eur Urol. 1999;35:16.
40. Queralto M, Portier G, Cabarrot PH, et al. Preliminary results of peripheral transcutaneous neuromodulation in the treatment of idiopathic fecal incontinence. Int J Colorectal Dis. 2006;21:670–2.
41. Hotouras A, Thaha MA, Boyle D, et al. Short-term outcome following percutaneous tibial nerve stimulation (PTNS) for faecal incontinence: a single-centre prospective study. Colorectal Dis. 2012;14:1101–5.
42. Thin NN, Horrocks EJ, Hotouras A, et al. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. Br J Surg. 2013;100:1430–47.
43. Knowles CH, Horrocks EJ, Bremner SA, et al. Percutaneous tibial nerve stimulation versus sham electrical stimulation for the treatment of faecal incontinence in adults (CONFIDeNT): a double-blind, multicentre, pragmatic, parallel-group, randomised controlled trial. Lancet 2015;366:1640–8.
44. Tjandra JJ, Lim JF, Hiscock R, et al. Injectable silicone biomaterial for fecal incontinence caused by internal anal sphincter dysfunction is effective. Dis Colon Rectum. 2004;47:2138–46.
45. Graf W, Mellgren A, Matzel KE, et al. Efficacy of dextranomer in stabilised hyaluronic acid for treatment of faecal incontinence: a randomised, sham-controlled trial. Lancet. 2011;377:997–1003.
46. Mellgren A, Matzel KE, Pollack J, Nasha Dx Study Group, et al. Long-term efficacy of NASHA Dx injection therapy for treatment of fecal incontinence. Neurogastroenterol Motil. 2014;26:1087–94.
47. Ratto C, Parello A, Donisi L, et al. Novel bulking agent for faecal incontinence. Br J Surg. 2011;98:1644–52.
48. Barussaud ML, Mantoo S, Wyart V, et al. The magnetic anal sphincter in faecal incontinence: is initial success sustained over time? Colorectal Dis. 2013;15: 1499–503.
49. Herman RM, Berho M, Murawski M, et al. Defining the histopathological changes induced by nonablative radiofrequency treatment of faecal incontinence – a blinded assessment in an animal model. Colorectal Dis. 2015;17:433–40.
50. O´Connell R, Laurberg S, Lehur PA, et al. Surgery for fecal incontinence. 6th International Consultation on Incontinence, in press.

Constipation

10

Charles H. Knowles

10.1 Etiology

Constipation is not a disease but rather a symptom that can result from numerous diseases. Constipation can thus be described as primary or secondary, depending on whether the etiology of disordered bowel function is presumed to reside within the bowel neuromuscular apparatus itself (primary) or whether there is an obvious local or systemic cause (secondary). Secondary constipation can be further subdivided on the basis of etiology (Table 10.1), whereas for primary constipation, the most useful initial consideration is whether constipation is a transient short-term problem (often called "simple" constipation) or a chronic condition. The term *idiopathic* is often used in the context of primary chronic constipation on the basis that the current understanding of the exact disease pathogenesis is limited.

The various etiologies of secondary constipation are not considered further here, although these inform clinical history taking and investigations (see below). Simple constipation can result from various factors including diet, lack of exercise or immobility, and poor fluid intake. There is no single unified etiology for chronic (idiopathic) constipation. Rather, clinicians are faced with piecing together a multitude of clinical and research observations based on a variety of disparate approaches. These are summarized below.

10.1.1 Observed Colonic Physiological Abnormalities

Colonic motility problems, abnormalities of colonic reflexes, and the lack of a normal response to physiological stimuli may all contribute to constipation and can be directly recorded using pancolonic manometric methods [2]. High-amplitude propagated contractions (HAPCs) are responsible for luminal transit (mass movements) and defecation. Several studies have shown a reduced frequency of HAPCs in patients with slow-transit constipation [3]. In addition, constipated patients may demonstrate a lack of spatiotemporal regional linkage between propagated sequences (in health, a series of two or three colonic propagated sequences may be linked to span the length the colon) [4].

There is normally an increase in the frequency of HAPCs after a meal. This response is often absent in patients with constipation. Colonic motor activity normally increases upon awakening and decreases upon sleeping, with conflicting reports as to whether such increases are absent or reduced in patients with constipation [5]. Similarly, some studies have shown no difference

C.H. Knowles, MB, BChir, PhD, FRCS
National Centre for Bowel Research and Surgical Innovation, 1st floor Abernethy Building, 2 Newark St, London E1 2AT, UK
e-mail: c.h.knowles@qmul.ac.uk

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_10

Table 10.1 Classification system for constipation based on etiology

Primary (idiopathic) constipation	
Simple constipation	Factors include exercise, dietary fiber intake, hydration
Chronic constipation	Delayed colonic transit and/or pelvic floor dysfunction
	Constipation predominant irritable bowel syndrome
	Idiopathic megacolon or megarectum (rare)
Secondary constipation	
Gastrointestinal causes	
Colorectal	Malignant neoplasms, inflammatory strictures, diverticular disease
	Secondary megacolon or megarectum (Hirschsprung disease and other rare causes)
Anal	Atresia or malformation (after corrective surgery)
	Hereditary internal anal sphincter hypertrophy
	Anal stenosis
Extragastrointestinal causes	
Metabolic and endocrine	Hypothyroidism, diabetes, hypercalcemia, chronic renal failure, pregnancy
Neurological	Degenerative central nervous system diseases (e.g., multiple sclerosis, Parkinson disease)
	Spinal or pelvic nerve lesions
	Autonomic neuropathies
Drugs	Opioids, anticholinergics, antidepressants, anticonvulsants
Psychological	Severe endogenous depression
	Eating disorders
Other	Scleroderma, Ehlers Danlos syndrome, Chagas disease, amyloidosis

Modified from Knowles [1]

in the nocturnal suppression of colonic motor activity in constipated patients when compared with controls [5], whereas others have reported an absence of nocturnal suppression. It is suggested that the lack of diurnal variation may indicate a neuropathic cause of constipation. In healthy controls, intravenous injection of the cholinergic agonist edrophonium and rectal infusion of chenodeoxycholic acid [6] increased the frequency of HAPCs; this response is absent in constipated patients and might signify disturbed cholinergic function [6].

It is known that mechanical stimulation of the rectum can inhibit the activity of the small intestine and colon. These studies point toward the existence of reflex pathways [4], abnormalities of which may potentially lead to constipation. Voluntary suppression of evacuation can lead to prolonged total and regional intestinal transit time, indicating that constipation can be "learned" [7] and reinforcing the concept that problems of defecation cannot be divorced from those of the colon (an important point in therapy).

10.1.2 Observed Anorectal Physiological Abnormalities

Defecation is dependent not only on the delivery of stool of an appropriate consistency to the rectum but also on the combined functions of the rectum and pelvic floor to permit subsequent voluntary evacuation. The analogy of a "tube of toothpaste" is useful in considering the act of defecation: the tube needs to be full, and the user needs to know that it is full, be able to squeeze it, and remove the cap at the appropriate time. Such coordinated actions incorporate biomechanical properties, structural integrity, and an intact nerve supply to the rectum and anus [8]. Decreased rectal sensation (rectal hyposensitivity) [9], reduced or uncoordinated rectal motor activity, and abnormal biomechanical properties of the rectal wall (usually increased rectal compliance) have all been reported in patients with chronic constipation. The important contribution of dynamic structural abnormalities of the rectum (mainly rectocele and intussusception) and pelvic floor

dysfunction (dysynergic defecation) to the etiology of constipation are addressed in Chap. 11.

10.1.3 Observed Colonic Histological Abnormalities

The subject of gastrointestinal (GI) neuromuscular pathology is one that is, in general, fraught with technical and interpretative uncertainties [10, 11] – and the study of colonic tissue in chronic constipation is no exception. The interested reader should access more detailed information from specific reviews (see Ref. [10]). Accepting issues of selection bias (patients undergoing colectomy are not representative of the whole), technical processing (many data are based on outdated histologic techniques, such as silver staining), reporting (do subtle differences actually deviate from normality?), and interpretation (do findings have a causal relationship with the observed clinical phenotype?), the following observations of patients with chronic constipation (mainly based on the study of patients with slow-transit constipation) are briefly summarized:

1. Bona fide enteric neuropathy [11] is probably not a common finding.
2. Widely reported changes in functional subsets of enteric neurons [12, 13] or glia may have biological relevance but currently have little diagnostic utility.
3. Well-established developmental, degenerative, and inflammatory myopathic phenotypes [11] are at best an uncommon finding.
4. Quantitative reductions in the numbers of interstitial cells of Cajal (pacemaker cells) are the most consistent finding [14], although standardized approaches are required for diagnosing individual patients in clinical practice [10].

10.1.4 Brain-Gut Influences

The central nervous system can influence GI functions by hard wiring (autonomic nervous system), neuroendocrine functions (hypothalamo-pituitary axis), and immune modulation. Depression, anxiety, and traumatic life events such as sexual and physical abuse are more common among women with severe constipation [15, 16]. While in general such studies have shown clearer associations with irritable bowel syndrome and dysynergic defecation, it is known from studies of healthy volunteers that transit can be delayed at will [7], suggesting that behavioral factors may also influence colonic function. This may be the mechanism involved in constipation arising from toilet avoidance behavior, which is often seen in young children or in frequent travelers such as airplane crewmembers.

10.1.5 Other Etiologies

A plethora of studies have addressed hypotheses such as altered intestinal absorption, changes in sex hormones, altered endogenous opioid balance, autoimmune mechanisms, infective agents, and laxative toxicity. None provide conclusive evidence; however, in light of the strong female predominance of slow-transit constipation (see below), experimental evidence for downregulation of smooth-muscle contractile G proteins and upregulation of inhibitory G proteins caused by the overexpression of progesterone receptors [17] is probably the most attractive current line of reasoning.

10.2 Incidence

Constipation is one of the most common chronic disorders of the digestive tract, affecting between 2 and 35 % of the general population [18]. Similar prevalence rates of 0.7–29.6 % have been reported for constipation in the pediatric literature [19]. Systematic review and meta-analysis of general adult population studies, excluding convenience sampling and using a mix of self-reporting and specific diagnostic criteria, yielded a pooled prevalence of 14.0 % [20]. In the United States alone, constipation accounts for approximately 2.5 million physician visits a year, and tertiary care for constipation was estimated to cost an average of US$2,752 per patient in the late 1990s. The wide range of prevalence

estimates for constipation is secondary to variations in populations studied, definitions used for constipation (see below), and methods used for the surveys.

It is readily evident (and fortunate) that these survey estimates cannot possibly represent the prevalence of clinically significant chronic constipation – that is, one in five of the UK population will not be attending my clinic! A recent UK cohort study of 3.8 million patients in primary care helps provide some sense regarding this question [21]. In that cohort, 1.3 % per annum consulted their general practitioner for constipation. This figure remained constant over a 5-year period and included all common causes (e.g., pregnancy and drug use). Approximately 40 % of patients required repeat prescriptions for laxatives, and 32 % were refractory to two or more laxatives, suggesting a maximum prevalence of chronic constipation of approximately 0.4 % (i.e., 1 in 250 adults).

10.3 Epidemiology

Most studies have reported a higher prevalence of self-reported constipation among women than men, with a male-to-female ratio ranging from 1.01 to 3.77 [18, 22] and a median of 2.2 [20]. This ratio is much more pronounced in patients with chronic idiopathic constipation attending tertiary care [23]. There is an increased prevalence of constipation among nonwhites, with white-to-nonwhite ratios between 1.13 and 2.89 [18, 20, 24]. Some geographic variations exist, with lower prevalence in southeast Asia [20]. Subjects with a low income have a significantly higher rate of constipation than subjects with a high income [20]. Several studies have reported an increase trend toward constipation with increasing age, and a meta-analysis confirmed this relationship [20].

10.4 Classification

10.4.1 Etiology

The classification of constipation based on etiology has already been presented here (primary vs. secondary). One further method of classification is based on bowel diameter. While this seems logical, in practice (excluding acute causes such as mechanical obstruction and acute colonic pseudo-obstruction) bowel dilatation (megacolon) is extremely rare, thus limiting the usefulness of this approach (megacolon and megarectum are addressed separately at the end of the chapter in Sect. 10.7).

10.4.2 Symptoms

There is no universally agreed definition of *constipation*. It is a general term that embraces a range of conditions where a subject is dissatisfied with their ability to expel stool. Symptoms can include infrequent bowel movements (usually fewer than three movements a week), hard stools that are difficult to pass, a need to strain excessively (or a need for manual maneuvers to pass stool), a sense of incomplete bowel movement, and excessive time spent on the toilet. Others may describe even more diverse symptoms such as general abdominal discomfort, nausea, lethargy, and back pain. Patients and doctors often have different perceptions of what constitutes "constipation." Clinicians often use the frequency of defecation, stool weight, colonic transit studies, and other anorectal physiology investigations to diagnose constipation [25], whereas self-reported constipation is subjective and influenced by social customs. A traditional criterion for constipation (i.e., fewer than three bowel movements per week) was only reported by 9 % respondents with constipation in an epidemiological survey in the United States. By contrast, 38 % reported a sense of incomplete bowel movement, 24 % reported unsuccessful attempts at moving their bowels, and 20 % reported abdominal pain, bloating, or a sense of outlet blockage. Bowel infrequency is also a less common symptom than defecatory difficulty (especially straining) in other general population studies [22] and in patient cohorts with well-defined chronic constipation [22].

Because of the variation in perceptions of constipation, consensus criteria have been proposed by experts to aid diagnosis, evidence-based management, and further research. One of the most widely used diagnostic criteria, the

Rome criteria, was proposed by an international panel of experts and is presently in its third iteration (Rome III) [26]. Rome III defines functional constipation solely based on symptoms: the presence of two or more of six listed symptoms in at least 25 % of defecations (over the past 3 months, with symptom onset at least 6 months before diagnosis and only in the absence of sufficient criteria to diagnose irritable bowel syndrome [IBS]): hard stools, straining, sensation of incomplete evacuation, sensation of anorectal blockage, the use of manual maneuvers during evacuation, and infrequent bowel movements (<3 movements/week). The Rome III criteria recognize subgroups of functional constipation based on symptoms and physiological tests, which implies that the experts consider symptoms alone to be inadequate to identify subtypes of functional constipation in clinical practice. The other widely accepted diagnostic criterion was proposed by the American College of Gastroenterology Chronic Constipation Task Force. They defined constipation more simply, as unsatisfactory defecation characterized by infrequent stools, difficult stool passage, or both for at least the previous 3 months. Difficult stool passage includes straining, hard/lumpy stool, difficulty passing stool, incomplete evacuation, prolonged time on toilet, or the need for manual maneuvers to pass stool [27].

10.4.3 Measurements

Patients with chronic constipation may be referred for specialist investigations (see below). Using measures of transit and evacuation, constipation can be subdivided into two main categories: slow-transit constipation and evacuatory disorders; a large proportion of patients has both findings. Another group has no obvious abnormality; this is sometimes termed *normal-transit constipation*. Ragg et al. [28] investigated 541 patients with chronic constipation and found that 53 % had outlet obstruction, 5 % had isolated slow-transit constipation, 29 % had coexistent outlet obstruction and slow-transit constipation, and 12 % had normal-transit constipation. In another series of >5,000 UK patients, these figures were similar (45 %, 10 %, 35 %, and 10 %, respectively).

Slow-transit constipation is defined by a prolonged colonic transit time (in reality, most methods actually determine a prolonged whole-gut transit time). As an isolated phenomenon, this is most commonly observed in young women with constipation dating from early childhood and is associated with infrequent spontaneous bowel movements (once a week or fewer), bloating, and abdominal discomfort or pain [23] (the term *colonic inertia* has been applied to this relatively rare condition in a subgroup of patients). It is more commonly observed in combination with a defecation disorder, where the transit disturbance may be secondary to outlet obstruction and reflex inhibition of colonic contractile activity (see section on observed colonic physiology).

Defecatory disorders (also referred to as evacuation disorders and outlet obstruction) are characterized by difficulty evacuating stool once it reaches the rectum. Common causes include functional abnormalities of the anal sphincter or pelvic floor and dynamic structural abnormalities such as rectocele, intussusception, and excessive perineal descent (see Chap. 11).

Normal-transit constipation is an ill-defined condition in which stool passes through the intestine at a normal rate, the frequency of bowel movements and evacuation are normal, yet patients perceive that they are constipated [29]. Patients frequently also experience abdominal pain and bloating, and may have psychosocial issues [16, 25]. This group probably has considerable clinical overlap with constipation-predominant IBS.

10.5 Diagnostics

10.5.1 Clinical History

When a patient presents with constipation, a thorough history determines whether constipation represents a new complaint, that is, one that may indicate a change in bowel habits. The patient should be asked specifically about the frequency and consistency of bowel movements and the

progress of such changes over time (as well as other alarming symptoms such as rectal bleeding, anorexia, and weight loss). On this basis, with additional information regarding family history, previous colon cancer screening, and other GI investigations, an informed decision can be made regarding whether structural intraluminal investigation of the colon is required. Other organic causes of constipation may be deduced by appropriate history-taking and biochemical investigation. With the exclusion of treatable secondary causes, if the history is short and multiple previous therapies have not already been tried, then the patient may be first considered to have "simple" constipation that can be managed with reassurance and lifestyle advice (fiber, fluids, and exercise), with or without simple laxative therapy.

In patients with chronic symptoms, after excluding a secondary cause, the focus should shift to the investigation and management of chronic (idiopathic) constipation. This decision is helped by overwhelming epidemiological evidence that patients with chronic idiopathic constipation are usually female (≥90 %) [23] and often have symptoms from early childhood or puberty (at least 50 %) [23] or problems that start after pelvic surgery (e.g., hysterectomy, childbirth). Thus the history should ascertain the duration and mode of onset of symptoms. In relation to onset, it may sometimes be necessary to tactfully query regarding a history of physical or sexual abuse [15, 16]. It is helpful to systematically document the main symptoms that in the patient's mind constitute a problem, since this has some bearing on treatment decisions and subsequent monitoring of effectiveness. Several questions form detailed scoring systems to systematically facilitate this in a research context (e.g., the Cleveland Clinic Constipation [30] and Knowles Eccersley Scott Symptom scores); psychometrically validated patient-reported outcome measures are also now available (e.g., the Patient Assessment of Constipation Symptoms and Patient Assessment of Constipation Quality of Life questionnaires) [31]. In routine practice, however, it is sufficient to list in the patient's record the presence or absence (with some indication of degree) of each symptom. I specifically ask about the following, with and without laxative use (if relevant):

Frequency of spontaneous or assisted bowel opening	Painful defecation
Stool consistency	Digitation (vaginal or anal)
Straining	Abdominal pain
Incomplete/unsuccessful evacuation	Bloating

In addition, brief questioning can determine the coexistence of other symptoms attributable to pelvic floor disorders, such as stress and urge urinary incontinence, vaginal bulging, or prolapse. The remaining history should document prescribed and self-administered laxatives (and the therapeutic benefit of each) and also provide an impression of the quality of the diet with respect to fiber and fluid intake.

10.5.2 Clinical Examination

A poor nutritional status should prompt a search for a secondary cause, including occult carcinoma, widespread dysmotility syndromes such as chronic intestinal pseudo-obstruction (see below), and eating disorders. An abdominal examination should be conducted to look for scars, any significant abdominal distention, tenderness, or masses. Bloating is a common and expected finding with idiopathic constipation, but significant distension, tenderness, or masses should prompt a full investigation.

All patients presenting with constipation should undergo a rectal examination. The perineum and anus should be examined for evidence of fecal incontinence, which may indicate impaction and overflow. Fecal incontinence and chronic constipation coexist to some degree in 40 % patients; marked soiling of the underwear is especially associated with the rare diagnosis of megarectum. Scarring (e.g., from episiotomy), sentinel pile formation secondary to underlying fissure, external hemorrhoids, or prolapse may also be present. The degree of perineal descent upon straining, indicative of pelvic floor weakness, should also be determined visually (>3 cm

is usually considered abnormal, and complete effacement of the natal cleft or ballooning of the perineum indicates significant global pelvic floor weakness). A digital rectal examination can allow a diagnosis of impaction, provide a rough measure of anal tone at rest and upon squeezing, and ascertain obvious sphincter defects. Further, an effort should be made to look for any anterior defect in the rectovaginal septum leading to a rectocele. Upon removing the digit from the anus, it is sometimes possible to appreciate the presence of an intra-anal intussusception/mucosal prolapse, which is "dragged out" with the examining digit. It is questionable whether digital examination gives a reliable diagnosis of pelvic floor dyssynergia. It is, however, usual practice to ask the patient to simulate defecation (push maneuvre) two or three times, whereupon an experienced examiner can gain an impression of pelvic floor contraction or failure to relax during straining. Further, significant intussusception (intrarectal or intra-anal) may push on the examining finger. Anoscopy and proctoscopy should be performed if there is any history of rectal bleeding and may indicate fissure or internal piles. A urogynecological examination is desirable in all patients with suspected pelvic multiorgan prolapse.

10.5.3 Investigations

While the findings from the history or physical examination may indicate a possible secondary cause of constipation, making further investigation mandatory, it is also typical practice in patients with chronic constipation to exclude certain secondary causes by investigation, even though the diagnostic utility of such investigations is acknowledged to be low (the most common undiagnosed systemic disease is hypothyroidism). Thus serum electrolyte, creatinine, calcium, and glucose hemoglobin concentrations are usually measured and thyroid function tests performed. The approach taken for a structural investigation of the colon when patients have no suspected intraluminal pathology varies internationally and on the basis of available resources. In the United States, for patients older than 50 years, the baseline risk of colorectal cancer is sufficiently high that screening colonoscopy is recommended, even in the absence of alarming symptoms. These older patients should therefore undergo routine colonoscopy, and many authors recommend that patients younger than 50 years undergo routine flexible sigmoidoscopy. Routine biopsies have no benefit. This approach is being increasingly adopted in Europe. My view is that at some stage it is worth assessing the rectum and colon so that subsequent management (which may be protracted or unsuccessful) can start with baseline reassurance that no organic disease is present. Barium enema (or, as an alternative, computed tomography pneumocolon) can still be a useful investigation in this instance because it yields more information on colonic diameter (for rare cases of megacolon) and the distribution and severity of diverticular disease, which may coexist and be responsible in part for symptomatology (Fig. 10.1).

In patients with chronic constipation in whom basic laxatives have failed, further specialist investigative tests may be warranted, although opinions differ on how rigorous such investigations should be and when in the treatment algorithm they should be performed. While there is a general lack of evidence that targeted management strategies are superior to empirical stepwise treatments in early pharmacologic and behavioral interventions, it is at least generally agreed that such tests are mandatory if surgery is considered [32, 33]. Finally, it should be noted that all tests are dependent on adequate normative data (relevant for the patient's sex and age), the expertise of the investigator, and correct interpretation in the context of the clinical information. Table 10.2 lists standard and advanced tests. A plain abdominal radiograph that can be reviewed immediately in the outpatient setting is particularly useful as a screening tool for determining whether the symptoms mentioned by patients actually correlate with evidence of fecal loading, and they may be shown to the patient to aid discussion.

The mainstay for the rapid evaluation of colonic transit is the radiopaque marker study [34]. Though variations in technique exist in

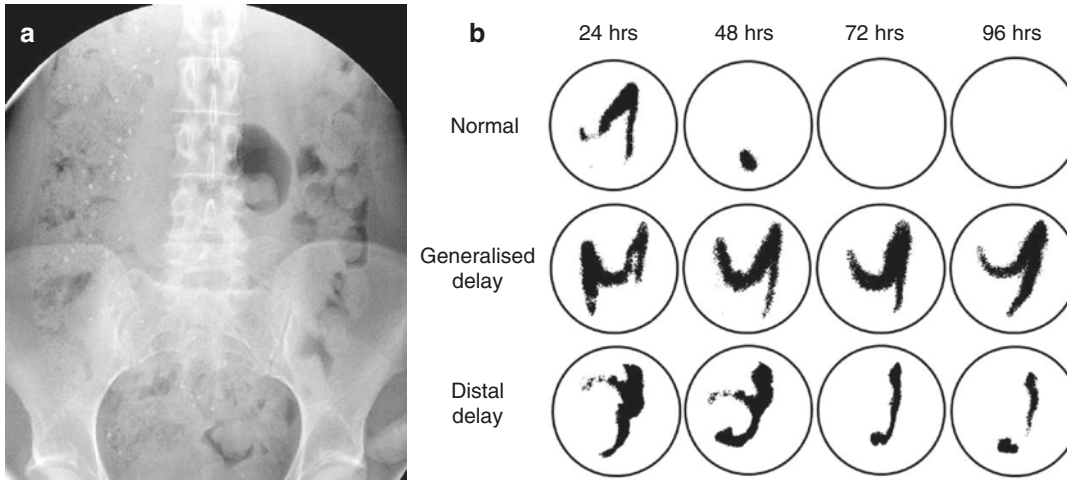


Fig. 10.1 (**a**) Slow colonic transit: radio-opaque marker study. All markers remain in the proximal colon at 100 h. (**b**) In^{111} Isotope scintigraphy showing normal progression of an isotope in a healthy control, generalized slow transit, and distal delay (Courtesy of Dr. Mark Scott, Barts Health NHS Trust)

Table 10.2 Specialist investigations for chronic constipation

Measure	Standard	Advanced
Colonic transit	Radio-opaque marker study	Colonic isotope scintigraphy
Colonic contractile activity	–	Colonic manometry
Rectal evacuation	Balloon expulsion test	Magnetic resonance proctography
	Fluoroscopic evacuation proctography	Isotope scintigraphic proctography
Anal sphincter contraction	Anal manometry	High-resolution anorectal manometry
Rectal sensory testing	Simple balloon distension	Rectal barostat distension
Rectoanal inhibitory reflex	Balloon and anal manometry	Integrated barostat-manometry

terms of the number of markers, the interval to radiography, and the definition of *slow transit*, the basic premise is that a number of markers (small pieces of plastic tubing prepackaged in gelatin capsules) are ingested, and an abdominal radiograph (which includes the pelvis) is taken at a particular interval. The patient abstains from using laxatives for the duration of the study. In patients with significant numbers of retained markers (based on control data), slow whole-gut transit is diagnosed (Fig. 10.2a). Alternatively, regional transit can be measured by radioscintigraphy [35] (Fig. 10.2b) or using a wireless motility capsule [36]. These techniques are valid but not widely available. On the basis of radio-opaque marker studies, approximately 40% of patients with chronic constipation have delayed transit [32]. Abnormal transit may be demonstrated either throughout the colon or within a limited portion thereof (most commonly the sigmoid colon and the rectum). With regard to the latter, it is unresolved whether such markers represent a primary disturbance of rectosigmoid motility or are retained secondary to a primary problem of evacuation, which is also present in more than half of patients with slow-transit constipation.

The simplest direct test of evacuation is the fixed-volume (50 mL) water-filled rectal balloon expulsion test [37, 38], which is performed in a seated position on a commode. Expulsion is defined as abnormal if there is a failure to expel with 1 min of effort for men and 1.5 min for women. It should be kept in mind, however, that as many as 12% of patients with normal pelvic floor function have difficulty with balloon expulsion in this setting, and that balloon expulsion can only

determine the ability to expel the balloon, *not* the underlying mechanism leading to failed expulsion. Thus, in patients who remain refractory to therapy (see below), more advanced tests of evacuation may be indicated. Many specialist centers use fluoroscopic evacuation proctography with installation of barium porridge into the rectum and evacuation on a radiolucent commode [39, 40]. The proportion of contrast evacuated and the time taken to evacuate are recorded, as are "functional" (i.e., pelvic floor dyssynergia) and "structural" features deemed obstructive to defecation (e.g., rectocele, enterocele and intussusception) [38, 40, 41] (Fig. 10.2a). Magnetic resonance proctography is gaining in popularity. It has the advantages of avoiding ionizing radiation and global appreciation

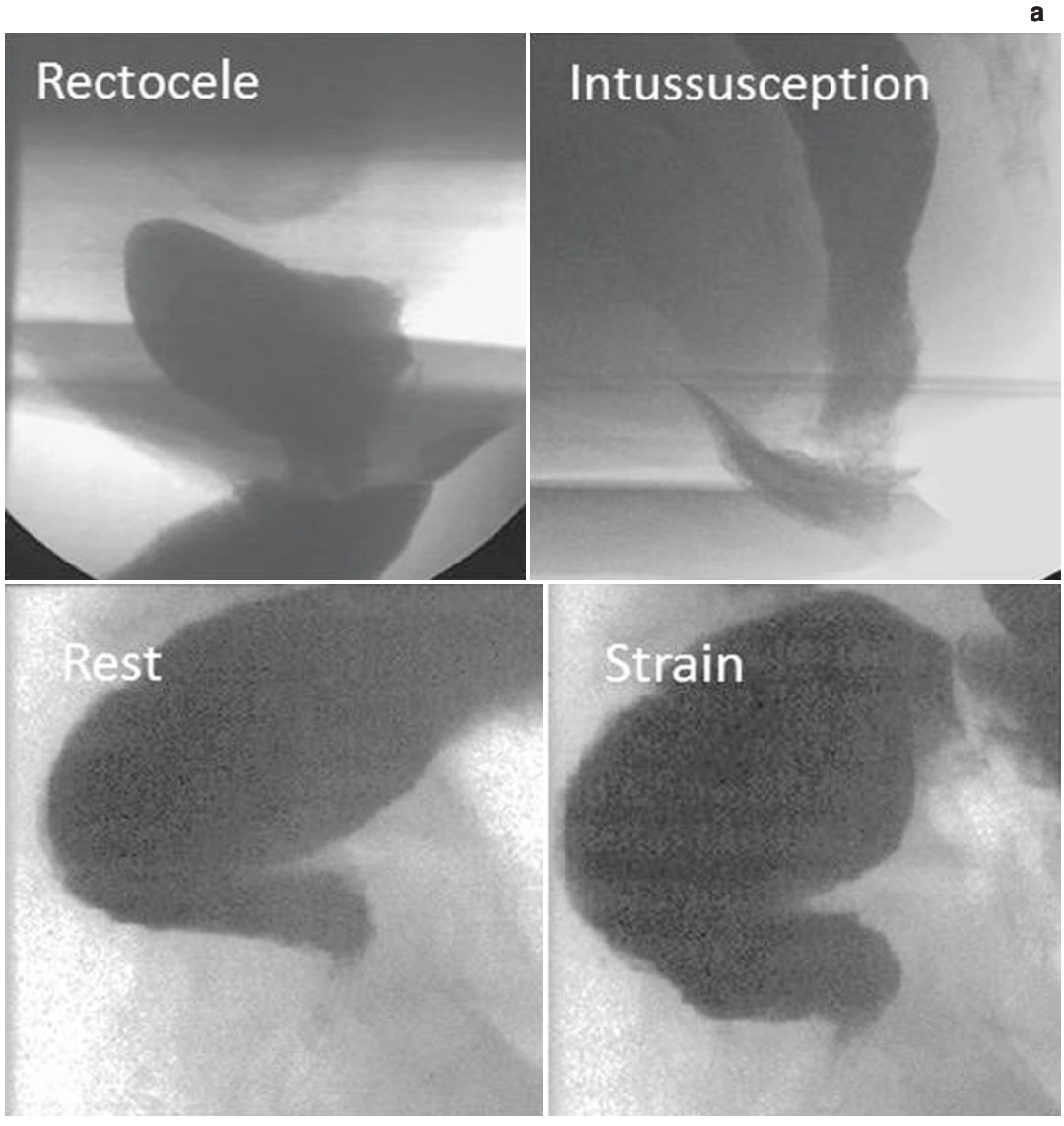


Fig. 10.2 (**a**) Fluoroscopic evacuation proctograms with common abnormalities highlighted. (**b**) High-resolution anorectal manometry traces from patients with chronic constipation, showing normal relaxation of the anal sphincter in response to the push maneuver, and a patient with dyssynergic defecation in whom there is an increase in rectal pressure but a concomitant strong paradoxical contraction of the anal sphincter (Courtesy of Dr. Mark Scott, Barts Health NHS Trust)

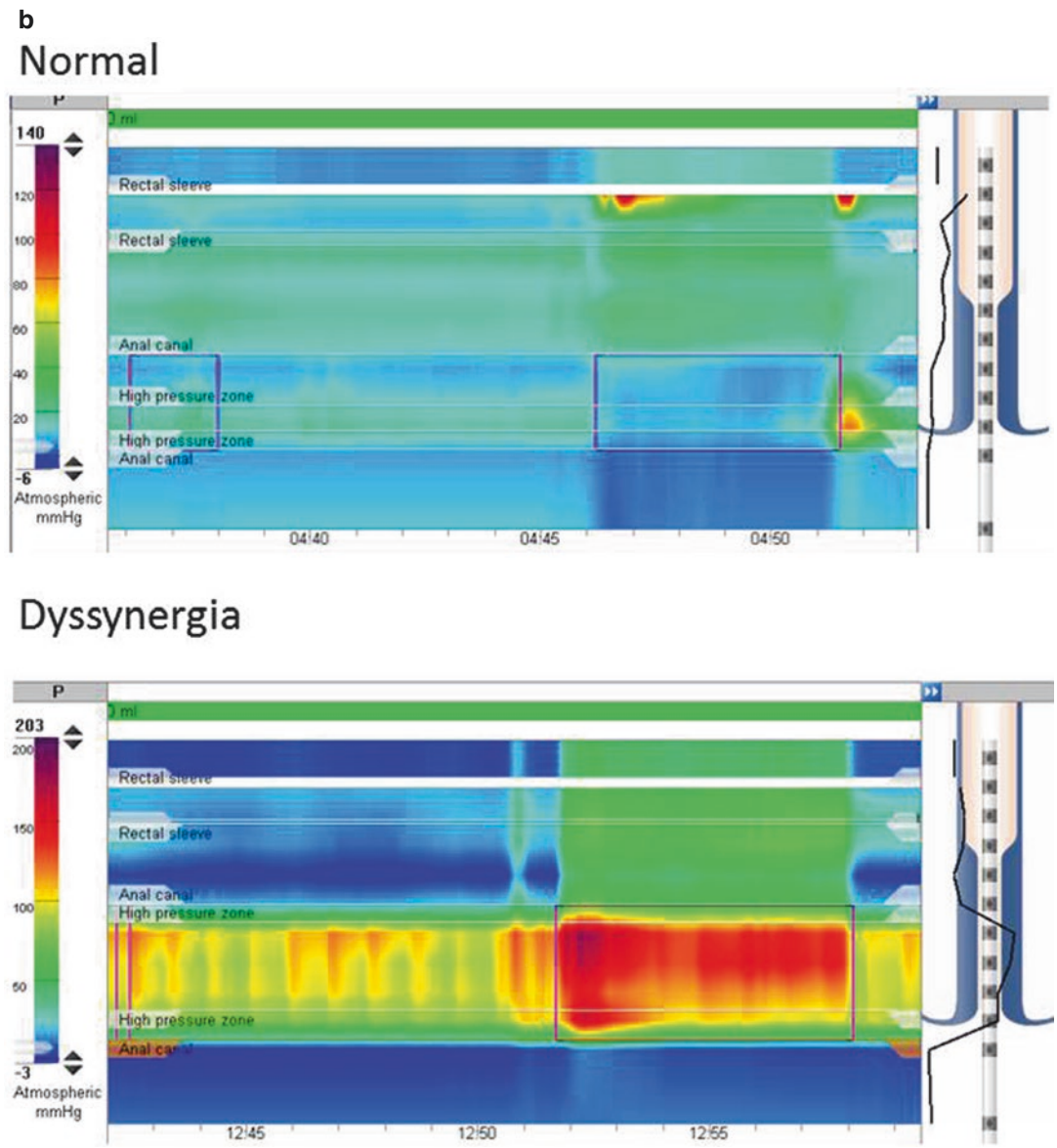


Fig. 10.2 (continued)

tion of pelvic floor structures in all compartments; it is, however, technically challenging in the sitting position and may underdetect abnormalities in the supine position.

In addition to the balloon expulsion test, pelvic floor evaluation generally involves manometry. Using standard (usually water-perfused) manometry, anal canal pressures are recorded at 1-cm intervals throughout the anal canal during rest and squeeze. A balloon is then rapidly expanded within the distal rectum and used to assess the rectoanal inhibitory reflex (relaxation of the internal sphincter to rectal distention). The presence of this reflex rules out adult Hirschsprung disease (HSCR; a rare cause of constipation in adults; see below). In many centers the ability of a patient to sense rectal progressive volumetric balloon distension [42] is also determined, since the loss of the urge to defecate may be caused by blunted rectal sensation (rectal hyposensation) [9]. In patients with a

suspected defecatory disorder, manometry can be used during a push maneuver to demonstrate either paradoxical contraction or inadequate relaxation of the pelvic floor muscles (dyssynergic defecation) or inadequate propulsive forces (or a combination of both) [43]. The utility of manometry in the diagnosis of dyssynergia [38] is contentious, however, and has been further questioned by recent studies using high-resolution manometry [44] (Fig. 10.2b). Finally, urodynamic testing may be indicated if combined surgery on multiple pelvic compartments is considered.

10.6 Treatment

10.6.1 Medical (Nonsurgical) Therapy

The following information is relevant to all patients with chronic constipation, although the use of oral drugs probably has the most relevance for transit disorders, whereas rectal laxatives, behavioral therapy, and anal irrigation are most relevant for defecation disorders (Chap. 11) (Fig. 10.3).

10.6.1.1 Laxatives

Many treatments can be initiated without prior specialist physiologic investigation. Following a detailed history, the patient's past drug use must be documented and can guide further therapy. The evidence base for an exact protocol of laxative use is poor (see Ref. [45]); only polyethylene glycol–based osmotic laxatives have been rigorously subjected to trials in the modern age of randomized controlled trials (RCTs) [46]. Nevertheless, stool softeners (e.g., docusate), stimulant laxatives (e.g., senna and bisacodyl), and osmotic laxatives (e.g., polyethylene glycol, lactulose, magnesium salts) may be used alone or in combination with good effect. Bulking agents often cause further abdominal pain and bloating in patients with chronic constipation. In addition, attempts to prescribe such products (like encouraging further dietary fiber intake, exercise, and fluids) are, in general, met with hostility by patients who exhausted such measures many years before, and they lead to an erosion of trust. In the absence of evidence, I make the following practical suggestions:

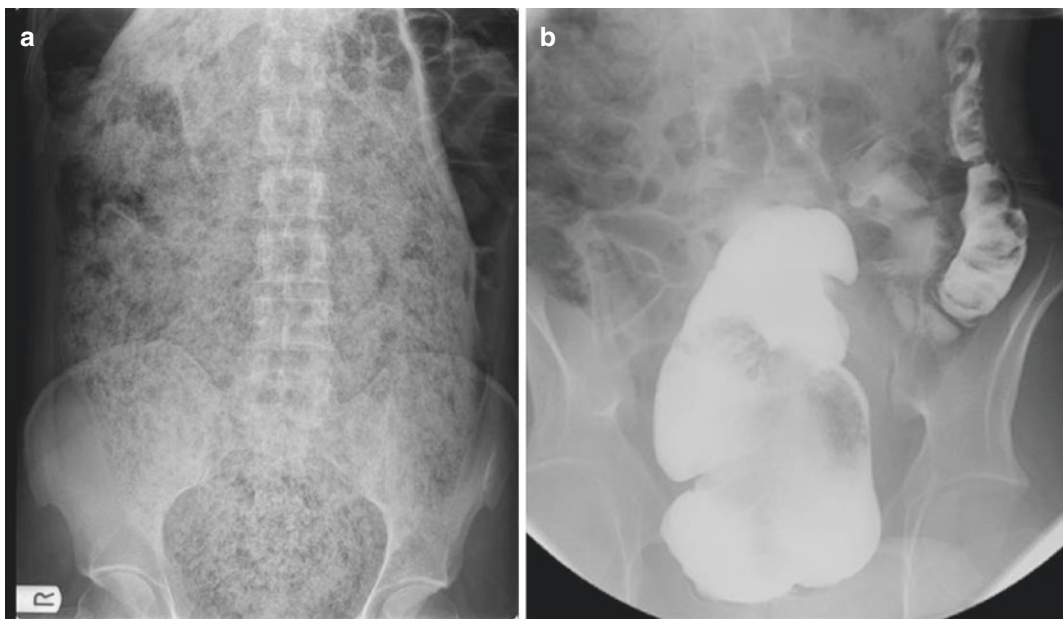


Fig. 10.3 (**a**) Plain film of a young male adult with gross idiopathic megarectum. (**b**) Barium enema in a different young male adult with a more modest megarectum (Courtesy of Dr. Mark Scott, Barts Health NHS Trust)

- Reassure the patient that modern laxatives do not damage the bowel.
- Try to stop the current use of all laxatives; that is, do something definite (this is referred to as "switching" in the psychiatric literature).
- Consider the use of rectal laxatives (with or without oral purgatives) in patients with defecatory symptoms; these often will not have been tried.
- Consider laxative dose titration (e.g., magnesium salts, Movicol sachets).
- Prescribe and monitor the chosen therapy at a fixed interval – say, 3 months (monitoring can be performed by specialist nurses).
- Warn the patient of side effects but emphasize the need for compliance with a regular dose (avoid intermittent reactive use of laxatives).
- Rotate the laxative type regularly at intervals to avoid tolerance.

10.6.1.2 Prokinetics and Secretagogues

Although laxatives are widely used by patients with chronic constipation, it is generally acknowledged that at least 50 % of patients remain dissatisfied with their results [47]. A theoretical problem with all classical laxative therapies is their bioavailability in the colon. All require transport to the colon (to reach the site of action), and some require metabolism via the enteral flora to produce active products (e.g., hydrolysis of stimulant laxatives). Further, laxatives are often poorly tolerated because of pain (mainly stimulant) or unpredictable diarrhea, with or without incontinence (mainly osmotic). Given the burden of disease, much has been invested to find newer classes of drugs to treat chronic constipation. To date, three drug classes are now marketed for chronic constipation and allied symptoms:

1. Selective serotonin receptor subtype 4 (5-HT_4) agonists (prokinetic)
2. CIC-2 chloride channel activators (intestinal secretagogue)
3. Guanylate cyclase-C receptor agonists (intestinal secretagogue and visceral hyperalgesic)

The main development in the 5-HT_4 agonist class is prucalopride. This drug has much greater selectivity to the 5-HT_4 receptor than 5-HT_4 agonists withdrawn from the market, such as tegaserod and cisapride. In particular, it has no proven effect on the QTc interval caused by activation of the cardiac conducting system channels, which led to arrhythmias with less selective drugs. Prucalopride has been the subject of three rigorous pivotal phase III trials, with pooled data available on >2,000 patients [48], and has also been trialed in the elderly. Abundant cross-species data (including humans) show that prucalopride leads to increases in propagated colonic contractile activity, leading to coordinated mass movements and spontaneous defecation. It has an acceptable side effect profile and is now licensed in Europe and the United States for women with chronic constipation, among whom it has a some effect in approximately 50 % patients [48]. In particular, it has a significant advantage over laxatives in terms of reducing rather than increasing abdominal pain and bloating. Two drugs, lubiprostone (Amitiza; a CIC-2 chloride channel activator) and linaclotide (Linzess; a heat-stable enterotoxin homologue guanylate cyclase C receptor activator) accelerate colonic transit in humans by mediating luminal secretion. Lubiprostone is reported to cause problematic nausea in approximately 20 % of patients [49]. Linaclotide is licensed for the treatment of constipation-predominant IBS [50] and, based on experimental evidence, may have particular benefit for patients in whom pain caused by visceral hypersensitivity is the main complaint.

10.6.1.3 Behavioral Therapy

In most practices patients are first referred to specialist nurses for a variety of nurse-led behavioral interventions to improve defecatory function. A range of cohort studies [51], RCTs [52], reviews, guidelines [38], and a meta-analysis [53] attest to the general success of this approach. However, opinion varies greatly concerning the complexity of intervention required, and practice varies remarkably. The most basic form of behavioral therapy comprises "habit training." This involves

optimizing dietary patterns to maximize the gastrocolic response and the morning clustering of colonic high-amplitude propagated contractions, which propel contents toward the rectum for subsequent evacuation. Advice is given on diet (to optimize intake of liquids and fiber) and about the frequency and duration of toilet visits and posture. Patients are also instructed on basic gut anatomy and function, and gain an appreciation of how psychological and social stresses may influence gut function. Simple pelvic floor and balloon expulsion exercises are often included.

More complex forms of therapy include instrument-based biofeedback learning techniques [51, 54]. Particularly favored in the United States, these provide direct visual computer-based biofeedback of pelvic floor activity. This (usually nurse-led) therapy retrains the patient to appropriately contract abdominal and relax pelvic floor muscles during defecation; the patient receives feedback of anal and pelvic floor muscle activity as recorded by surface electromyography, anal pressure sensors, or digital examination by the therapist. Several controlled trials and meta-analyses provide data on biofeedback outcomes in comparison with sham or alternative treatments (see the review in Ref. [32]). Opinions vary on which patient groups benefit most, with some favorable [51] and unfavorable results [52] for patients with slow-transit constipation. However, most would agree that this treatment is best targeted at those with defecatory disorders and particularly those with proven dyssynergia. Success rates range from approximately 70–90 % in adults with defecatory disorders [52], and a meta-analysis of three RCTs give an odds ratio of success over placebo of 3.7 (95 % confidence interval, 2.1–6.3) [53]. Training may have to be reinforced at intervals but is generally sustained over the long term. Of note, there has been no multicenter or adequately powered RCT of biofeedback versus habit training alone in unselected patients with chronic constipation. Further, most publications advocating biofeedback have come from specialist centers with considerable investment in these techniques; much less favorable reports come when biofeedback is the "devested" comparator [55].

10.6.1.4 Anal Irrigation

Anal irrigation using a variety of commercially available devices has been rapidly disseminated internationally over the past 3–5 years, first in patients with neurological injury [56] and subsequently in other groups with constipation. Despite a lack of published data other than from small selected case series, it is generally considered to be the next step for patients failing other nurse-led interventions. There are, however, ongoing concerns regarding the longevity of treatment and complications. While therapy might seem best directed toward those with defecatory disorders, audit data suggest efficacy in patients with all forms of chronic constipation [57].

10.6.2 Surgical Treatment

Surgical procedures directed at the anorectum and pelvic floor for defecatory disorders are covered in Chap. 11.

10.6.2.1 Colectomy

Until relatively recently, colonic excision was the only popularized form of surgery to address slow-transit constipation. It is a fact that colectomy has a "finality" that separates it not only from medical treatments but also from most other invasive interventions for constipation. The results of colectomy have been extensively reviewed [33, 58], with overall success rates varying between 40 and 100 %. It is probable that colectomy peaked in popularity in the mid-1990s; its application has gradually declined since publications of more modest longer-term results became available and the potential for serious complications and poor functional outcomes was realized. Nevertheless, most would agree that colectomy continues to have a limited role as a treatment option for highly selected patients with proven slow-transit constipation but normal or completely treated [59] evacuation who have failed all nonsurgical interventions and in whom symptoms are sufficiently severe to contemplate major surgery. Such surgery should only be undertaken in specialized centers where

techniques required for selection are available. Colectomy with ileorectal anastomosis has the most consistent results, leading to a median stool frequency of three per day (ranging from one to five per day). Unfortunately, surgery may not satisfactorily alleviate other symptoms (e.g., abdominal discomfort or bloating), and patients should be made aware of this possibility before the operation. Overall, the majority of well-selected patients are satisfied with the results of surgical treatment [59]; however, long-term postoperative complications, particularly small-bowel obstruction, are common. In addition, patients may manifest symptoms of a more global GI dysmotility disorder in the long term. To give an idea of selectivity, it is my practice to perform about two colectomies per annum among the hundreds of patients seen annually. The procedure can now be performed laparoscopically [60], making this a more attractive for young female patients. It is hoped that this will also reduce the disproportionately high incidence of adhesional small-bowel obstruction seen after colectomy in patients with slow-transit constipation [33].

10.6.2.2 Neuromodulation

The role of sacral nerve stimulation (SNS) is contentious. The publication of a multicenter European trial in 2010 showing a beneficial effect of SNS in 39 of 62 patients with chronic constipation (63 %) who predominantly had slow-transit constipation [61] has been followed by several less encouraging reports. Mechanistically, SNS increases pancolonic anterograde propagated sequences in patients with slow-transit constipation; however, more recent data from the same group suggest that such changes only occur with suprasensory stimulation [62]. Controlled studies are required, particularly since SNS is not cheap, but the attraction of this minimally invasive treatment, and the possibility to test patients before implanting the stimulator, make it a promising tool for patients who might otherwise progress to colectomy [58].

10.6.2.3 Stoma

A stoma may be used as a definitive procedure, as a guide for further treatment, or to salvage failed or complicated prior surgical intervention. Few published data support its evidence-based use; however, an ileostomy may be used as a guide to colectomy, and subsequent resection can be avoided if ileostomy output is unsatisfactorily high or symptoms such as pain and bloating are untouched by diversion [63]. As a definitive procedure, both colostomy and ileostomy have been described for a diversity of disorders characterized by constipation, including spinal cord injury, megacolon, and chronic idiopathic constipation. There is little evidence in adults to guide the choice of ileostomy or colostomy, but some studies report high complication rates of ileostomy, and slow-transit constipation may be unsatisfactorily treated by colostomy.

The Malone anterograde continent enema technique may be an option for refractory slow-transit constipation but has been used more frequently in patients with severe defecatory disorder when conservative methods and pelvic floor surgery have failed or are contraindicated [64]. In patients with previous appendicectomy or in whom the appendix cannot be satisfactorily used, cecostomy may be effected using a percutaneous Chait tube or by more complex surgical techniques [65]. In general, success rates are lower in adults [64, 65] than in children: approximately 50 % versus 80 % (see below). In the long-term, complications such as stoma stenosis or leakage, or failure to effectively treat symptoms commonly require revision (>50 % at 3 years), reversal, or conversion to a formal stoma [65].

10.7 Special Considerations

10.7.1 Megarectum and Megacolon

As noted above, the finding of chronic visceral dilatation in concert with chronic constipation is rare and may often point to a secondary cause such as central neurological disease, autonomic neuropathy (diabetes and paraneoplastic syndrome), connective tissue disease, and Chagas disease. In such instances, global dysmotility may also manifest with dysphagia, gastric emptying disturbances, and small-bowel dysmotility with or without dilatation (the latter is termed

Table 10.3 Nomenclature in acute and chronic nonmechanical visceral dilatation

Region	Small bowel	Colon
Time course		
Acute	Ileus	Acute colonic pseudo-obstruction
Chronic	Intestinal pseudo-obstruction	Megacolon

chronic intestinal pseudo-obstruction). Chronic dilatation of the rectum or colon is termed *megarectum* or *megacolon*, respectively, although they frequently coexist (sometimes termed *megabowel*). When no secondary cause is evident, the term *idiopathic* is applied. Table 10.3 should serve as an aid to understanding the globally confusing nomenclature in this area.

Idiopathic megarectum in its classic form is, in my opinion, a distinct condition from megacolon. The condition nearly always starts in infancy or early childhood, is predominant in males [66], and is usually associated with psychobehavioral conditions, for example, variants of autism (a casual genetic link was just recently established [67]), learning disorders [66], or neurological disorders. In this situation it is widely assumed that chronic inhibition of defecatory behavior leads to a bolus distension of the rectum. The resulting megarectum may be huge (the size of a full-term pregnancy) (Fig. 10.2), and the condition is terribly debilitating for the child and parents because of the pain and overflow incontinence, including nocturnal encopresis [66]. The management of this condition is difficult and almost always involves surgery at some stage (this is reviewed extensively elsewhere). By contrast, idiopathic megacolon is, in my view, more akin to an extreme, rare variant of slow-transit constipation. It is thus a female-predominant condition that presents during childhood or adulthood [66]. In general, such colons become flaccid and fail to generate useful propulsive motility, despite maximal pharmacologic intervention. The management of such patients usually requires colonic resection and/or a stoma. Referral to a specialist center is recommended for patients with idiopathic megabowel.

10.7.2 Hirschsprung Disease

HSCR is a genetically determined intestinal obstruction syndrome (OMIM 142623) that occurs in approximately 1 in 5,000 live births and is predominant in males (male-to-female ratio of 4:1 in short-segment HSCR and 2:1 in long-segment HSCR). The classical form is short-segment (also called type I HSCR), affecting approximately 60–85 % of cases and characterized by a failure of enteric nervous system (ENS) formation (aganglionosis) restricted to the rectum and, in continuity, a short portion of the colon distal to the splenic flexure. In the rarer form, affecting approximately 15–25 % of cases, the aganglionic segment is longer (type II HSCR) and extends proximally to affect more of the bowel, including the entire colon (8–10 %) or even the entire intestine. A variety of single-gene defects have been detected in approximately 40 % patients and are more common in the familial and syndromic forms [68].

HSCR is often included in discussions of chronic constipation because some adults or older children with either megarectum or megacolon may have previously undetected classic or "very short segment disease" [69]. Clinical features may resemble megacolon (classic disease) or megarectum (short-segment disease) [69]. A demonstration of the rectoanal inhibitory reflex is included in standard anorectal manometry protocols (see investigation section), and its presence excludes HSCR. I have never seen a patient with conclusively proven adult HSCR, and although deep submucosal or strip myectomy rectal biopsies are occasionally performed in adults, it could be concluded that this presentation is extremely rare, at least among Western populations in the modern age of pre- and postnatal diagnoses.

References

1. Knowles CH, Madoff RD. Chronic constipation. In, Ashley SW (Ed): ACS Surgery 7, Principles and Practice, 2013; Decker Intellectual Properties.
2. Dinning PG, Di Lorenzo C. Colonic dysmotility in constipation. Best Pract Res Clin Gastroenterol. 2011;25(1):89–101. Epub 2011/03/09.
3. Bassotti G, Gaburri M, Imbimbo BP, Rossi L, Farroni F, Pelli MA, et al. Colonic mass movements in idiopathic

chronic constipation. Gut. 1988;29(9):1173–9. Epub 1988/09/01.
4. Dinning PG, Smith TK, Scott SM. Pathophysiology of colonic causes of chronic constipation. Neurogastroenterol Motil: Off J Eur Gastrointest Motil Soc. 2009;21 Suppl 2:20–30. Epub 2009/10/15.
5. King SK, Catto-Smith AG, Stanton MP, Sutcliffe JR, Simpson D, Cook I, et al. 24-Hour colonic manometry in pediatric slow transit constipation shows significant reductions in antegrade propagation. Am J Gastroenterol. 2008;103(8):2083–91. Epub 2008/06/20.
6. Dinning PG, Bampton PA, Kennedy ML, Lubowski DZ, King D, Cook IJ. Impaired proximal colonic motor response to rectal mechanical and chemical stimulation in obstructed defecation. Dis Colon Rectum. 2005;48(9):1777–84. Epub 2005/06/28.
7. Klauser AG, Voderholzer WA, Heinrich CA, Schindlbeck NE, Muller-Lissner SA. Behavioral modification of colonic function. Can constipation be learned? Dig Dis Sci. 1990;35(10):1271–5. Epub 1990/10/01.
8. Palit S, Lunniss PJ, Scott SM. The physiology of human defecation. Dig Dis Sci. 2012;57(6):1445–64. Epub 2012/03/01.
9. Gladman MA, Lunniss PJ, Scott SM, Swash M. Rectal hyposensitivity. Am J Gastroenterol. 2006;101(5): 1140–51. Epub 2006/05/16.
10. Knowles CH, Farrugia G. Gastrointestinal neuromuscular pathology in chronic constipation. Best Pract Res Clin Gastroenterol. 2011;25(1):43–57. Epub 2011/03/09.
11. Knowles CH, De Giorgio R, Kapur RP, Bruder E, Farrugia G, Geboes K, et al. Gastrointestinal neuromuscular pathology: guidelines for histological techniques and reporting on behalf of the Gastro 2009 International Working Group. Acta Neuropathol. 2009;118(2):271–301. Epub 2009/04/11.
12. Wattchow D, Brookes S, Murphy E, Carbone S, de Fontgalland D, Costa M. Regional variation in the neurochemical coding of the myenteric plexus of the human colon and changes in patients with slow transit constipation. Neurogastroenterol Motil: Off J Eur Gastrointest Motil Soc. 2008;20(12):1298–305. Epub 2008/07/30.
13. King SK, Sutcliffe JR, Ong SY, Lee M, Koh TL, Wong SQ, et al. Substance P and vasoactive intestinal peptide are reduced in right transverse colon in pediatric slow-transit constipation. Neurogastroenterol Motil: Off J Eur Gastrointest Motil Soc. 2010;22(8):883–92. e234. Epub 2010/06/10.
14. He CL, Burgart L, Wang L, Pemberton J, Young-Fadok T, Szurszewski J, et al. Decreased interstitial cell of cajal volume in patients with slow-transit constipation. Gastroenterology. 2000;118(1):14–21. Epub 1999/12/28.
15. Drossman DA, Leserman J, Nachman G, Li ZM, Gluck H, Toomey TC, et al. Sexual and physical abuse in women with functional or organic gastrointestinal disorders. Ann Intern Med. 1990;113(11):828–33. Epub 1990/12/01.
16. Wald A, Hinds JP, Caruana BJ. Psychological and physiological characteristics of patients with severe idiopathic constipation. Gastroenterology. 1989;97(4): 932–7. Epub 1989/10/01.
17. Xiao ZL, Pricolo V, Biancani P, Behar J. Role of progesterone signaling in the regulation of G-protein levels in female chronic constipation. Gastroenterology. 2005;128(3):667–75. Epub 2005/03/15.
18. Stewart WF, Liberman JN, Sandler RS, Woods MS, Stemhagen A, Chee E, et al. Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. Am J Gastroenterol. 1999;94(12):3530–40. Epub 1999/12/22.
19. van den Berg MM, Benninga MA, Di Lorenzo C. Epidemiology of childhood constipation: a systematic review. Am J Gastroenterol. 2006;101(10):2401–9. Epub 2006/10/13.
20. Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(9):1582–91. quiz 1, 92. Epub 2011/05/25.
21. Shafe AC, Lee S, Dalrymple JS, Whorwell PJ. The LUCK study: laxative usage in patients with GP-diagnosed constipation in the UK, within the general population and in pregnancy. An epidemiological study using the General Practice Research Database (GPRD). Ther Adv Gastroenterol. 2011;4(6):343–63. Epub 2011/11/02.
22. Pare P, Ferrazzi S, Thompson WG, Irvine EJ, Rance L. An epidemiological survey of constipation in Canada: definitions, rates, demographics, and predictors of health care seeking. Am J Gastroenterol. 2001;96(11):3130–7. Epub 2001/11/28.
23. Preston DM, Lennard-Jones JE. Severe chronic constipation of young women: 'idiopathic slow transit constipation'. Gut. 1986;27(1):41–8. Epub 1986/01/01.
24. Drossman DA, Li Z, Andruzzi E, Temple RD, Talley NJ, Thompson WG, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci. 1993;38(9):1569–80. Epub 1993/09/01.
25. Ashraf W, Park F, Lof J, Quigley EM. An examination of the reliability of reported stool frequency in the diagnosis of idiopathic constipation. Am J Gastroenterol. 1996;91(1):26–32. Epub 1996/01/01.
26. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130(5):1480–91. Epub 2006/05/09.
27. An evidence-based approach to the management of chronic constipation in North America. Am J Gastroenterol. 2005;100 Suppl 1:S1–4. Epub 2005/07/13.
28. Ragg J, McDonald R, Hompes R, Jones OM, Cunningham C, Lindsey I. Isolated colonic inertia is not usually the cause of chronic constipation. Colorectal Dis: Off J Assoc Coloproctology G B Irel. 2011;13(11):1299–302. Epub 2010/10/21.

29. Glia A, Lindberg G, Nilsson LH, Mihocsa L, Akerlund JE. Constipation assessed on the basis of colorectal physiology. Scand J Gastroenterol. 1998;33(12):1273–9. Epub 1999/02/04.
30. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum. 1996;39(6):681–5. Epub 1996/06/01.
31. Dubois D, Gilet H, Viala-Danten M, Tack J. Psychometric performance and clinical meaningfulness of the Patient Assessment of Constipation-Quality of Life questionnaire in prucalopride (RESOLOR) trials for chronic constipation. Neurogastroenterol Motil: Off J Eur Gastrointest Motil Soc. 2010;22(2):e54–63. Epub 2009/09/19.
32. Camilleri M, Bharucha AE. Behavioural and new pharmacological treatments for constipation: getting the balance right. Gut. 2010;59(9):1288–96. Epub 2010/08/31.
33. Knowles CH, Scott M, Lunniss PJ. Outcome of colectomy for slow transit constipation. Ann Surg. 1999;230(5):627–38. Epub 1999/11/24.
34. Hinton JM, Lennard-Jones JE. Constipation: definition and classification. Postgrad Med J. 1968;44(515):720–3. Epub 1968/09/01.
35. Scott SM, Knowles CH, Newell M, Garvie N, Williams NS, Lunniss PJ. Scintigraphic assessment of colonic transit in women with slow-transit constipation arising de novo and following pelvic surgery or childbirth. Br J Surg. 2001;88(3):405–11. Epub 2001/03/22.
36. Rao SS, Kuo B, McCallum RW, Chey WD, DiBaise JK, Hasler WL, et al. Investigation of colonic and whole-gut transit with wireless motility capsule and radiopaque markers in constipation. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2009;7(5):537–44. Epub 2009/05/07.
37. Barnes PR, Lennard-Jones JE. Balloon expulsion from the rectum in constipation of different types. Gut. 1985;26(10):1049–52. Epub 1985/10/01.
38. Bharucha AE, Dorn SD, Lembo A, Pressman A. American gastroenterological association medical position statement on constipation. Gastroenterology. 2013;144(1):211–7. Epub 2012/12/25.
39. Womack NR, Williams NS, Holmfield JH, Morrison JF, Simpkins KC. New method for the dynamic assessment of anorectal function in constipation. Br J Surg. 1985;72(12):994–8. Epub 1985/12/01.
40. Palit S, Bhan C, Lunniss PJ, Boyle DJ, Gladman MA, Knowles CH, et al. Evacuation proctography: a reappraisal of normal variability. Colorectal Dis: Off J Assoc Coloproctol G B Irel. Neurogastroenterol Motil. 2016;28(10):1589–98.
41. Shorvon PJ, Mchugh F, Somers S, Stevenson GW. Defecographic findings in young healthy-volunteers. Gut. 1987;28(10):A1361–2.
42. Jameson JS, Chia YW, Kamm MA, Speakman CTM, Chye YH, Henry MM. Effect of age, sex and parity on anorectal function. Br J Surg. 1994;81(11):1689–92.
43. Scott SM, Gladman MA. Manometric, sensorimotor, and neurophysiologic evaluation of anorectal function. Gastroenterol Clin N Am. 2008;37(3):511–38. vii. Epub 2008/09/17.
44. Ratuapli SK, Bharucha AE, Noelting J, Harvey DM, Zinsmeister AR. Phenotypic identification and classification of functional defecatory disorders using high-resolution anorectal manometry. Gastroenterology. 2013;144(2):314–22. e2. Epub 2012/11/13.
45. Emmanuel AV, Tack J, Quigley EM, Talley NJ. Pharmacological management of constipation. Neurogastroenterol Motil. 2009;21 Suppl 2:41–54. Epub 2009/10/15.
46. Corazziari E, Badiali D, Bazzocchi G, Bassotti G, Roselli P, Mastropaolo G, et al. Long term efficacy, safety, and tolerabilitity of low daily doses of isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in the treatment of functional chronic constipation. Gut. 2000;46(4):522–6. Epub 2000/03/15.
47. Wald A, Scarpignato C, Mueller-Lissner S, Kamm MA, Hinkel U, Helfrich I, et al. A multinational survey of prevalence and patterns of laxative use among adults with self-defined constipation. Aliment Pharmacol Ther. 2008;28(7):917–30. Epub 2008/07/23.
48. Camilleri M, Kerstens R, Rykx A, Vandeplassche L. A placebo-controlled trial of prucalopride for severe chronic constipation. N Engl J Med. 2008;358(22):2344–54. Epub 2008/05/30.
49. Johanson JF, Drossman DA, Panas R, Wahle A, Ueno R. Clinical trial: phase 2 study of lubiprostone for irritable bowel syndrome with constipation. Aliment Pharmacol Ther. 2008;27(8):685–96. Epub 2008/02/06.
50. Chey WD, Lembo AJ, Lavins BJ, Shiff SJ, Kurtz CB, Currie MG, et al. Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. Am J Gastroenterol. 2012;107(11):1702–12. Epub 2012/09/19.
51. Chiotakakou-Faliakou E, Kamm MA, Roy AJ, Storrie JB, Turner IC. Biofeedback provides long-term benefit for patients with intractable, slow and normal transit constipation. Gut. 1998;42(4):517–21. Epub 1998/06/09.
52. Chiarioni G, Salandini L, Whitehead WE. Biofeedback benefits only patients with outlet dysfunction, not patients with isolated slow transit constipation. Gastroenterology. 2005;129(1):86–97. Epub 2005/07/14.
53. Enck P, Van der Voort IR, Klosterhalfen S. Biofeedback therapy in fecal incontinence and constipation. Neurogastroenterol Motil: Off J Eur Gastrointest Motil Soc. 2009;21(11):1133–41. Epub 2009/07/02.
54. Chiarioni G, Whitehead WE, Pezza V, Morelli A, Bassotti G. Biofeedback is superior to laxatives for normal transit constipation due to pelvic floor dyssynergia. Gastroenterology. 2006;130(3):657–64. Epub 2006/03/15.
55. Lehur PA, Stuto A, Fantoli M, Villani RD, Queralto M, Lazorthes F, et al. Outcomes of stapled transanal rectal resection vs. biofeedback for the treatment of outlet obstruction associated with rectal intussusception and

rectocele: a multicenter, randomized, controlled trial. Dis Colon Rectum. 2008;51(11):1611–8. Epub 2008/07/22.
56. Christensen P, Krogh K, Buntzen S, Payandeh F, Laurberg S. Long-term outcome and safety of transanal irrigation for constipation and fecal incontinence. Dis Colon Rectum. 2009;52(2):286–92. Epub 2009/03/13.
57. Emmanuel AV, Krogh K, Bazzocchi G, Leroi AM, Bremers A, Leder D, et al. Consensus review of best practice of transanal irrigation in adults. Spinal Cord. 2013;51(10):732–8. Epub 2013/08/21.
58. Knowles CH, Dinning PG, Pescatori M, Rintala R, Rosen H. Surgical management of constipation. Neurogastroenterol Motil. 2009;21 Suppl 2:62–71. Epub 2009/10/15.
59. Nyam DC, Pemberton JH, Ilstrup DM, Rath DM. Long-term results of surgery for chronic constipation. Dis Colon Rectum. 1997;40(3):273–9. Epub 1997/03/01.
60. Kessler H, Hohenberger W. Laparoscopic total colectomy for slow-transit constipation. Dis Colon Rectum. 2005;48(4):860–1. Epub 2005/03/16.
61. Kamm MA, Dudding TC, Melenhorst J, Jarrett M, Wang Z, Buntzen S, et al. Sacral nerve stimulation for intractable constipation. Gut. 2010;59(3):333–40. Epub 2010/03/09.
62. Dinning PG, Hunt LM, Arkwright JW, Patton V, Szczesniak MM, Wiklendt L, et al. Pancolonic motor response to subsensory and suprasensory sacral nerve stimulation in patients with slow-transit constipation. Br J Surg. 2012;99(7):1002–10. Epub 2012/05/05.
63. Wong SW, Lubowski DZ. Slow-transit constipation: evaluation and treatment. ANZ J Surg. 2007;77(5):320–8. Epub 2007/05/15.
64. Hirst GR, Arumugam PJ, Watkins AJ, Mackey P, Morgan AR, Carr ND, et al. Antegrade continence enema in the treatment of obstructed defaecation with or without faecal incontinence. Tech Coloproctol. 2005;9(3):217–21. Epub 2005/12/06.
65. Lees NP, Hodson P, Hill J, Pearson RC, MacLennan I. Long-term results of the antegrade continent enema procedure for constipation in adults. Colorectal Dis: Off J Assoc Coloproctology G B Irel. 2004;6(5):362–8. Epub 2004/09/01.
66. Gattuso JM, Kamm MA. Clinical features of idiopathic megarectum and idiopathic megacolon. Gut. 1997;41(1):93–9. Epub 1997/07/01.
67. Bernier R, Golzio C, Xiong B, Stessman HA, Coe BP, Penn O, et al. Disruptive CHD8 mutations define a subtype of autism early in development. Cell. 2014;158(2):263–76. Epub 2014/07/08.
68. Panza E, Knowles CH, Graziano C, Thapar N, Burns AJ, Seri M, et al. Genetics of human enteric neuropathies. Prog Neurobiol. 2012;96(2):176–89. Epub 2012/01/24.
69. Luukkonen P, Heikkinen M, Huikuri K, Jarvinen H. Adult Hirschsprung's disease. Clinical features and functional outcome after surgery. Dis Colon Rectum. 1990;33(1):65–9. Epub 1990/01/01.

Defecation Disorders

11

Laurent Siproudhis and Paul-Antoine Lehur

Dyschezia refers to the inability to efficiently and rapidly empty the rectum of its contents on demand. Defecation disorders involve both functional and anatomic considerations when symptoms related to obstructed defecation coexist with abnormal anal function (anismus), rectocele, intussusception, or overt rectal prolapse. Symptoms are a source of discomfort and significantly impair the quality of life of afflicted patients. Management requires a thorough clinical and functional assessment to identify the underlying cause. Medical treatment and pelvic floor retraining are first-line treatments. Various surgical approaches currently available are designed to correct anatomic abnormalities in order to improve function and may be performed in selected patients.

L. Siproudhis, MD, PhD (✉)
Service des Maladies de l'Appareil Digestif, CHU Pontchaillou, Rue Henri Le Guilloux,
35033 Rennes Cedex 09, France
e-mail: laurent.siproudhis@chu-rennes.fr

P.-A. Lehur, MD, PhD
Clinique de chirurgie digestive et endocrinienne, Institut des Maladies de l'Appareil Digestif (IMAD), Hôtel-Dieu. 1, place Ricordeau, 44093 Nantes Cedex 01, France

11.1 Definition – Epidemiology

Impaired defecation is a commonly reported symptom. It is covered by the general term *constipation*, which refers to infrequent or qualitatively inadequate defecation when compared with the normal scheme (Appendix 1). Defecation disorders, also called "outlet obstruction/delay" or "dyschezia," are integrated into the Rome III definition of chronic constipation (Table 11.1).

While the exact prevalence of constipation of the outlet delay type is unknown, it is recognized as a common health problem. In several population surveys, the prevalence of symptoms compatible with outlet obstruction has been as high as 30 %. It is accepted that about one-third of patients who present to their physician complaining of constipation demonstrate evidence of outlet obstruction [1]. Studies from referral centers also show a higher incidence of outlet delay than slow-transit constipation (60 % vs. 30 %, with the two types of constipation combined in 5 % of cases).

Defecation disorders occur significantly more frequently in women than in men. Prevalence increases with advancing age in both sexes, and the elderly, especially women, are frequently affected. The reasons for the female predisposition toward evacuation problems include pelvic floor alteration related to childbirth through vaginal delivery, long-lasting and excessive straining

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_11

Table 11.1 Rome III definitions of functional defecation disorders (www.romecriteria.org/criteria/)

Diagnostic criteria for functional constipation
1. Must include two or more of the following:
(a) Straining during at least 25 % of defecations
(b) Lumpy or hard stools in at least 25 % of defecations
(c) Sensation of incomplete evacuation for at least 25 % of defecations
(d) Sensation of anorectal obstruction/blockage for at least 25 % of defecations
(e) Manual maneuvers to facilitate at least 25 % of defecations (e.g., digital evacuation, support of the pelvic floor)
(f) Fewer than three defecations per week
2. Loose stools are rarely present without the use of laxatives.
3. Insufficient criteria for irritable bowel syndrome
Functional defecation disorders
Diagnostic criteria[a]
1. The patient must satisfy diagnostic criteria for functional constipation**
2. During repeated attempts to defecate, must have at least two of the following:
(a) Evidence of impaired evacuation, based on balloon expulsion test or imaging
(b) Inappropriate contraction of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or <20 % relaxation of the basal resting sphincter pressure by manometry, imaging, or electromyography
(c) Inadequate propulsive forces assessed by manometry or imaging
Dyssynergic defecation
Inappropriate contraction of the pelvic floor or <20 % relaxation of the basal resting sphincter pressure with adequate propulsive forces during attempted defecation
Inadequate defecatory propulsion
Inadequate propulsive forces with or without inappropriate contraction or <25 % relaxation of the anal sphincter during attempted defecation

[a]Criteria fulfilled for the past 6 months, with symptom onset at least 6 months before diagnosis
**As described here above

when passing stool, postmenopausal hormonal estrogen deprivation, previous hysterectomy, and association with urogenital prolapse and urinary incontinence. A genetic predisposition to pelvic organ prolapse is also recognized as a predisposing factor.

11.2 Etiology – Pathophysiology

Impaired defecation may result from various functional and/or anatomic disorders combined in a complex syndrome that is still not completely understood.

11.2.1 Functional Anal Obstruction

Inappropriate contraction of the pelvic floor or ineffective relaxation of striated muscles on the pelvic floor during attempted defecation impedes the passage of stool. Anal dyssynergia or anismus refers to this situation. Neurologic disorders such as spinal cord lesions and multiple sclerosis may also be responsible. In rare instances the functional obstruction is due to the ineffective inhibition of the internal anal sphincter with failure of the rectoanal inhibitory reflex, as occurs in Hirschsprung disease, Chagas disease, and hereditary myopathy of the internal anal sphincter. This feature may be encountered in association with pelvic organ prolapse [2].

11.2.2 Rectal Inertia – Rectal Hyposensitivity – Megarectum

The failure to increase intra-abdominal/intrarectal pressure to a level sufficient to allow defecation frequently occurs in elderly or debilitated patients and accumulates stool in the rectum,

leading to fecal impaction (or fecaloma). In some conditions, defined as "rectal inertia" or "megarectum" and occurring in young patients, the rectum and often the distal sigmoid colon dilate and attempts to evacuate are ineffective. Abnormal rectal sensation during rectal filling, termed *rectal hyposensitivity* (blunted rectum), may be present and is caused by diabetes mellitus, multiple sclerosis, cerebrospinal disease, or direct injury to the pelvic nerves during hysterectomy or following disc (L5–S1) surgery.

11.2.3 Excessive Perineal Descent

Perineal descent during defecation that exceeds 4 cm is associated with evacuation difficulties. It is caused by weakness of the pelvic floor support as a consequence of stretching of or stress on the nerves, ligaments, and muscles of the pelvis during childbirth. Perineal descent may be associated with sacral nerve damage, secondary muscular atrophy, and eventually fecal incontinence, leading to the so-called descending perineum syndrome. It is, however, unclear whether perineal descent itself induces dyschezia.

11.2.4 Anatomic Defects and Deformities of the Rectal Reservoir

In addition to functional disorders, anatomic abnormalities may lead to impaired rectal evacuation. Any prolapsing organ pressing on mechanoreceptors adjacent to the rectum may give the patient the perception of impending defecation and disturb the normal evacuation process.

- Rectocele is defined as a herniation of the anterior rectal wall into the posterior vagina.
- Enterocele is the insinuation of a viscus (the small bowel or sigmoid colon) between the posterior vaginal wall and rectum into a herniated pouch of Douglas.
- Rectal intussusception (also known as "internal procidentia" or "occult rectal prolapse") is defined as an incomplete, nonexteriorized rectal prolapse. Infolding of the rectal wall is a common finding in healthy individuals, but high-grade intussusception reaching the anal canal may contribute to defecation disorders.

11.3 Diagnostics

11.3.1 Symptoms

History-taking is essential in defining what symptom causes the patient the most problems. Questions must assess various factors:

- Presence of an urge to defecate (patients with colonic inertia rarely have a need, but patients with defecation disorders have the urge to defecate daily)
- Bowel frequency, stool consistency, and size (best assessed using the Bristol stool chart)
- Use of laxatives, suppositories, and enemas
- Duration of the problem and the circumstances in which it occurs
- Maneuvers and digitations that the patient performs to help him-/herself evacuate
  - Vaginal digitation suggests a rectocele
  - Leaning forward on the toilet seat suggests an enterocele
  - Massaging lateral to the anus suggests poor rectal contractility
  - Use of enemas and/or suppositories may suggest megarectum
  - Supporting the perineum is used in abnormal perineal descent

Typical symptoms of obstructed defecation, with variations according to the type of disorder, are presented in Table 11.2. These symptoms are best assessed using standardized questionnaires specifically designed for this purpose [3] (Table 11.3). A diary of gastrointestinal complaints and defecation habits can be helpful. The presence of fecal incontinence is also established and, if present, scored. Abdominal pain and bloating may be present, as irritable bowel syndrome is frequently associated with defecation disorders. Associated urogynecologic symptoms

Table 11.2 Symptoms to be searched in defecation disorders

Inability to empty the rectum (sometimes even for soft or liquid stool)
Excessive and prolonged straining efforts and time spent in toilets
Feeling of incomplete and/or fragmented, unsatisfactory evacuation
Pain and perineal discomfort in the standing position and/or at defecation
Need for (intra-anal, perineal, or vaginal) stimulation and manual evacuation
Rectal bleeding and mucous discharge
Use of laxatives, suppositories, enemas

Table 11.3 Severity of disease index for obstructed defecation

	Score				
Variables	0	1	2	3	4
Mean time spent on the toilet	≤5 min	6–10 min	11–20 min	21–30 min	>30 min
Attempts to defecate per day, *n*	1	2	3–4	5–6	>6
Anal/vaginal digitations	Never	>1/month, <1/ week	Once a week	Two to three per week	Every defecation
Use of laxatives	Never	>1/month, <1/ week	Once a week	Two to three per week	Every day
Incomplete/fragmented defecation	Never	>1/month, <1/ week	Once a week	Two to three per week	Every defecation
Straining during defecation	Never	<25 % of the time	<50 % of the time	<75 % of the time	Every defecation
Stool consistency	Soft	Hard	Hard and few	Fecaloma formation	

This score, ranging from 0 (normal) to 31 points, has been validated and is recommended for the assessment of patients and for research purposes [3]

including urinary incontinence, dyspareunia, and manifestations of urogenital prolapse must also be identified.

Any history of proctologic, obstetric, gynecologic, and/or urologic conditions should be carefully established. Obtaining psychological or psychiatric advice is relevant in select cases, particularly if surgery is contemplated. Underlying personal problems are frequently present, and this patient population more likely to have suffered some form of sexual abuse during childhood and is more depressed than a normal population.

11.3.2 Examination – Clinical Findings

After an abdominal examination, the patient is placed in the lithotomy position for a complete perineal and anorectal examination. The following must be clinically assessed:

- Descent/elevation of the perineum on command, at inspection
  - Inability to coordinate pelvic floor relaxation with failure of the perineum to descend more than 1 cm upon straining (frozen perineum) strongly favors anismus.
- Anal resting tone and squeeze pressure on digital examination and the integrity of the sphincteric ring
  - Anismus is evoked in the case of hypertonia.
  - Fecal incontinence and soiling may result from low anal tone or chronic impaction.
- Presence of anal stenosis
- Presence of associated hemorrhoidal disease, mucosal prolapse, or full-thickness prolapse
  - Insertion of a proctoscope allows an anterior wall prolapse, an internal prolapse, or the beginning of an external prolapse to be visualized upon straining.
- Rectovaginal wall and anterior rectal wall integrity to identify a rectocele or an enterocele
  - Enterocele is not easy to distinguish on simple clinical grounds (vaginal and rectal examination, bidigital examination, speculum examination, standing position).

  - Vaginal bulging is graded as I (intravaginal), II (reaching the introitus), or III (exteriorized).
  - Rectoceles are classified according to their position relative to the vagina: low (with thinning of the perineal body and sometimes anal sphincter disruption), middle, and high (commonly associated with enterocele).
- Entire pelvic floor and the relationship of the rectum to the remainder of the pelvic organs to document anterior compartment prolapse (uterine, cystocele, or vaginal vault) and urinary incontinence.

11.3.3 Workup

Most patients clinically identified as suffering from defecation disorders require a series of tests to assess anorectal and colonic function for further management (Table 11.4). These methods, used for evaluation in constipated patients, give objective measurements of colorectal function. However, their limitations must be kept in mind and the results analyzed in light of the symptoms and clinical findings [4].

The presence of an organic cause of constipation (e.g., cancer, stricture from any cause) is excluded by appropriate means – usually colonoscopy. Information from a standard gynecologic workup (mammography, pelvic ultrasound, cervicovaginal smears) is obtained as appropriate.

11.3.4 Dynamic Defecography

Dynamic changes in the anatomic structures of the pelvis are studied during simulated defecation.

11.3.5 Standard Dynamic Defecography

Technique: A semisolid artificial barium stool is injected into the rectum with concomitant filling of the small bowel, usually also the vagina and bladder. The patient is placed on a specially designed commode. Lateral video-radiographs are taken before, during, and after defecation.

Table 11.4 Tests eventually required when assessing disordered defecation

Dynamic defecography
Anorectal physiology tests
Colonic transit time
Endoanal ultrasound
Urological/gynecological workup

Defecographic parameters include the

- position of the pelvic floor
- anorectal angle at rest and during straining and evacuation
- opening of the anal canal and time to and completeness of emptying

A rectocele, if present, is defined by its size, barium trapping, and incomplete evacuation (Fig. 11.1). Rectal intussusception is graded according to its distance from the anal canal. Enteroceles can be identified during the evacuation phase. Nonrelaxing puborectal muscle may be recognized and may delay or prevent evacuation (anismus). This technique is useful since it allows the dynamic assessment of both rectal wall prolapse and rectal emptying. Results must be interpreted with caution and related to the symptoms and physical findings; small rectoceles and minor rectal intussusception occur in up to 50 % of healthy subjects, and their clinical significance is unclear.

11.3.5.1 Dynamic Magnetic Resonance Imaging

This investigation tends to replace barium defecography because its fast image acquisition yields data similar to that from standard defecography without the need for radiation. It also helps to characterize associated pelvic organ prolapse (Fig. 11.2). Using a standard magnetic resonance imaging system, the patient is asked to evacuate in the left lateral position, not a physiological position as is used with conventional defecography. Moreover, dynamic magnetic resonance imaging is not sensitive enough to detect intrarectal intussusception.

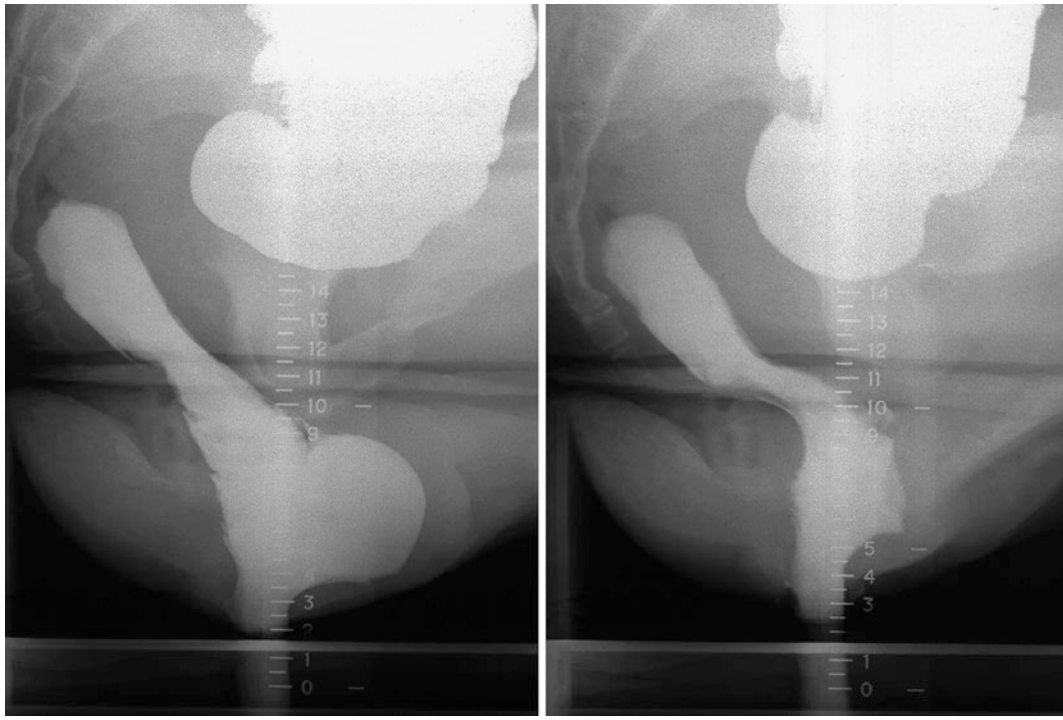


Fig. 11.1 Standard dynamic defecography with bowel barium filling. Evacuation series: rectocele and low-grade rectal intussusception (no enterocele), moderate perineal descent (*left*). Patient digitating to empty the rectocele by using the fingers to put pressure on the vaginal bulge (*right*)

11.3.5.2 Defecation Scintigraphy

The efficiency of defecation is measured by calculating the percentage of artificial radiolabeled stool evacuated from the rectum. Healthy individuals evacuate 60 % of stool in 10 s. Because of its limited availability, its use in clinical practice is uncommon.

11.3.6 Anorectal Physiology Tests

These include standard manometry, the assessment of rectal sensation/rectal wall properties, and the balloon expulsion test.

High resting anal pressures suggest the presence of anismus. Absence of the rectoanal inhibitory reflex raises the possibility of adult Hirschsprung disease. Patients with defecation disorders have inappropriate contraction of the pelvic floor and anal sphincter while straining.

Rectal sensation and rectal wall properties can be tested by controlled balloon distension of the rectum. Recorded measurements are the volume at which the first sensation is experienced, the volume that elicits a desire to defecate, and the maximal tolerated volume.

The balloon expulsion test is a cheap, easy to perform, and reproducible method used to assess the ability to empty the rectum. Patients with dysfunction of the pelvic floor and anismus often fail to expel the balloon.

11.3.7 Colonic Transit Time

Colonic transit may be studied using several methods, the simplest and most popular of which involves the ingestion of radiopaque markers. The markers are followed along the large bowel with abdominal radiographs. Patients with transit times longer than 72 h are classified as having slow-transit constipation. Scintigraphic methods to determine panintestinal transit are also available. These methods are

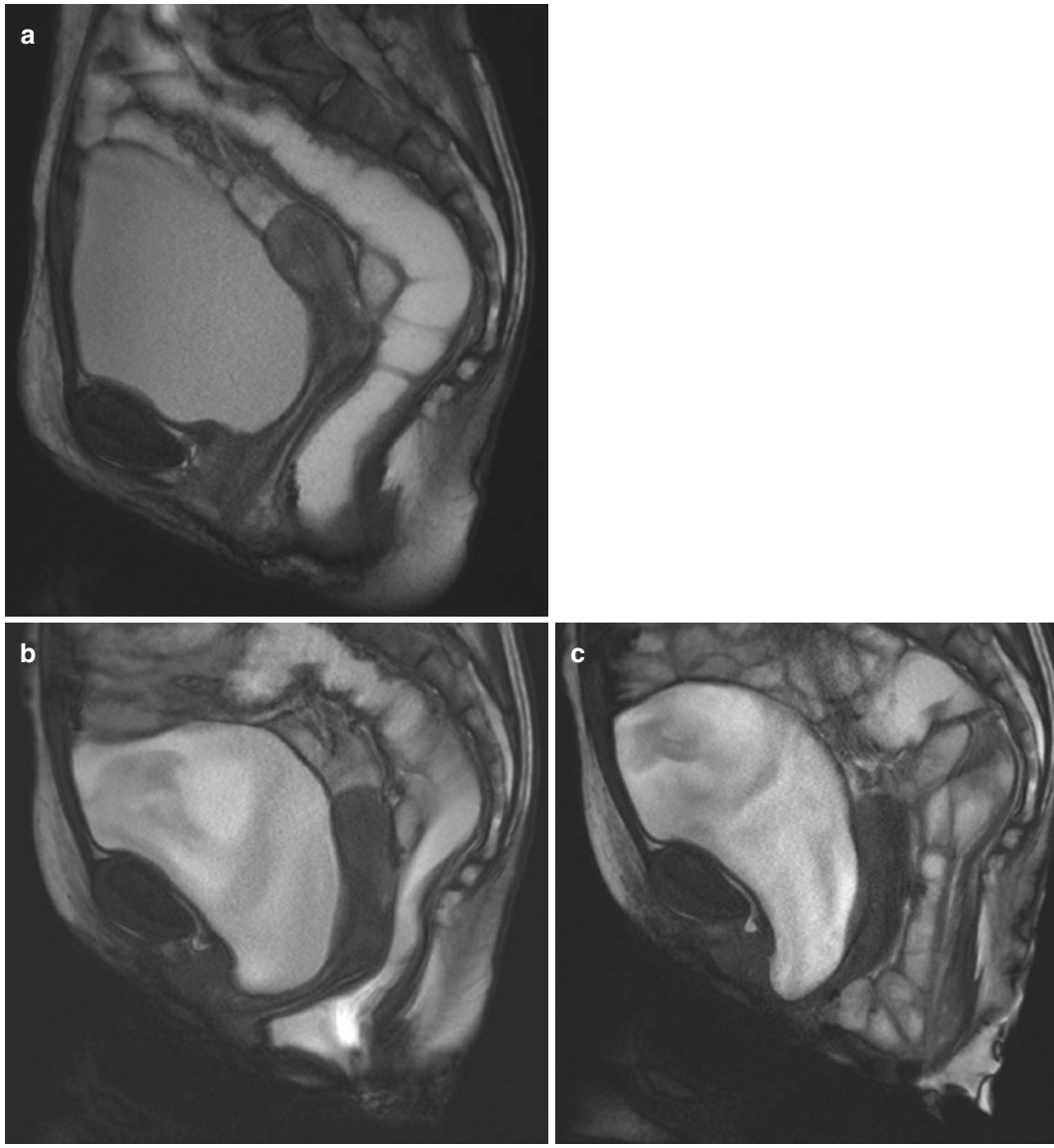


Fig. 11.2 Dynamic defecographic magnetic resonance imaging series in the same patient. (**a**) At rest. (**b**) First stage of rectal evacuation with the presence of an anterior rectocele. (**c**) End of rectal evacuation: the empty rectum leaves room for a large sigmoidocele reaching the perineum. Associated prolapse of the anterior compartment (bladder and uterus)

not, however, sensitive enough to detect abnormalities of rectal emptying.

11.3.8 Endoanal Ultrasound

Endoanal ultrasound is required in cases of fecal incontinence to document anal sphincter tears. It may affect the surgical approach.

11.3.9 Electromyographic Studies

The electromyographic (EMG) activity of the external anal and puborectalis muscles can be recorded either by needle or surface electrodes to detect the absence of relaxation or inappropriate contraction of the sphincters during attempted expulsion; this is indicative of anismus. The EMG signal may later be used during

biofeedback therapy. The lack of specificity of this test and the considerable overlap measures in selected groups of incontinent and constipated patients is not really helpful for diagnosis of perineal neuropathy or for prognostic considerations.

11.3.10 Urological Workup

Voiding studies are needed in the case of associated urinary incontinence or symptoms that have to be searched for systematically.

11.4 Treatment

11.4.1 Conservative Treatment

Dietary and hygienic measures are recommended as first-line treatment and improve symptoms in 30–60 % of patients. Simple measures include increasing fiber (20–25 g/day) and noncaffeinated, nonalcoholic fluid intake. Illustrated explanations of the defecatory process and advice on positioning on the toilet seat, the use of suppositories and small enemas, and manually supporting the perineum are simple and helpful primary care measures to reassure the patient.

One of the best evaluated strategies is a carbon dioxide–releasing suppository, which has been shown to be more effective than a placebo for the relief of symptoms of dyschezia and is associated with a good safety profile [5]. It also significantly enhances the efficacy of retraining in patients with anismus [6].

11.4.2 Biofeedback Therapy – Pelvic Floor Retraining

Behavioral relaxation techniques may reestablish normal rectal expulsion. Patients with constipation secondary to pelvic floor dysfunction are guided through a retraining program to relax the pelvic floor muscles during straining.

Biofeedback is a well-established treatment modality. Several techniques are available: the ambulatory or in-patient approach, a microballoon system, surface EMG recording, or an anal EMG probe. Overall, two-thirds of patients with anismus achieve success with pelvic floor retraining. Several controlled trials have shown a benefit of retraining over "dietary [changes] and/or laxatives" alone in patients with obstructed defecation related to an anismus [7, 8]. However, new trials are necessary to better assess the level of benefit biofeedback could provide.

11.4.3 Surgical Techniques

Surgical treatment of defecation disorders aims at correcting anatomic abnormalities with the intent that correction will improve function. Disorders in which surgery should be considered include nearly exclusively rectocele, intussusception, and enterocele.

11.4.3.1 Methods

The approach can be from three directions: transrectal (through the anal canal), transvaginal or transperineal, or transabdominal either by Pfannenstiel laparotomy or more often nowadays through a laparoscopic approach.

Transanal Approach

Transanal repair addresses the anorectal component of rectoceles. The patient is placed in the jack-knife or lithotomy position. The anal canal is opened with a retractor to expose the lower rectum.

- Option 1. Anterior (longitudinal or transversal) plication of the rectal wall and resection of excess mucosa allow correction of rectocele (Sullivan–Khubchandani technique).
- Option 2. Stapled transanal rectal resection (or Transtar) procedure using either circular or curved linear staplers is currently performed more frequently. The technique allows

resection of the anterior and posterior rectal walls, correcting both rectocele and intussusception while restoring the normal shape of the rectal ampulla [9]. An internal Delorme operation has also been proposed to treat high-grade internal prolapse.

Transperineal or Transvaginal Approach

By contrast, the transvaginal/transperineal approach corrects the rectocele using a transverse perineal and/or a vertical vaginal incision. After exposing the whole of the rectovaginal septum, the anterior rectal wall is plicated from outside, a vaginal sacrospinous ligamentopexy (Richter procedure) can be performed, and the levator ani are plicated (levatorplasty), taking great care to not reduce the vaginal introitus. In large or recurrent defects, some surgeons insert various types of mesh to add support. Because of a high risk of complications (extrusion, dyspareunia), the use of mesh through a vaginal approach is no longer recommended. This approach allows anal sphincter repair in addition to rectocele repair, if required. The pouch of Douglas can also be resected using this approach.

Transabdominal Approach

Through an open or (preferably) a laparoscopic approach, mesh inserted into the rectovaginal septum and suspended without tension to the sacral promontory (colpopexy vaginorectopexy or ventropexy) allows for the correction of deep enteroceles, sigmoidoceles, and rectoceles; supports the associated rectal intussusception; and elevates a deep pouch of Douglas [10–12]. This technique, the so-called laparoscopic ventral mesh rectopexy (LVMR) (see also Chap. 12), differs from standard rectopexy in that it avoids dorsolateral mobilization of the rectum and does not endanger the pelvic autonomic innervation.

Some authors have supported a combined abdominal *and* perineal approaches to achieve complete rectovaginal suspension (Zaccharin procedure), which is not commonly performed. Rectovaginal mesh suspension is easily combined on demand or systematically with bladder/anterior vaginal wall suspension for urogenital prolapse.

11.4.3.2 Results – Outcome

The level of evidence in the literature is poor with regard to any surgical approach for a defecation disorder. A wide spectrum of results has been reported for rectocele repair, combined with variable criteria for surgery, and no clear difference has been shown between the transrectal and transvaginal/transperineal approaches. The outcome of surgery is often difficult to predict. The patient must be informed and understand that whatever technique is tried, there is a risk of failure.

Patients should be given realistic expectations and must be warned that symptoms may persist following surgery. Incomplete or no resolution of the problem, as well as the appearance of new symptoms of variable severity, may define failure of the surgical approach. Complications following transanal repair include the onset of fecal incontinence, and a decrease in anal sphincter pressures has been reported after this procedure. Stapled procedures offered better improvement than biofeedback/retraining in a randomized controlled study [13]. However, the urgency to defecate and incontinence during early follow-up and recurrence during late follow-up are the main limitations of this approach [9, 14]. Dyspareunia may occur after transvaginal repair. In women with pelvic organ prolapse, sacral colpopexy has superior outcomes to a variety of vaginal procedures, including sacrospinous colpopexy, uterosacral colpopexy, and transvaginal mesh [15]. These benefits must be balanced against a longer operating time, a longer time to return to activities of daily living, and the increased cost of the abdominal approach. Constipation symptoms often increase after conventional rectopexy but do not often occur following LVMR [12]. This technique has been widely developed over the past decade: the laparoscopic approach or robot-assisted methods have been standardized, even allowing day-care surgery in selected tertiary centers.

11.4.3.3 Indications for Surgery – Special Conditions

Surgery can be discussed for patients with defecation disorders who are unresponsive to dietary measures and rehabilitative therapy (Appendix 2).

- Nonrelaxing puborectalis or anismus: Surgical treatment for this condition (unilateral or bilateral division of the external anal sphincter muscle or puborectalis, for instance) has been abandoned. Some benefit can be obtained with botulinum toxin (Botox) injection to reduce hypertonia and muscle bulk.
- Perineal descent: This is not a surgical condition. Pelvic floor retraining can be offered but has limited success. Prevention is recommended (atraumatic childbirth, limited straining when passing stool, pelvic floor exercises).
- Rectocele: Frequently asymptomatic, a rectocele can be an incidental finding on examination and on defecography that does not require surgery. The selection of patients for surgical intervention for symptomatic rectocele remains an area of debate. Currently accepted criteria for patient selection for surgery are a need for rectal/vaginal digitation to facilitate rectal evacuation, rectal and/or vaginal symptoms for longer than 12 months that are not improved by increasing dietary fiber, and a rectocele larger than 3 or 4 cm in diameter on defecography with only partial emptying.
- Enterocele. Abdominal approach and mesh suspension is recommended in younger patients. In older or fragile patients, perineal repair gives satisfactory results at lesser risk and is therefore the preferred option.
- Rectal intussusception: The role of surgery in this condition is controversial; however, LVMR gives good results and could be offered especially in patients with fecal incontinence associated with outlet obstruction. Other options are perineal approaches – either internal Delorme procedure or the more widely used stapled transanal rectal resection (Transtar).
- Megarectum – slow-transit constipation: Vertical reduction rectoplasty and concomitant sigmoidectomy have been proposed for the treatment of idiopathic megarectum. In the most severe cases, and when defecation disorders are associated with slow-transit constipation, there may be an indication for antegrade colonic enemas using a Malone-type cecostomy for easier bowel management. Refractory cases may end up with an ileostomy or colostomy.
- Adult Hirschsprung disease: This uncommon cause of outlet obstruction can be diagnosed on anorectal manometry when the rectoanal inhibitory reflex is absent. The patient should then undergo a full-thickness rectal biopsy to confirm the absence of ganglion cells in the bowel wall. For ultrashort aganglionosis, lateral internal sphincterotomy or anorectal myectomy are recommended.

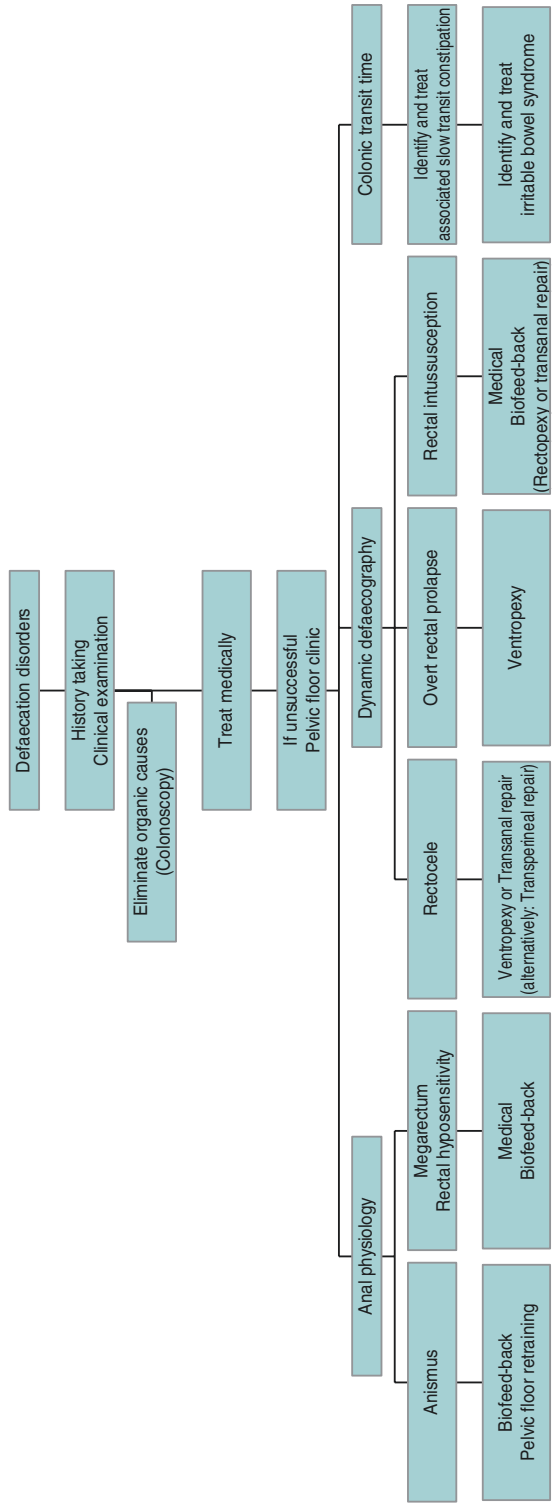
Conclusion

Defecation disorders represent a complex field for which detailed assessment of the terminal bowel anatomy and function is needed. A multidisciplinary approach as developed in "pelvic floor clinics" is a useful adjunct to the traditional colorectal approach. In this difficult area of functional disorders, providing information to the patient and his/her relatives is essential, especially when surgery is considered.

Appendix 1 Normal Defecation

Normal defecation
The process by which the rectum normally empties is complex. It requires a series of coordinated actions of the colon, rectum, pelvic floor, and anal sphincter muscles
Physiological steps of a successful evacuation of the bowel:
Mass movement in the sigmoid colon moves a fecal bolus to the rectum and may initiate the urge to defecate. The sensation of rectal filling plays a key role in normal defecation.
Distension of the rectum results in relaxation of the internal anal sphincter (the so-called rectoanal inhibitory reflex) and secondary reflex contraction of the external sphincter to prevent incontinence.
Discrimination between solid or liquid stool and gas is allowed by exposure of the sensory receptor–rich anal transitional zone to the rectal contents. The rectoanal inhibitory reflex is therefore known as the "sampling reflex" and is of paramount importance in social behavior.
If socially convenient, defecation can be attempted by adopting a sitting position. Flexion of the hips relaxes the pelvic floor and facilitates the passage of stools by opening the anorectal angle.
Straining is performed by contracting the diaphragm and abdominal wall (Valsalva maneuver). It increases the intra-abdominal and intrarectal pressures. Contraction of the rectal wall also participates in this pressure increase. Meanwhile, the anal sphincters and puborectalis muscle relax. Tightening of iliococcygeus muscles stabilizes the levator plate to counterbalance the intra-abdominal push. Inversion of the pressure gradient between the rectum and the anal canal allows stool evacuation

Appendix 2 Flow Chart: How to Manage a Defecation Disorder



References

1. Siproudhis L, Pigot F, Godeberge P, Damon H, Soudan D, Bigard MA. Defecation disorders: a French population survey. Dis Colon Rectum. 2006;49(2):219–27.
2. Siproudhis L, Dautrème S, Ropert A, Briand H, Renet C, Beusnel C, Juguet F, Rabot AF, Bretagne JF, Gosselin M. Anismus and biofeedback: who benefits? Eur J Gastroenterol Hepatol. 1995;7(6):547–52.
3. Altomare DF, Spazzafumo L, Rinaldi M, Dodi G, Ghiselli R, Piloni V. Set-up and statistical validation of a new scoring system for obstructed defaecation syndrome. Colorectal Dis. 2008;10(2):84–8.
4. Videlock EJ, Lembo A, Cremonini F. Diagnostic testing for dyssynergic defecation in chronic constipation: meta-analysis. Neurogastroenterol Motil. 2013;25(6):509–20.
5. Tarrerias AL, Abramowitz L, Marty MM, Coulom P, Staumont G, Merlette C, Berger V, Savarieau B, Ducrotté P. Efficacy of a CO2-releasing suppository in dyschezia: a double-blind, randomized, placebo-controlled clinical trial. Dig Liver Dis. 2014;46(8):682–7.
6. Cotelle O, Cargill G, Marty MM, Bueno L, Cappelletti MC, Colangeli-Hagège H, Savarieau B, Ducrotté P. A concomitant treatment by CO2-releasing suppositories improves the results of anorectal biofeedback training in patients with dyschezia: results of a randomized, double-blind, placebo-controlled trial. Dis Colon Rectum. 2014;57(6):781–9.
7. Rao SS, Valestin J, Brown CK, Zimmerman B, Schulze K. Long-term efficacy of biofeedback therapy for dyssynergic defecation: randomized controlled trial. Am J Gastroenterol. 2010;105(4):890–6.
8. Chiarioni G, Whitehead WE, Pezza V, Morelli A, Bassotti G. Biofeedback is superior to laxatives for normal transit constipation due to pelvic floor dyssynergia. Gastroenterology. 2006;130(3):657–64.
9. Ribaric G, D'Hoore A, Schiffhorst G, Hempel E, TRANSTAR Registry Study Group. STARR with CONTOUR® TRANSTAR™ device for obstructed defecation syndrome: one-year real-world outcomes of the European TRANSTAR registry. Int J Colorectal Dis. 2014;29(5):611–22.
10. Wong M, Meurette G, Abet E, Podevin J, Lehur PA. Safety and efficacy of laparoscopic ventral mesh rectopexy for complex rectocele. Colorectal Dis. 2011;13(9):1019–23.
11. Mercer-Jones MA, D'Hoore A, Dixon AR, Lehur P, Lindsey I, Mellgren A, Stevenson AR. Consensus on ventral rectopexy: report of a panel of experts. Colorectal Dis. 2014;16(2):82–8.
12. D'Hoore A, Penninckx F. Laparoscopic ventral recto(colpo)pexy for rectal prolapse: surgical technique and outcome for 109 patients. Surg Endosc. 2006;20(12):1919–23.
13. Lehur PA, Stuto A, Fantoli M, Villani RD, Queralto M, Lazorthes F, Hershman M, Carriero A, Pigot F, Meurette G, Narisetty P, Villet R, ODS II Study Group. Outcomes of stapled transanal rectal resection vs. biofeedback for the treatment of outlet obstruction associated with rectal intussusception and rectocele: a multicenter, randomized, controlled trial. Dis Colon Rectum. 2008;51(11):1611–8.
14. Van Geluwe B, Stuto A, Da Pozzo F, Fieuws S, Meurette G, Lehur PA, D'Hoore A. Relief of obstructed defecation syndrome after stapled transanal rectal resection (STARR): a meta-analysis. Acta Chir Belg. 2014;114(3):189–97.
15. Maher C, Feiner B, Baessler K, Schmid C. Surgical management of pelvic organ prolapse in women. Cochrane Database Syst Rev. 2013;(4):CD004014.

Rectal Prolapse, Intussusception, Solitary Rectal Ulcer

12

André D'Hoore

12.1 Introduction

Rectal prolapse is an uncommon but disabling condition that requires surgical correction not only to treat related symptoms but to prevent progressive anal sphincter damage. In total rectal prolapse the rectum protrudes through the anal opening. With time, manual reduction may be required. Mucous discharge and frank fecal soiling are common.

Considerable controversy remains regarding the most appropriate surgical technique. Surgery aims to correct anatomy and should result in improved anorectal function without postoperative functional sequelae. In Europe, laparoscopic ventral mesh rectopexy has gained widespread acceptance, but the type of mesh used (synthetic vs. biological) is a timely debate.

Rectal intussusception, also referred at as internal rectal prolapse, is a common finding on defecograpy. Deep intussusception (into the anal canal) can lead to fecal incontinence and has been linked to obstructed defecation (OD). The need for surgery in rectal intussusception remains highly controversial, especially in the setting of OD.

Solitary rectal ulcer is a benign condition. Lesions, with mild proctitis surrounding them, are situated on the anterolateral side of the rectum, usually located 4–8 cm from the anal verge. Mucosal trauma and related ischemia are generally accepted as cause of solitary rectal ulcer. It is important to evoke this diagnosis because solitary rectal ulcer may be confused both clinically and histologically with carcinoma of the rectum.

12.2 Total Rectal Prolapse

Rectal prolapse is defined as a full-thickness rectal intussusception protruding through the anus. Using cinedefecography, Broden and Snellman [1] were able to demonstrate that rectal prolapse is an intussusception rather than a sliding hernia through a pelvic fascia defect (Moschcowitz [2]).

12.2.1 Epidemiology

Rectal prolapse is predominantly a female pathology (sex ratio, 10:1) and the finding of two ages at which peak incidence occurs may well reflect the underlying pathophysiology. In the younger group of patients, a history of obstructed defecation and prolonged straining seems to precede rectal prolapse. In aged patients, rectal prolapse is often part of a more complex pelvic organ prolapse related to a weakened pelvic floor

A. D'Hoore, MD, PhD
Department of Abdominal Surgery, University Hospitals of Surgery, Leuven, Belgium
e-mail: andre.dhoore@uzleuven.be

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_12

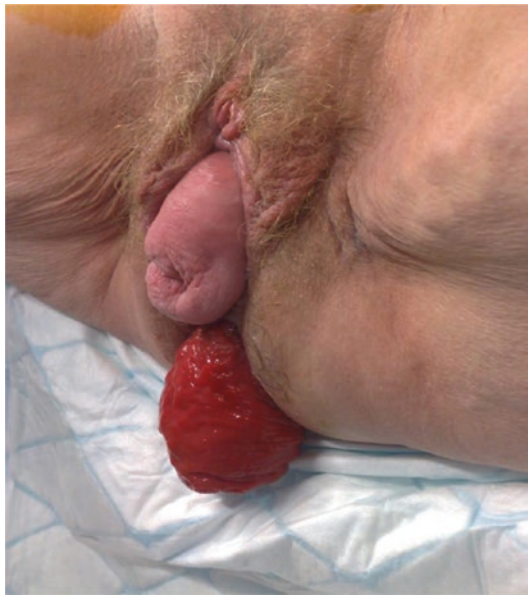


Fig. 12.1 External rectal prolapse and uterine prolapse upon straining

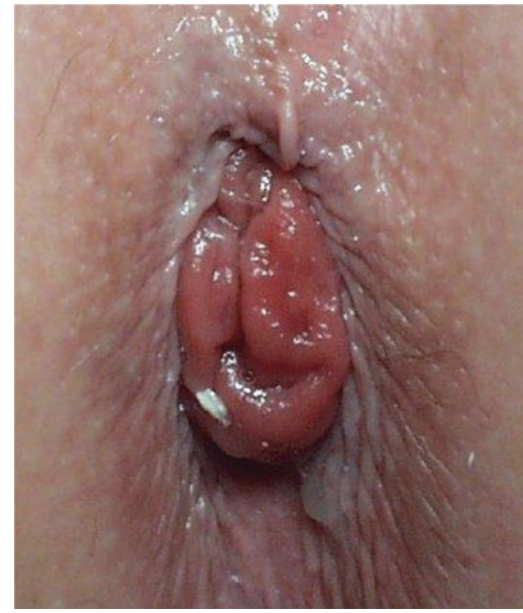


Fig. 12.2 Differential diagnosis: circular mucosal prolapse

(Fig. 12.1). Childbearing certainly can contribute to the development of pelvic floor laxity; however, half of women with rectal prolapse are nulliparous.

In males the condition is unrelated to age. There is a variable association with psychiatric illness [3].

12.2.2 Clinics

Symptoms include the sensation of a lump protruding during defecation. Either spontaneous reduction occurs at the end of straining, or there is the need to manually reposition the prolapsed rectum.

Mucous discharge and soiling are common. Anal bleeding with tenesmus and pain could reveal a solitary rectal ulcer.

Symptoms related to anorectal dysfunction are common and differ: constipation (obstructed defection), predominant in younger patients, and fecal incontinence, occurring most often in aged patients. Some degree of fecal incontinence is noted in about 60–80 % of patients. The development of fecal incontinence in rectal prolapse is multifactorial: mechanical stretch of the sphincters, pudendal neuropathy, repetitive stimulation of the rectoanal inhibitory reflex, and impaired rectoanal motility all result in a low resting anal pressure [4].

Constipation is present preoperatively in up to 60 % of patients. Most patients have a pattern of obstructed defecation. Slow-transit colonic constipation is rarely seen in this clinical setting [5].

Rectal prolapse should be differentiated from mucosal anal prolapse, anterior mucosal prolapse, and prolapsing hemorrhoids (Fig. 12.2). A solitary rectal ulcer, especially the exophytic polypoid type should be differentiated from a rectal adenocarcinoma.

A complete examination of the pelvic floor should be performed to assess the presence of a descent of the middle and/or anterior pelvic compartment. A pathologic descent of the pelvic floor (descending perineum syndrome) should be noted, as this can contribute to persistent postoperative dysfunction.

If the prolapse is not visible during the clinical examination, the patient should be asked to sit on a commode and bear down to reproduce the prolapse.

12.2.3 Technical Investigations

In general, flexible endoscopy is advisable to exclude a neoplasm or a lead point lesion as a cause of the prolapse. A finding of extensive

diverticular disease also could influence the type of surgery.

Isolated erythema or ulceration of the anterolateral rectal wall is the cardinal feature of solitary rectal ulcer syndrome, and biopsy can reveal a typical histology with fibrous obliteration of the lamina propria.

Although clinically evident, colpo-cystodefecography or dynamic magnetic resonance imaging of the rectum can provide additional information on the extent of prolapse of other pelvic compartments. This could be helpful in tailoring the surgical approach. Anorectal manometry has added value only in the setting of clinical research.

A radiopaque marker study is appropriate in patients with a history suggesting slow-transit constipation. It should be noted that nearly one-third of the patients with outlet delay constipation present with delayed overall large-bowel transit [6].

12.2.4 Surgical Repair

The aim of surgical treatment is to correct the prolapse, restore continence, and prevent postoperative constipation. Some anatomic features are constant findings and reflect the rationale for some of the surgical approaches: full-thickness intussusception, a deep pouch of Douglas, defective fixation of the rectum to the sacrum, a redundant sigmoid colon, and a weakened pelvic floor and anal sphincter muscles.

A large number of operations for rectal prolapse have been described, reflecting their defectiveness. No particular scientific reason seems to explain the popularity of a specific approach, and the surgeon's choice is mostly based on anecdotal and/or personal experiences.

These operations can be categorized as either abdominal or perineal. Table 12.1 provides an overview of techniques that have been used.

Based on a Cochrane Database systematic review, abdominal approaches seem to result in a reduced prolapse recurrence rate. Residual incontinence is less frequent after abdominal approaches. Postoperative constipation, on the other hand, seems to be linked to mesh rectopexy, especially when lateral ligament ligation (extensive rectal mobilization) is performed. Bowel resection during rectopexy was associated with lower rates of postoperative constipation. Nevertheless, the limited number of relevant trials, their small sample sizes, and other methodological weaknesses severely limit their usefulness for guiding practice [8].

It seems appropriate that surgeons master a perineal as well as an abdominal technique. All abdominal procedures should be performed laparoscopically, which can result in shorter hospital stays and lower costs [9].

Laparoscopic ventral mesh rectopexy has gained wide spread acceptance in Europe and has become the procedure of choice fit patients requiring prolapse repair.

12.2.4.1 Perineal Approaches

Perineal approaches are generally reserved for patients who are too frail to withstand an abdominal approach or general anesthesia. Perineal procedures can be performed under regional anesthesia (a spinal or sacral block) and in the lateral decubitus position.

Table 12.1 Defecographic grading of a prolapse

	Grade I	Grade II	Grade III
Rectocele	<2 cm	2–4 cm	>4 cm
Enterocele	Proximal one-third of the vagina	Middle one-third	Lower one-third
Intussusception	Above puborectal	At puborectal	In the anal canal
Sigmoidocele [7]	Above the pubococcygeal line	At the pubococcygeal line	Below the pubococcygeal line
Descending perineum		>4 cm Descent upon straining	

Delorme Mucosectomy [10]

This technique was described in 1900 by the French military surgeon Edmond Delorme. It involves stripping the mucosa of the prolapsed rectum (sparing the muscular tube). A circular incision starts about 1 cm cephalad to the dentate line (to safeguard the internal anal sphincter). The submucosa is infiltrated with a diluted adrenaline solution, which facilitates the dissection. By placing interrupted sutures around the circumference, the muscle layer is plicated; this reduces the prolapse above the anal canal. The mucosal sleeve covers the plication and is anastomosed to the anal canal (Fig. 12.3).

This technique is better adapted to treat smaller rectal prolapses. A modified technique has been proposed, adding a postanal repair to reduce the enlarged hiatus [11].

Perineal Rectosigmoidectomy (Altemeier Procedure) [12, 13]

In contrast to the Delorme procedure, a full-thickness resection of the prolapse is performed (rectum, rectosigmoid) with a coloanal anastomosis (Fig. 12.4). The prolapse is everted and a full-thickness incision is performed 1.5 cm above the dentate line.

Opening the pelvic pouch allows the surgeon to palpate in order to determine whether a redundant loop of sigmoid colon should be resected. All mesenterial vessels should be ligated with care. The colon should reach the line of anastomosis without any tension. Septic complications and suture-line dehiscence are rare, probably because of the weakness of the remaining sphincter.

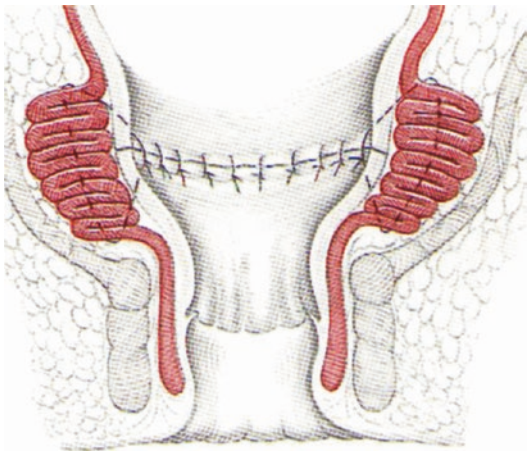


Fig. 12.3 Schematic representation of a Delorme mucosectomy and rectal muscle wall plication (From Mann CV, Glass RE, *Surgical Treatment of Anal Incontinence*, 2nd edition. London: Springer-Verlag; 1997)

Outcomes of Perineal Procedures

1. *Recurrence*

   Recurrence rates after Delorme mucosectomy vary from 4 % to 38 %; these values certainly reflect the duration of follow-up and patient selection. In a large series of 101 primary procedures, Watts and Thompson [14] showed that a cumulative recurrence rate of about 40 % at 5 years can be expected. An even higher incidence of recurrence (60 % at 2 years) was recorded for repeat Delorme procedures.

   The incidence of recurrence rates after the Altemeier procedure is lower and varies between 0 % and 15 %. Recurrence probably reflects inadequate resection [15].

2. *Functional Outcome*

   Perineal procedures have yielded poor functional outcomes with respect to fecal incontinence and urgency. The resection or plication of the rectal reservoir (in a situation of already-reduced sphincter function) further jeopardizes fecal continence [16]. Recovery of fecal continence is unpredictable.

   – Perineal colonic pouch

     To overcome this problem, Yoshioka et al. [17] suggested constructing a colonic *J*-pouch of the peranaly mobilized sigmoid.

   – Additional levatorplasty

     In addition to the classical Altemeier procedure, posterior or anterior buttressing has been proposed. The muscular edges of the puborectal muscle can be identified, allowing either a posterior or anterior levatorplasty to be performed using nonabsorbable sutures. This reduces the hiatus (postanal repair). In an interesting study, Agachan et al. [18] demonstrated that after perineal rectosigmoidectomy with levatorplasty not only were incontinence scores improved, recurrence was also reduced.

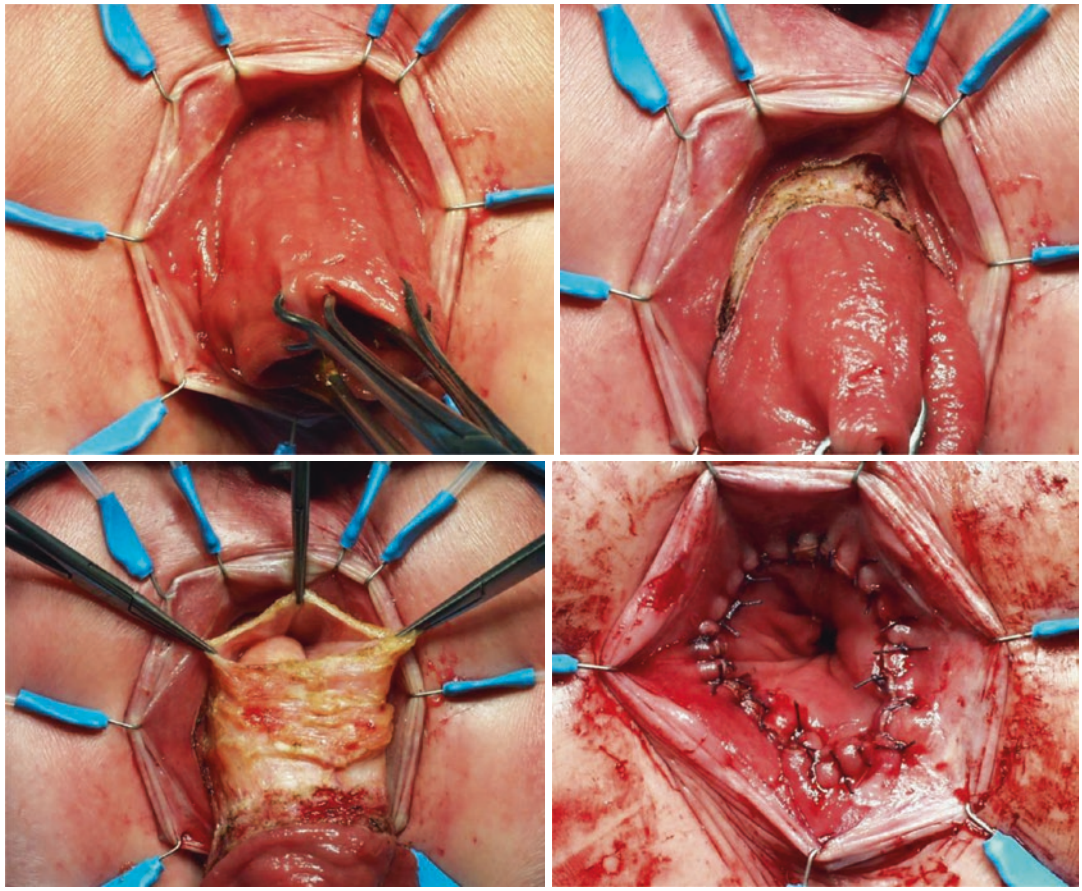


Fig. 12.4 Intraoperative steps of the Altemeier procedure

Choice of Perineal Operation

Perineal procedures are indicated in frail, old patients with extensive morbidity. Smaller prolapses can be treated by Delorme mucosectomy. In larger prolapses, a perineal resection with dorsal levatorplasty is advisable. In the rare scenario of an incarcerated and gangrenous rectal prolapse, a perineal resection is indicated; abdominal rectopexy cannot be performed.

In young, healthy, male patients the use of a Delorme procedure is certainly worth considering because it avoids the risk for pelvic autonomic nerve injury.

12.2.4.2 Abdominal Approaches

Preservation of the rectal ampulla is important to allow recovery of fecal continence. Most abdominal suspension techniques rely on the same surgical principle: mobilization of the rectum, reduction of the prolapse, and fixation of the elevated rectum to the sacrum. Fixation can be performed using either sutures or mesh. The mesh can be placed in different positions, and the type of mesh can vary (synthetic vs. biological). A resection of a redundant sigmoid colon can be added.

Suture Rectopexy

This technique was first described by Cutait [19] in 1959. Nonresorbable sutures are used to fix the mesorectum of the elevated rectum to the presacral fascia and sacral promontory.

Suture Rectopexy with Sigmoid Resection

This procedure is also referred to as the "Frykman-Goldberg procedure" [20] and is still

very popular in the United States. The procedure was initially intended to reduce the recurrence rates of suture rectopexy by resecting the redundant sigmoid colon. It significantly reduces the incidence of postoperative constipation, but adding a resection potentially increases the risk for complications.

Posterior Mesh Rectopexy

In the original Wells procedure [21], a polyvinyl alcohol sponge (Ivalon) was inserted posterior to the mobilized mesorectum to stimulate inflammatory adhesion-fixation of the bowel to the presacral fascia. Later the same procedure was performed using polypropylene or Teflon mesh (Fig. 12.5).

Anterior Sling Rectopexy

In the Ripstein procedure [22], an anterior sling of fascia lata or synthetic material is positioned in front of the rectum and sutured to the sacral promontory. To overcome the risk of bowel obstruction, a modified technique (McMahan-Ripstein) [23] includes a posterior fixation of the mesh to the presacral fascia; the lateral mesh is anteriorly sutured to the rectum, deliberately leaving an anterior gap (Fig. 12.5).

Lateral Mesh Rectopexy

In the so-called Orr-Loygue procedure [24, 25], lateral fixation (using either fascia lata strips or synthetic material) between the elevated rectum and the sacral promontory at both sides of the rectum is performed. This is done after full mobilization of the rectum.

Laparoscopic Ventral Mesh Rectopexy (or Rectocolpopexy)

Laparoscopic ventral mesh rectopexy (LVR) was first described by D'Hoore and Penninckx [26]. The laparoscopic dissection is limited to the anterior aspect of the rectum (rectovaginal septum), avoiding the risk of autonomic nerve damage. A synthetic mesh is sutured to the anterior aspect of the rectum to avoid further intussusception and fixed to the sacral promontory. If the uterosacral ligaments are lax, they can be

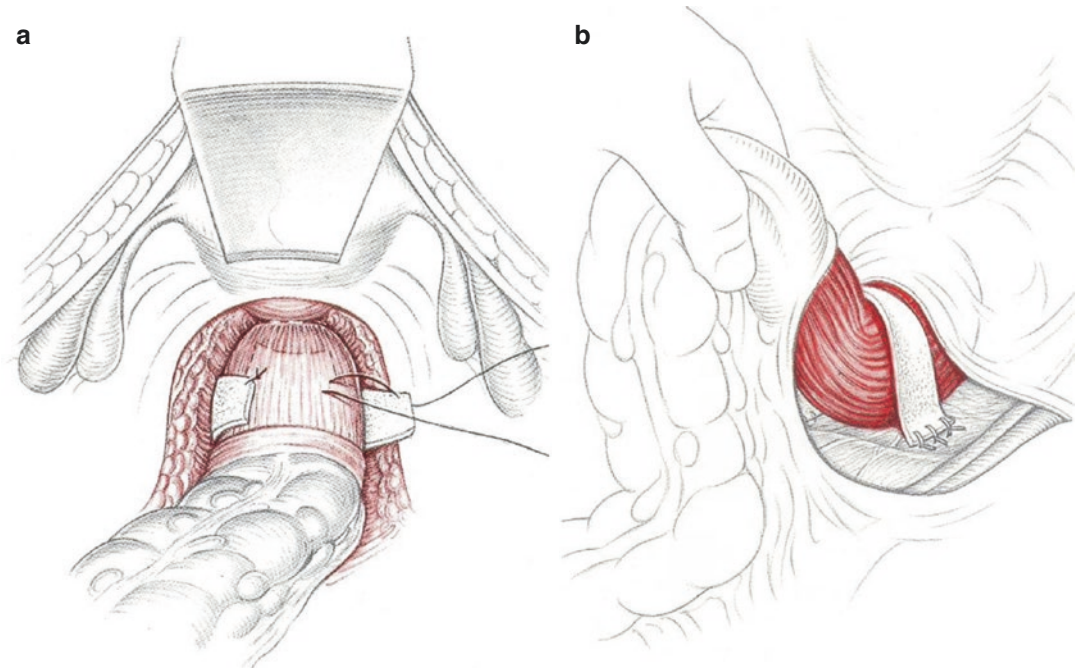


Fig. 12.5 Classical mesh rectopexy: Wells procedure (**a**). Ripstein procedure (**b**) (From Mann CV, Glass RE, *Surgical Treatment of Anal Incontinence*, 2nd edition. London: Springer-Verlag; 1997)

hooked to the same mesh. Any descent of the vaginal vault can be restored by performing a colpopexy using the same mesh. The peritoneum is closed over the synthetic mesh to elevate the neo-Douglas and to avoid further adhesion to the mesh. The unique position of the mesh further reinforces the rectovaginal septum. It therefore can be used in the presence of a complex rectocele (Fig. 12.6).

The same procedure can be performed in male patients. Dissection is limited to the level of the seminal vesicles, and no attempt is made to dissect posterior to the prostate. Care should be taken to avoid any damage to the hypogastric nerve at the site of the sacral promontory.

Outcome of Classical Rectopexy

1. *Recurrence*
   Any abdominal procedure that involves extensive rectal mobilization and fixation seems to be more effective than perineal procedures. Recurrence rates in most series vary between 0 % and 5 % [27, 28].
2. *Functional Outcome*
   Certainly, abdominal rectopexy provides a patient the best chances of maintaining or regaining fecal continence. Unfortunately, postoperative constipation is a significant problem and has consistently been reported to occur in up to half of patients [29].
   Different mechanisms can contribute to this phenomenon (mesh obstruction, rectal wall fibrosis). Autonomic nerve damage secondary to full mobilization of the rectum may result in disturbed rectosigmoid motility [30–33].

Outcome of LVR

Based on the safety of the technique (conversion to laparotomy rate of 2.9 %), a low long-term recurrence rate, and favorable long-term functional outcomes (low de novo constipation),

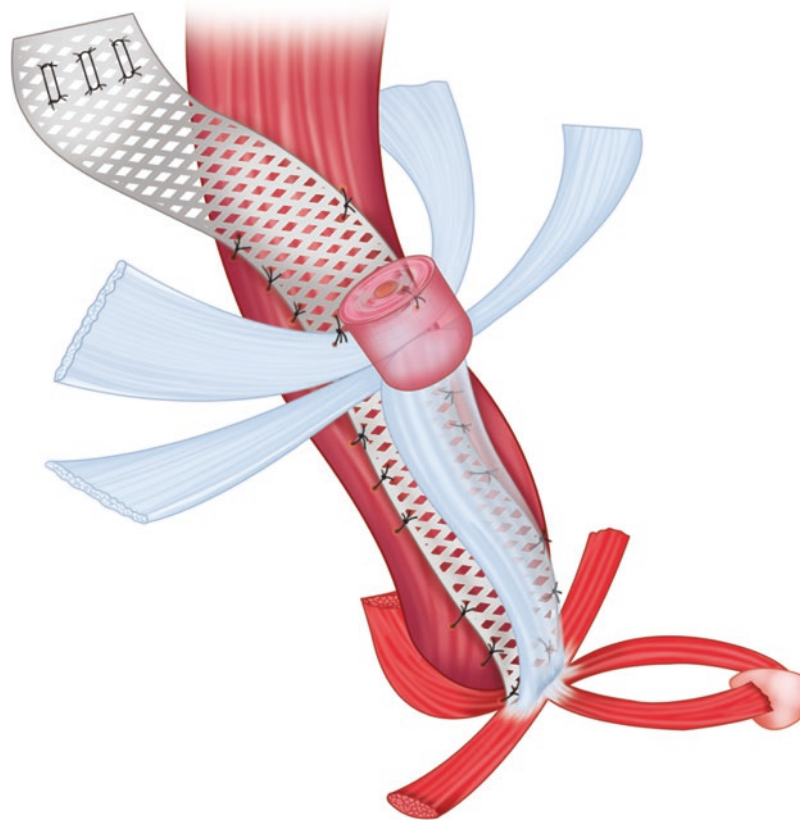


Fig. 12.6 Laparoscopic ventral mesh recto(colpo)pexy

LVR emerges as an efficient procedure for the treatment of patients with total rectal prolapse. It has gained wide acceptance as the procedure of choice in Europe.

12.3 Choice of Abdominal Operation

Laparoscopic ventral recto(colpo)pexy has become the procedure of choice to treat most patients with rectal prolapse. Resection rectopexy (Frykman-Goldberg) can be of interest in those patients with extensive diverticular disease.

Despite using a nonresorbabale synthetic mesh, in a pooled analysis of two series (919 patients), D'Hoore et al. reported a septic complication rate of 2.3 % at a median follow-up of 44 months. More data are needed to be able to compare outcomes after LVR using either a synthetic or biological mesh.

12.4 Internal Rectal Prolapse and Solitary Rectal Ulcer Syndrome

Controversy over the significance of internal prolapse and the role of surgical correction is ongoing [34].

Rectal intussusception or internal rectal prolapse is a common finding on evacuation proctography in normal volunteers. A limited degree of intussusception may occur during defecation as a mechanism of rectal emptying [35].

By contrast, a circumferential full-thickness intussusception into the anal canal (grade III internal prolapse; (Fig. 12.7) can be the cause of obstructed defecation (incomplete evacuation, excessive strain, sensation of anorectal blockage), incontinence, and mucous discharge [36]. Trauma at the site of the intussusception may lead to a rectal ulcer (solitary rectal ulcer syndrome [SRUS]), causing anal pain and bleeding [37]. Internal prolapse and anismus contribute to the development of SRUS.

There also remains debate over the concept of rectal intussusception as a precursor of total rectal prolapse [38]. This was recently challenged by Collinson et al. [39], who showed a slow chronological progression along the spectrum from internal to external prolapse over a time frame of 10–15 years.

12.4.1 Technical Investigations

Patients with a defecatory dysfunction (obstructed defecation,) deserve a thorough evaluation that includes the following:

1. Scoring of anorectal dysfunction using validated questionnaires and scores
2. Dynamic imaging (colpo-cysto-defecography or magnetic resonance defecography)

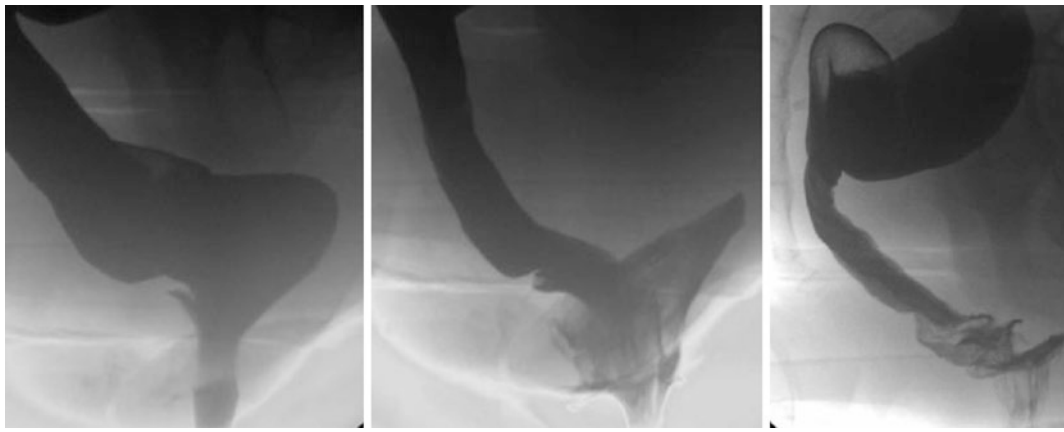


Fig. 12.7 Grade III rectal intussusception seen on an evacuation proctogram (progressive strain)

3. Extensive anorectal manometry, including defecometry to distinguish different forms of dyssynergia [40]
4. Neurologic investigation if necessary
5. Rectoscopy with biopsy (for suspected SRUS)

12.4.2 Treatment

In spite of the well-defined anatomic deficit, conservative treatment is indicated as a first-line therapy for most patients.

For clinicians, it is almost impossible to judge the relative impact of the anatomic defect and the common anorectal dysfunction causing a patient's symptoms.

1. Conservative dietary therapy (a high-fiber diet) with biofeedback (certainly in the case of documented anismus or dyssynergia) is the mainstay of treatment [41]. Topical treatment often fails to heal rectal ulcers.
2. Surgery can be considered in patients who fail optimized conservative therapy. "Prophylactic" surgery seems to be inappropriate in view of actual data regarding the natural history of the condition.
   - *Endoanal Delorme*
     Berman et al. [42] reported successful results after an endoanal Delorme procedure for rectal intussusception. However, technical difficulties have limited its implementation.
   - *Classical mesh rectopexy*
     As mentioned above, classical posterior rectopexy results in constipation in about half of patients and therefore is considered an ineffective treatment for internal rectal prolapse [43].
   - *Laparoscopic ventral recto(colpo)pexy*
     After LVR for total rectal prolapse, a significant improvement in symptoms of obstructed defecation is noted in about 80 % of patients. The Oxford group extensively investigated the role of LVR in patients with internal prolapse:
     1. Wijffels et al. [44] pointed to fecal incontinence as a frequent symptom of high-grade internal prolapse.
     2. Patients with internal rectal prolapse and fecal incontinence benefit from LVR as much as patients with external rectal prolapse [45]
     3. Sacral nerve stimulation does not perform as well in patients with internal prolapse and fecal incontinence; therefore LVR should be performed first [46].
     4. The same results for relief of complaints of obstructed defecation have been reported in patients with external and internal rectal prolapses [47].

     There remains debate over the exact role of LVR in patients with internal prolapse and anorectal dysfunction, especially those with long-standing obstructed defecation.
     Table 12.2 summarizes outcome data after LVR for external and internal rectal prolapse repair.
   - Stapled transanal rectal resection procedure
     This technique consists of a stapled transanal rectal resection (STARR), which allows resection of a rectal intussusception correction of a rectocele [48]. This technique certainly is less invasive than laparoscopic procedures and can eventually be performed in a day-case setting. Promising results have been reported [49, 50]; however, severe complications can occasionally occur, and the technique may induce or worsen symptoms of fecal urge and urge incontinence [51]. A modified STARR was recently developed using a new dedicated device, the CCS-30 Transtar (Ethicon-Endosurgery) [52].

Table 12.2 Outcome data for laparoscopic ventral mesh rectopexy

Author	Patients (N)	Indication	FU (m)	OD (% improvement)	FI (% improvement)	Recurrence (%)
Auguste (2006)	54	ERP	12	70	72.4	7.4
Samaranaya (2009) (review)	223	ERP/IRP	3–61	66–90.3	69–90	
Collinson (2009)	75	IRP	12	86	85	
Wong (2011)	84	IRP	29	37	3.5	
Laurette (2012)	30	ERP (n = 2) IRP (n = 28)	30	57.9 76.9	76.2 65.4	3.3
Maggiori (2013)	33	ERP	42	72	90	6
Gosselink (2014)	91	ERP (n = 41) IRP (n = 50)	12		50 48	2.3
Rondall (2104)	190	ERP	29		93	3.2
MacKenzie (2014)	636	ERP (n = 149) IRP (487)	21	56.7	89.7	
D'Hoore A Consten E (2015) (accepted)	919	ERP (n = 242) IRP (n = 687)	44.3	70.5	80.2	8.2

FU follow-up, *OD* obstructed defecation, *FI* fecal incontinence, *ERP* external rectal prolapse, *IRP* internal rectal prolapse

Conclusion

The emergence of laparoscopic ventral rectopexy and STARR led to a reappraisal of the role of surgery in the treatment of patients with internal rectal prolapse. Nevertheless, extensive clinical and technical evaluations of a patient is necessary to obtain a successful outcome. There certainly is a lack of prospective and prospective randomized data to allow definitive conclusions.

References

1. Broden B, Snellman B. Procidentia of the rectum studied with cinedefecography: a contribution o the discussion of causative mechanism. Dis Colon Rectum. 1968;11:330–47.
2. Moschcowitz AV. The pathogenesis, anatomy and cure of prolapse of the rectum. Surg Gynecol Obstet. 1912;15:7–21.
3. Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. Curr Probl Surg. 2001;38:771–832.
4. Williams JG, Wong WD, Jensen L, Rothenberger DA, Goldberg SM. Incontinence and rectal prolapse: a prospective manometric study. Dis Colon Rectum. 1991;34:209–16.
5. Metcalf AM, Loening-Baucke V. Anorectal function and defecation dynamics in patients with rectal prolapse. Am J Surg. 1988;155:206–10.
6. Chaussade S, Khyari A, Roche H, Garret M, Gaudric M, Couturier D, et al. Determination of total and segmental colonic transit time in constipated patients. Dig Dis Sci. 1989;34:1168–79.
7. Jorge JM, Yang YK, Wexner SD. Incidence and clinical significance of sigmoidoceles as determined by a new classification system. Dis Colon Rectum. 1994;37:1112–7.
8. Bachoo P, Brazezelli M, Grant A. Surgery for complete rectal prolapse in adults. Cochrane Database Syst Rev. 2000;(2):CD001758.
9. Purkayastha S, Tekkis P, Athansiou T, Aziz O, Paraskevas P, Ziprin P, Darzi A. A comparison of open vs lap abdominal rectopexy for full-thickness rectal prolapse: a meta-analysis. Dis Colon Rectum. 2005;48:1930–40.
10. Delorme RL. Communication sur le traitement des prolapsus du rectum totale par l'excision de la muquese rectal ou recto-colique. Bull Mem Soc Chir Paris. 1900;26:499–518. *Translated in Dis Colon Rectum* 1985; 28:544–553.
11. Lechaux JP, Lechaux D, Perez M. Results of Delorme's procedure for rectal prolapse: advantages of a modified technique. Dis Colon Rectum. 1995;38:301–7.
12. Altemeier WA, Giuseppi J, Hoxworth P. Treatment of extensive prolapse of the rectum in aged or debilitated patients. Arch Surg. 1952;65:72.
13. Altemeier WA, Culbertson WR, Schowengerdt C, et al. Nineteen years experience with the one-stage perineal repair of rectal prolapse. Ann Surg. 1971;173:993.
14. Watts AM, Thompson MR. Evaluation of Delorme's procedure as a treatment for full-thickness rectal prolapse. Br J Surg. 2000;87:218–22.

15. Takesue Y, Yokoyama T, Murakami Y, et al. The effectiveness of perineal rectosigmoidectomy for the treatment of rectal prolapse. Surg Today. 1999;29: 290–3.
16. Penninckx F, D'Hoore A, Sohier S, Kerremans R. Abdominal resection rectopexy versus Delorm's procedure for rectal prolapse: a predictable outcome. Int J Colorectal Dis. 1997;12:49–50.
17. Yoshioka K, Ogunbiyi OA, Keighley MRB. Pouch perineal rectosigmoidectomy gives better functional results than conventional rectosigmoidectomy in elderly patients with rectal prolapse. Br J Surg. 1998;85:1525–6.
18. Agachan F, Reissman P, Pfeiffer J, et al. Comparison of three perineal procedures for the treatment of rectal prolapse. South Med J. 1997;90:925–32.
19. Cutait D. Sacro-promontory fixation of the rectum for complete rectal prolapse. Proc R Soc Med. 1959;52(suppl):105.
20. Frykman HM, Goldberg SM. The surgical treatment of rectal procidentia. Surg Gynecol Obstet. 1969;129:1225–30.
21. Wells C. New operation for rectal prolapse. Proc R Soc Med. 1959;52:602–3.
22. Ripstein CB. Treatment of massive rectal prolapse. Am J Surg. 1952;83:68–71.
23. Mc Mahan JD, Ripstein CB. Rectal prolapse: an update on the rectal sling procedure. Am Surg. 1987;53:37–40.
24. Orr TG. A suspension operation for rectal prolapse. Ann Surg. 1947;126:833–40.
25. Loygue J, Nordlinger S, Cunci O, Malafosse M, Huguet C, Parc R. Rectopexy to the promontory for the treatment of rectal prolapse. Report of 256 cases. Dis Colon Rectum. 1984;27:356–9.
26. D'Hoore A, Penninckx F. Laparoscopic ventral recto(colpo)pexy for rectal prolapse. Surgical technique and outcome for 109 patients. Surg Endosc. 2006;20:1919–23.
27. Kuijpers HC. Treatment of complete rectal prolapse: to narrow, to wrap, to suspend, to fix, to encircle, to plicate or to resect? World J Surg. 1992;16:826–30.
28. Raftopoulos Y, Senagore AJ, Di Giuro G, Bergamaschi R, Rectal Prolapse Recurrence Study Group. Recurrence rates after abdominal surgery for complete rectal prolapse: a multicenter pooled analysis of 643 individual patient data. Dis Colon Rectum. 2005;48:1200–6.
29. Madiba TE, Baig MK, Wexner SD. Surgical management of rectal prolapse. Arch Surg. 2005;140: 63–70.
30. Dolk A, Broden G, Holmstrom B, Johansson C, Nilsson BY. Slow transit of the colon associated with severe constipation after the Ripstein procedure. A clinical and physiologic study. Dis Colon Rectum. 1990;33:786–90.
31. Siproudhis L, Ropert A, Gosselin A, Bretagne JF, Heresbach D, Raoul JL, et al. Constipation after rectopexy for rectal prolapse. Where is the obstruction? Dig Dis Sci. 1993;38:1801–8.
32. Scaglia M, Fasth S, Hallgren T, Nordgren S, Oresland T, Hulten L. Abdominal rectopexy for rectal prolapse. Influence of surgical technique on functional outcome. Dis Colon Rectum. 1994;37:805–13.
33. Speakman CTM, Madden MV, Nicholls RJ, Kamm MA. Lateral ligament division during rectopexy causes constipation but prevents recurrence:results of a prospective randomized study. Br J Surg. 1991; 78:1431–3.
34. Lundby L, Laurberg S. Laparoscopic ventral mesh rectopexy for obstructed defaecation syndrome: time for a critical appraisal. Colorectal Dis. 2015;17: 102–3.
35. Shorvon PJ, McHugh S, Diamant NE, Somes S, Stevenson GW. Defecography in normal volunteers : results and implications. Gut. 1989;30:1737–49.
36. Dvorkin LS, Gladman MA, Epstein J, Scott SM, Williams NS, Lunniss PJ. Rectal intussusception in symptomatic patients is different from that in asymptomatic volunteers. Br J Surg. 2005;92:866–72.
37. Vaizey CJ, Van den Bogaerde JB, Emannuel AV, Talbot JC, Nicholls RJ, Kamm MA. Solitary rectal ulcer syndrome. Br J Surg. 1998;35:1026–9.
38. Mellgren A, Schultz I, Johansson C, Dolk A. Internal rectal intussusception seldom develops into total rectal prolapse. Dis Colon Rectum. 1997;40:817–20.
39. Collinson R, Wijffels N, Cunningham C, Lindsey I. Laparoscopic ventral rectopexy for internal rectal prolapse: short-term functional results. Colorectal Dis. 2010;12:97–104.
40. Rao SSC, Mudipalli RS, Stessman M, Zimmerman B. Investigation of the utility of colorectal function tests and Rome II criteria in dyssyerngic defecation (anismus). Neurogastroenterol Motil. 2004;16:589–96.
41. Choi JS, Hwang YH, Salum MR, Weiss EG, Pikarsky AJ, Nogueras JJ, et al. Outcome and management of patients witrh large rectoanal intussusception. Am J Gastroenterol. 2001;96:740–4.
42. Berman JR, Manning DH, Dudley-Wright K. Anatomic specificity in the diagnosis and treatment of internal rectal prolapse. Dis Colon Rectum. 1985;28:816–26.
43. Orrom WJ, Bartolo DC, Miller R, Mortensen NJ, Roe AM. Rectopexy is an ineffective treatment for obstructed defaecation. Dis Colon Rectum. 1991;34:41–6.
44. Wijffels NA, Jones OM, Cunningham C, Bemelman WA, Lindsey I. What are the sympotms of internal prolapse? Colorectal Dis. 2013;15:368–73.
45. Gosselink MP, Adusumilli S, Gorissen KJ, Fourie S, Tuynman JB, Jones OM, Cunningham C, Lindsey I. Laparoscopic ventral rectopexy for fecal incontinence associated with high-grade internal rectal prolapse. Dis Colon Rectum. 2013;56:1409–14.
46. Prapasrivorakul S, Gosselink MP, Gorissen KJ, Fourie S, Hompes R, Jones OM, Cunningham C, Lindsey I. Sacral neuromodulation for faecal incontinence: is the outcome compromised in patients with high-grade internal rectal prolapse? Int J Colorectal Dis. 2015;30:229–34.

47. Collinson R, van Duivendijk P, Cunningham C, Lindsey I. Laparoscopic anterior rectopexy improves obstructed defecation in patients with rectal intussusception. Colorectal Dis. 2007; 9(Suppl1):31–104.
48. Boccasanta P, Venturi M, Salamina G, Cesana BM, Bernasconi F, Roviaro G. New trends in the surgical treatment of outlet obstruction : clinical and functional results in two novel transanal stapled techniques from a randomized controlled trial. Int J Colorectal Dis. 2004;19:359–69.
49. Boccasanta P, Venturi M, Stuto A, Bottini C, Caviglia A, Carriero A, et al. Stapled transanal rectal resection for outlet obstruction: a prospective multicenter trial. Dis Colon Rectum. 2004;47:1285–97.
50. Ommer A, Albrecht K, Wenger F, Walz MK. Stapled transanal rectal resection (STARR): a new option in the treatment of obstructive defecation syndrome. Langenbecks Arch Surg. 2006;391:32–7.
51. Dodi G, Pietroletti R, Milito G, Pescatori M. Bleeding, incontinence, pain and constipation after STARR for obstructed defecation. Tech Coloproctol. 2003;7: 148–53.
52. Renzi A, Talento P, Giardello C, Angelone G, Izzo D, Di Sarno G. Stapled trans-anal rectal resection (STARR) by a new dedicated device for the surgical treatment of obstructed defaecation syndrome caused by rectal intussusception and rectocel: early results of a multicenter prospective study. Int J Colorectal Dis. 2008;23(10):999–1005.

Irritable Bowel Syndrome

13

Heiner Krammer, Franka Neumer,
and Laura Gruner

Irritable bowel syndrome (IBS) is characterized by chronic abdominal symptoms and irregular bowel movements without any cause that can be revealed by routine diagnostic assessment. The pathophysiology of IBS has recently come to be better understood, and new therapeutic approaches have been developed. These advances were considered and assessed regarding their relevance to clinical practice in the framework of an interdisciplinary S3 guideline [8].

13.1 Definition

Irritable bowel syndrome (IBS) is present when all three of the following criteria are fulfilled:

- The patient has chronic symptoms, that is, symptoms lasting longer than 3 months (e.g., abdominal pain, bloating), that are ascribed by both the patient and the physician to the gut, and that are usually accompanied by an altered bowel habit.
- The symptoms are why the patient consulted the physician for help and/or is worried, and are so strong that they significantly impair the patient's quality of life.
- It is a precondition that no changes are present that are characteristic of other diseases that are likely to be the cause of the symptoms.

This new definition thus differs from all its predecessors. Manning and colleagues were the first to propose key symptoms ("Manning criteria") [11] to help in the diagnosis of IBS. The Rome I, II, and III criteria are the results of multinational consensus workshops. The Rome classification system characterizes IBS in terms of multiple physiological determinants contributing to a common set of symptoms rather than a single disease entity. Table 13.1 lists the symptom-based criteria that have been established to date for the diagnosis of IBS.

IBS-related symptoms overlap with those of other diseases. Experienced clinicians often diagnose these disorders on symptoms alone, but because functional disorders are much more common than organic diseases, any diagnostic strategy is likely to have a deceptively high positive predictive value.

H. Krammer, MD (✉) • F. Neumer, MD
L. Gruner, MD
Praxis für Gastroenterologie und Ernährungsmedizin
am End-und Dickdarmzentrum,
Mannheim, Germany
e-mail: krammer@magendarm-zentrum.de;
lgruner@gmx.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_13

Table 13.1 Symptom-based criteria established to date for the diagnosis of irritable bowel syndrome

Manning criteria	Pain relieved by defecation
	More frequent stools at the onset of pain
	Looser stools at the onset of pain
	Visible abdominal distension
	Passage of mucus
	Feeling of incomplete evacuation
Rome I criteria	*Abdominal pain or discomfort for at least 3 months with at least one of the following symptoms*:
	Relief upon defecation
	Association with a change in the frequency of stools
	Associated with a change in the form of stools and two more of the following symptoms:
	Altered stool frequency and/or form, altered stool passage
	Passage of mucus
	Bloating or abdominal distension
Rome II criteria	*At least 12 weeks (not necessarily consecutive) in the preceding 12 months of abdominal discomfort or pain that has two of three features:*
	Relieved with defecation
	Onset associated with a change in the frequency of stool
	Onset associated with a change in the form (appearance) of stool
	Symptoms that cumulatively support the diagnosis of IBS:
	Abnormal stool frequency
	Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation)
	Passage of mucus
	Bloating or feeling of abdominal distension
Rome III criteria	*Diagnostic criteria[a] for IBS: recurrent abdominal pain or discomfort[b] at least 3 days per month in the past 3 months associated with two or more of the following*:
	1. Improvement with defecation
	2. Onset associated with a change in the frequency of stool
	3. Onset associated with a change in the form (appearance) of stool
	Subtyping IBS by predominant stool pattern:
	1. IBS with constipation (IBS-C): hard or lumpy stools ≥25 % and loose (mushy) or watery stools <25 % of bowel movements
	2. IBS with diarrhea (IBS-D): loose (mushy) or watery stools ≥25 % and hard or lumpy stools <25 % of bowel movements
	3. Mixed IBS (IBS-M): hard or lumpy stools ≥25 % and loose (mushy) or watery stools ≥25 % of bowel movements
	4. Unsubtyped IBS: insufficient abnormality of stool consistency to meet criteria for IBS-C, -D, or -M

[a]Criteria fulfilled for the past 3 months, with symptom onset at least 6 months before diagnosis
[b]*Discomfort* means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency at least 2 days a week during screening evaluation is required for subject eligibility

13.2 Epidemiology

IBS is one of the most common disorders seen in gastrointestinal clinical practice. The overall prevalence is similar (10–20 %) in most industrialized countries. These findings reflect the tremendous impact of IBS on social costs related to health care use, drug consumption, and absences from work. The exact prevalence of IBS is poorly defined, probably because of the different definitions and clinical criteria used to define the syndrome.

This certainly underestimates the real prevalence of IBS, as only one in three patients seeks treatment. Those who do consult a doctor report more severe symptoms and an increased level of

psychological disturbance (anxiety, depression, and sleep disturbance) than those who do not.

IBS is commonly believed to be a female-predominant disease. IBS symptoms are at least twice as common in women as in men. The reasons why women seem to be more prone to IBS than men are unknown, although health-seeking behavior and other factors may play a role in this gender difference. The first presentation of patients to a physician often occurs between the ages of 30 and 50 years, and reporting frequency decreases among older people.

13.3 Etiology/Pathophysiology

Since the mid 1990s, significant advances have been made in the understanding of the pathophysiology of IBS. However, interactions/interrelationships between causal and secondary alterations are unclear. For many patients the most consistent, and probably interrelated, characteristics are:

- Altered intestinal motility
- Visceral hypersensitivity
- Bowel dysfunction after infection (altered intestinal microbiota)
- Dietary factors
- Stress and psychological comorbidity

13.3.1 Altered Motility

Abnormal small-intestinal and colonic motility has been demonstrated in patients with IBS, and in some patients it has been shown to correlate with symptoms. Abnormalities of intestinal motility may lead not only to the onset of pain but also to bloating and, if the abdominal motility results in changes in intestinal transit, constipation and diarrhea.

13.3.2 Visceral Hypersensitivity

Patients with functional bowel diseases exhibit decreased tolerance of pain upon balloon distension of the gut. This was first described in the rectum of patients with IBS almost 30 years ago and was subsequently confirmed by others. It is often also noted with air insufflation during colonoscopy. This phenomenon is referred to as visceral hyperalgesia. Explanations for this include an alteration of the sensitivity of sensory receptors through the recruitment of nociceptors in response to infection, intraluminal factors, ischemia, distension, and psychiatric factors. The neurons in the dorsal horn of spinal cord may experience increase excitability, and centrally there may be differences in the way the brain modulates afferent signals from the dorsal horn neurons through ascending pathways.

13.3.3 Gastrointestinal Infection (Altered Intestinal Microbiota)

There is an increased risk of patients developing IBS symptoms following an episode of gastrointestinal infection. It was shown that approximately one-third of patients hospitalized for infectious diarrhea had developed new IBS [13]. In most cases, persistent bowel dysfunction was noted in patients following documented *Campylobacter*, *Shigella*, and *Salmonella* gastroenteritis. Factors predisposing patients to persisting symptoms are the severity and duration of diarrhea, anxiety, depression, and somatization, as well as adverse life events. Mechanisms underlying IBS after infection are unclear, but immunological abnormalities at the intestinal level have been demonstrated in these patients, as has increased mucosal T lymphocytes and serotonin-producing enteroendocrine cells. Also, response to a pathogen is undoubtedly influenced by genetic factors that in turn influence immune response.

13.3.4 Dietary Factors

Many patients with IBS believe that their symptoms are related to food, and some have considerably restricted their diet by the time they consult a physician. The gut has an extensive immune system, but the current understanding

of how food antigens are processed in health and disease is limited. At present, no clinically useful marker is available to test for food hypersensitivity in IBS. Researchers have used both skin tests and serum immunoglobulins (IgG and IgE) as markers of food hypersensitivity in various disorders, including IBS, but published data are equivocal. Moreover, many unscrupulous practitioners benefit from the confusion, leading patients to more and more restricted and illogical diets.

The role of sugar malabsorption in the pathogenesis of IBS is still a debated problem. Demographic data show that the prevalence of sugar malabsorption among patients with IBS is similar to that found in controls. Symptoms such as diarrhea and bloating, can typically be reproduced by lactose intake and reduced once lactose is excluded from the diet. Lactose malabsorption may coexist with IBS. Nevertheless, a lactose-free diet is effective in improving symptoms in only about 10 % of patients with IBS.

True food allergy is much less common. It is usually not difficult to recognize whether food ingestion is associated with urticaria, asthma, eczema, angioedema, and rhinorrhea because of the high incidence of positive skin-prick or high radioallergosorbant scores. Such patients see an allergist rather than a gastroenterologist and are not usually thought to have IBS.

13.3.5 Stress and Psychological Comorbidity

Psychological observations have shown that psychological symptoms of anxiety and depression are more common among patients with IBS than among either healthy volunteers or patients with organic gastrointestinal diseases. More than 50 % of patients linked the onset of their symptoms to a stressful event such as employment difficulties, a death in the family, a surgical procedure, or marital stress. Clinicians agree that stress can cause symptoms of IBS, but it cannot be considered the only cause. The magnitude of psychological stress also correlates with symptomatic outcomes.

13.4 Symptoms

- Patients with IBS suffer from various gastroenterological symptoms. These include recurrent abdominal pain, altered bowel function, bloating, abdominal distension, a sensation of incomplete evacuation, and the increased passage of mucus (Table 13.1).
- In addition, several *nongastroenterological symptoms* are more frequent in patients with IBS, such as lethargy, poor sleep, fibromyalgia, backache, urinary frequency, and dyspareunia.
- Anxiety, depression, and somatization are frequent but do not reliably discriminate between IBS and other gastrointestinal diseases.
- Functional diseases such as IBS usually interfere with patients' comfort and their daily activities.
- On the other hand, IBS is a benign disorder, and there are no long-term organic complications such as cancer or colitis.

13.5 Diagnosis

The focus during diagnosis is on a careful history and the physical examination, supplemented by basic laboratory testing, abdominal ultrasound, and, in women, gynecological examination. After these have been performed, if results are normal, treatment may be started on a trial basis, even without a confirmed diagnosis (see section 13.5.2). This should be decided on an individual basis and is justified particularly in patients with mild, nonprogressive symptoms, but it does not allow a diagnosis of IBS to be made.

In patients with chronic diarrhea as an important symptom, a detailed diagnostic workup, including pathogen identification in the stool, and endoscopic and functional diagnostic examinations (with staged biopsies) are indicated. Confirmation of IBS in an adult requires an ileocolonoscopy.

The diagnostic procedure should be supplemented on an case-by-case basis by endoscopic, imaging, functional diagnostic, and, if relevant, other procedures to rule out other candidate diagnoses that can cause symptoms typical of

IBS. The criteria for this are the intensity and pattern of symptoms, the patient's age, the duration of symptoms, symptom dynamics, and a psychological assessment of the patient.

- IBS is basically a clinical diagnosis. Careful history-taking to record and classify the complex of symptoms is the key. A diagnosis of IBS is based on the identification of symptoms consistent with the syndrome (Table 13.1).
- The first step is a careful assessment of the patient's symptoms. Patients should be carefully interviewed. Ideally, no time limitation should exist because patients need to think about the diagnosis.
- Second, IBS is diagnosed after excluding structural or biochemical abnormalities that could indicate organic or other functional disorders.

Once a reliable initial diagnosis has been made, no repeat diagnostic procedure should be undertaken unless new aspects occur.

13.5.1 Physical Examination

- A physical examination should be performed during the first and as needed during any subsequent visits to exclude findings not consistent with IBS and to meet patients' expectations of a thorough evaluation.
- A pelvic examination is often indicated for lower abdominal/pelvic symptoms and/or if there is a change in menstrual pattern (in women).
- A rectal examination, particularly for patients reporting symptoms of incontinence and constipation, can help to identify a lax sphincter or paradoxical pelvic floor muscle contraction.

13.5.2 Investigation and Tests

- These tests include:
  - Complete blood cell count and sedimentation rate
  - Serum chemistry
  - Thyroid-stimulating hormone
  - Stool hemoculture
- Additional tests are performed depending on the age of the patient and the predominant clinical picture.
- Abdominal ultrasound contributes little in the evaluation of patients with suspected IBS.
- Colonoscopy is recommended for patients over the age of 50 because of the high pretest probability of colon cancer. In younger patients, the need to perform a colonoscopy or sigmoidoscopy is determined by clinical features suggestive of disease and may not be indicated.

Pain-Predominant Symptoms

- The persistence of pain often indicates additional imaging studies (e.g., computed tomography).

Constipation-Predominant Symptoms

- In patients with infrequent bowel movements, measurement of the whole-gut transit time may be indicated to differentiate between IBS and slow-transit constipation or outlet obstruction.
- When symptoms of dyschesia or incomplete evacuation are prominent, suggesting obstruction to defecation, defecography is recommended.

Diarrhea-Predominant Symptoms

- If diarrhea is persistent, a stool sample should be examined for pathological bacteria, ova, and parasites.
- Exocrine pancreas insufficiency should be excluded.
- Small-bowel biopsy and aspirate should be obtained to test for *Giardia lamblia* or sprue.
- A colonoscopy (possibly with ileoscopy) and multiple biopsies are necessary to exclude inflammatory bowel disease.
- Colonic biopsies can be considered to evaluate for collagenous or microscopic colitis.
- A breath hydrogen test to exclude bacterial overgrowth is helpful, especially when postprandial symptoms of bloating accompany the diarrhea.

- Lactose intolerance and other carbohydrate malabsorptions (e.g., fructose, sorbitol) are common causes of diarrhea.
- Rare causes of diarrhea include metabolic disorders such as diabetes (as a result of autonomic neuropathy and motility disorders), hormonal abnormalities (e.g., hyperthyroidism), other causes of malabsorption (e.g., chronic pancreatitis), and endocrine tumors secreting serotonin, vasoactive intestinal polypeptide, or gastrin.

13.6 General Management and Therapy

Making a definitive diagnosis helps both doctor and patient by reassuring them that it is unlikely that another alternative diagnosis will emerge over the ensuing years. Establishing a relationship of trust between physician and patient promotes treatment success. Physicians should avoid comments such as "it is untreatable" or "you will learn to live with it" because these quite obviously may result in despondency. However, patients often appreciate a short tutorial on the anatomy and physiology of the gut an being informed about the current theories of pathophysiology, such as motility and visceral sensitivity. Some information on the role of stress and psychological factors, if put in simple terms, is also recommended: for example, "stress can make symptoms worse but does not cause IBS." Individual triggering factors should be identified and taken into account.

The measure of any treatment plan is how much symptoms improve and how well the patient tolerates it. All treatments are trial treatments at first because it is impossible to predict the response to treatment in any particular case. This should be discussed with the patient beforehand.

Any treatment regimen that is successful can be continued, changed to a long-term or as-needed regimen, or interrupted for a trial withdrawal. If treatment success is inadequate, various drugs (and nondrug treatments) may be used in succession or in combination. Ineffective drugs should be terminated after 3 months at the most, after carefully weighing the risks and benefits to the particular patient. In some cases, especially in patients with severe symptoms that are refractory to treatment, off-label therapies may be worthwhile – if current scientific knowledge suggests there is a reason to expect relevant therapeutic utility. The same applies to active substances that to date are only licensed or approved for use abroad, although in this case, consultation with a specialized center is advisable.

13.6.1 Lifestyle Advice

Lifestyle advice means a careful dietary and lifestyle history to identify food fads or deficiencies, for example, and excess or lack of dietary fiber. Other common factors are lack of exercise and not allowing adequate and suitable time for regular defecation, which are particularly relevant to constipated patients with IBS. Patients should be instructed to keep a 2-week diary of symptoms, stressors, and dietary intake to identify any triggering factors.

13.6.2 Dietary Factors

Food products have variously been reported as perpetuating or treating IBS. For instance, patients may have excessively large intakes of indigestible carbohydrates, fruits, or caffeine, especially those who suffer from diarrhea and bloating. They may also benefit from a diet low in lactose and/or fructose. Constipated patients with low fiber intake should attempt a high-fiber diet. However, there is growing evidence that bran can increase the symptoms of IBS, whereas soluble forms of fiber (e.g., ispaghula) tend to be more effective and have fewer adverse effects such as bloating. Exclusion diets may be useful in controlling symptoms in some patients.

13.6.3 Psychological Comorbidities

To register the psychological comorbidities that are often present in patients with IBS, it is often enough to simply ask about anxiety disorders and depressive symptoms, and (carefully!) explore for a history of trauma and abuse. If appropriate, the patient should be referred for professional psychiatric/psychological/psychosomatic examination and/or care. Any signs of relevant psychosocial stress also indicate psychological diagnostic steps and possibly psychotherapy. At the same time, general medical care should be continued.

At the general and specialist medical level, basic psychotherapeutic intervention can often be carried out to favorable effect (e.g., using self-help strategies). Pure relaxation therapies (e.g., autogenic training) should not be used as monotherapy but should be combined with other measures. Costly and time-consuming psychological techniques (gut-directed hypnosis, cognitive behavioral therapy, psychodynamic therapy) are effective and should be integrated into an interdisciplinary therapy plan. Antidepressants may be indicated in the presence of psychological comorbidities (anxiety disorder, depression). Tricyclic antidepressants to treat the irritable bowel symptoms (diarrhea, pain; beware of constipation) should be given at doses lower than the usual; selective serotonin reuptake inhibitors in particular can also be given to patients with constipation-dominant IBS. However, irritable bowel symptoms seem not to respond to antidepressants in the absence of psychological comorbidities.

13.6.4 Targeted Symptom-Oriented Therapy

One of the most common problems facing clinicians treating patients with IBS is the lack of uniformity of symptoms. In the majority of cases, current pharmacological treatments have limited value. For those patients who require therapy for specific symptoms, however, the following treatments have been proven effective (summarized in Table 13.2).

13.6.4.1 Abdominal Pain and Bloating

- For pain and bloating, antispasmodic medication should be considered. These drugs have differing modes of action, some exhibiting anti–smooth muscle activity (phytotherapeutics; e.g., STW 5, mebeverine) and others anticholinergic activity (e.g., butylscopolamine).
- The guanylate cyclase-C agonist linaclotide, which has been shown to be effective in pain- and constipation-dominant IBS, is available in the United States and some European countries.
- Antidepressants can be used off label for treating IBS because they not only treat underlying depression but also modify gut motility and alter visceral nerve responses. However, tricyclic antidepressants can intensify constipation. That is why patients with a predominant symptom of pain who also suffer from constipation should be given selective serotonin reuptake inhibitors.
- Classical "analgesics" (e.g., acetylsalicylic acid, paracetamol/acetominophen, nonsteroidal anti-inflammatory drugs) are generally unsuitable, as are opioids and opioid agonists. Topical antibiotic therapy (rifaximin) is not yet recommended in the guidelines.
- A number of trials of probiotics in IBS, though patient numbers as well as treatment periods are rather small.

Diarrhea

- Loperamide slows transit through the small and large intestines and reduces stool frequency and urgency in patients with diarrhea-predominant IBS.
- Cholestyramine may also be considered since about 10% of patients with diarrhea-predominant IBS show evidence of bile salt malabsorption.
- Fiber supplements such as ispaghula husks and psyllium may be helpful to increase stool consistency.
- It may also be worth trying phytotherapeutics (e.g., STW 5), spasmolytics (e.g., mebeverine, butylscopolamine, peppermint oil), or—

Table 13.2 Symptom-directed therapy for irritable bowel syndrome

Pain-predominant	Antispasmodics (e.g., mebeverine, butylscopolamine)
	Linaclotide
	Herbal remedies (menthol, *Iberis amara*)
	Antidepressants (amitriptyline, *cave*: constipation)
	Selective serotonin reuptake inhibitors (fluoxetine)
Meteorism-predominant	Polydimethylsiloxane (dimethicone)
	Probiotics
	Herbal remedies (*I. amara*)
Diarrhea-predominant	Ispaghula husk, psyllium
	Loperamide
Constipation-predominant	Ispaghula husk, psyllium
	Linaclotide
	Probiotics
	Herbal remedies (*I. amara*)
	Osmotic laxatives (polyethylene glycol)
	Stimulating laxatives (bisocodyl, sodium picosulfate)
	CO_2 laxatives (suppositories) to support evacuation

especially where there is psychological comorbidity—tricyclic antidepressants. When symptoms are severe and refractory to treatment, a selective 5-HT_3 antagonist (e.g., alosetron) may be used, but only after carefully weighing the risks versus the benefits, because of its rare adverse effects (ischemic colitis, severe constipation).

Constipation

- Patients with IBS and constipation should try an increased intake of dietary fiber to increase stool weight and accelerate gut transit. In particular, psyllium and ispaghula husks are a useful alternative to wheat bran because they do not lead to meteorism and flatulence.
- The guanylate cyclase-C agonist linaclotide, which has been shown to be effective in pain- and constipation-dominant IBS, is available in the United States and some European countries.
- Probiotics such as *Escherichia coli* strain Nissle 1917, *Lactobacillus casei* strain Shirota, and *Bifidobacterium animalis* have been shown to increase stool frequency and soften stool consistency.
- Osmotic laxatives such as polyethylene glycol may be used.
- Stimulating laxatives such as bisocodyl or sodium picosulfate.
- In some cases lubiprostone, a chloride channel activator, may be tried, bearing in mind any contraindications and its restricted availability (it is licensed/approved for use in Switzerland and the United States).

The symptom-based therapy of IBS is summarized in Fig. 13.1.

13.7 Prognosis

IBS is generally regarded as a chronic relapsing condition. There is no cure for IBS, but symptoms can be managed with dietary changes, stress reduction, and, if necessary, medication. Therefore, the prognosis is likely to be individualized based on the patient's optimism and a successful management.

Previous abdominal surgery has a poor prognostic implication in IBS. Patients undergoing surgery are likely to be more symptomatic during the first postoperative year than are patients without IBS. Underlying reasons involve a questionable indication for the surgery and possible alterations in gut physiology following the procedure.

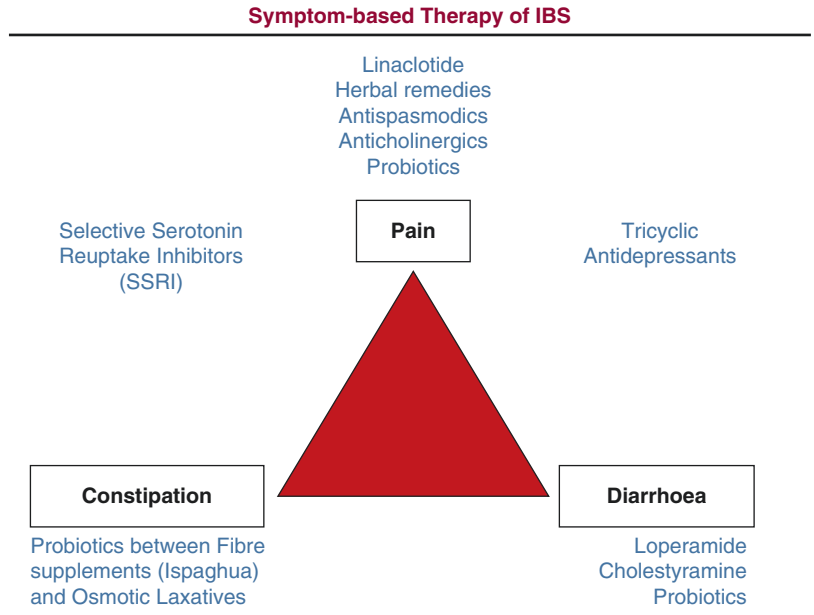


Fig. 13.1 Practical guide to the therapy of irritable bowel syndrome

Suggested Reading

1. Bonaz BL, Papillon E, Baciu M, Segebarth C, Bost R, LeBas J, Fournet J. Central processing of rectal pain in IBS patients: an MRI study. Gastroenterology. 2000;118(suppl):A615.
2. Camilleri M, Heading RC, Thompson WG. Clinical perspectives, mechanisms, diagnosis and management of irritable bowel syndrome. Aliment Pharmacol Ther. 2002;16:1407–30.
3. Corney RH, Stanton R. Physical symptom severity, psychological and social dysfunction in a series of outpatients with irritable bowel syndrome. J Psychosom Res. 1990;34:483–91.
4. Dapoigny M. Functional intestinal disorders. Diagnosis and treatment. Rev Prat. 1999;49:1559–64.
5. De Giorgio R, Barbara G, Stanghellini V, Cremon C, Salvidi B, De Ponti F, Corinaldesi R. Diagnosis and therapy of irritable bowel syndrome. Aliment Pharmacol Ther. 2004;20 Suppl 2:10–22.
6. Farthing MJ. Treatment options in irritable bowel syndrome. Best Pract Res Clin Gastroenterol. 2004;18:773–86.
7. Jones R. IBS: prime problem in primary care. Gut. 2000;46:7–8.
8. Layer P, et al. S3-Leitlinie Reizdarmsyndrom: Definition, Pathophysiologie, Diagnostik und Therapie. Gemeinsame Leitlinie der Deutschen Gesellschaft für Verdauungs- und Stoffwechselkrankheiten (DGVS) und der Deutschen Gesellschaft für Neurogastroenterologie und Motilität (DGNM). Z Gastroenterol. 2011;49(2):237–93.
9. Longstreth GF, Drossman DA. New developments in the diagnosis and treatment of irritable bowel syndrome. Curr Gastroenterol Rep. 2002;4:427–34.
10. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130:1480–91.
11. Manning AP, Thompson WG, Heaton KW, Morris AF. Towards positive diagnosis of the irritable bowel. BMJ. 1978;2:653–4.
12. Small PK, Loudon MA, Han CM, Noor N, Campbell FC. Large scale ambulatory study of post prandial jejunal motility in irritable bowel syndrome. Scand J Gastroenterol. 1997;32:39–47.
13. Spiller RC. Postinfectious irritable bowel syndrome. Gastroenterology. 2003;124:1662–71.
14. Thompson WG, Longstreth GF, Rossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut. 1999;45 suppl 2:II43–7.
15. Zimmerman J. Extraintestinal symptoms in irritable bowel syndrome and inflammatory bowel diseases: nature, severity, and relationship to gastrointestinal symptoms. Dig Dis Sci. 2003;48:743–9.

Inflammatory Bowel Disease: Ulcerative Colitis

14

P.J. Conaghan and N.J. Mc C. Mortensen

14.1 Definition

Ulcerative colitis (UC) is a chronic, relapsing idiopathic inflammation of the rectum and variable lengths of the adjoining colon.

14.2 Epidemiology

14.2.1 Incidence

The incidence of UC is relatively constant in the United States and northern Europe at about 12 cases per 100,000 adults and about 5 cases per 100,000 children younger than 16 years of age. The incidence is rising, however, in areas where it was previously low, such as southern Europe and East Asia [1, 2]. This may be in part the result of an increasing awareness of the condition and improved means of detection, but some of this increase is likely a real phenomenon. It has been attributed to a "Westernization" of the lifestyle in these countries, but an accurate cause is not known. Note that rates for isolated ulcerative proctitis are often excluded from these statistics.

14.2.2 Prevalence

The prevalence of UC reflects the incidence, although rates quoted vary widely in the literature. Rates for northern Europe are in the region of 100–250 per 100,000 but are as low as 20 per 100,000 in central/southern Europe. There is a higher prevalence among urban compared with rural populations. These geographical variations are reflected among migrants, in whom the rate of UC tends toward that of the host population, supporting the view that environmental factors play a major role in the pathogenesis of UC.

The onset of UC commonly occurs between 25 and 35 years of age, but it has a bimodal distribution, with a second smaller peak later in life (>60 years old). Younger age at onset is often associated with an aggressive disease course. Men and women are affected equally.

Many risk factors have been proposed for the development and exacerbation of UC. However, the literature is often contradictory.

- Cigarette smoking is the risk factor most strongly linked to UC. Current smoking is protective against the development of UC, reducing the risk to 40% of that of nonsmokers. However ex-smokers have the highest risk: 1.5–2 times greater than that of nonsmokers [3, 4].

P.J. Conaghan (✉)
Department of Colorectal Surgery, Royal Berkshire Hospital, Reading RG1 5AN, UK
e-mail: philip.conaghan@royalberkshire.nhs.uk

N.J. Mc C. Mortensen
Department of Colorectal Surgery, Oxford University Hospitals, Churchill Hospital, Headington, Oxford OX3 7LE, UK
e-mail: neil.mortensen@nds.ox.ac.uk

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_14

- Appendicectomy exerts a protective effect against the development of UC, reducing the risk to about 30 % of those who retain their appendix. However, the reduced rate of appendicectomy does not seem to have effected an equal rise in the incidence of UC, so the effect is likely to be minor [5].
- Prolonged use of nonselective nonsteroidal anti-inflammatory drugs, oral contraceptive pills, perinatal infections, social class, and various dietary substances have all been implicated in the development of UC, but the literature is inconclusive.

14.2.3 Etiology

The cause of UC is unknown, but it is likely to involve an inappropriate and exaggerated immune response in the colonic mucosa to antigens on colonic microflora brought about by environmental triggers in people who are genetically susceptible. In other words, a number of genes likely interact with environmental factors, and the trigger for inflammation may involve the colonic flora. These genetic, immunological, and microbiological factors are all interrelated.

14.2.4 Genetic Factors

The concordance rate of UC in monozygotic twins is quoted between 15 % and 20 %, compared with 2–5 % for dizygotic twins [6, 7]. The lifetime risk of developing UC for a first-degree relative of someone with the condition is 1.6 %, although this is higher for Jews [8]. This confirms a genetic influence in the development of UC, although its contribution is not as substantial as that seen in Crohn's disease. Some genes contribute to susceptibility to a broader inflammatory bowel disease (IBD), leading to the incidence of UC being greater among relatives of those with either UC or Crohn's disease and vice versa. The advent of genome-wide association studies have improved the understanding of the genetics of IBD, and 163 susceptibility genes are now considered loci for IBD, with the most important within the 6p locus, where evidence for linkage is strongest in the region of the human leukocyte antigen (HLA) genes [9–11]. Consistent with this, UC has associations with particular HLA genotypes. HLA-DR2 has a positive association with UC, which interestingly also has a positive association with the development of primary sclerosing cholangitis (PSC) and a negative association with the development of Crohn's disease. These genetic factors may also influence the clinical phenotype of the condition, especially in relation to the extraintestinal manifestations such as arthritis and PSC.

14.2.5 Immunological Factors

Immunological factors are closely linked with the genetic factors and in particular the patient's HLA genotype [10]. Appropriate levels of stimulatory and regulatory T cells and their respective cytokines maintain the immunological status quo of the colonic mucosa. Their importance is well demonstrated in experimental mouse models of colitis, where imbalance in the activation or number of these stimulatory or regulatory cells can lead to inflammation in certain circumstances.

The mucosal epithelium also plays a role in controlling immune functions. These epithelial cells can recognize conserved products unique to microorganisms (e.g., a lipopolysaccharide that coats some gram-negative bacteria) via Toll-like receptors and through these receptors can release cytokines, chemokines, and other pro- or anti-inflammatory substances. The cytokine response in UC is believed to be predominantly a dysregulated Th_2 response as opposed to the predominant Th_1 response in Crohn's disease.

14.2.6 Microbiological Factors

The inappropriate immune response may occur in response to colonic flora, and there has been suggestion that patients with UC fail to develop oral tolerance to luminal antigens in the gut. No specific bacteria have been identified as causative

agents, but people with different HLA genotypes may interact abnormally with different bacteria yet the same immune dysregulation may result to produce UC.

14.3 Symptoms and Signs

UC usually presents with bloody stool with an associated increase in stool frequency. The consistency of stool often depends on the extent of the disease: more extensive involvement leads to increased looseness of stool. Severe proctitis can present with constipation, although patients often pass blood and mucus independent of stool in these situations. Abdominal pain is more common in extensive disease, as are systemic symptoms such as fever, anorexia, and weight loss.

Some patients have extraintestinal manifestations of the disease, such as PSC and pyoderma gangrenosum, which are unrelated to the disease activity of the colitis, and others such as arthritis and erythema nodosum, which follow the clinical course of the gastrointestinal (GI) disease. The main symptoms are summarized in Table 14.1.

Abdominal examination is often unremarkable apart from mild tenderness. Significant tympanitic distension or any evidence of peritonism are of great concern and need urgent attention. During acute attacks the patient may become dehydrated, hypokalemic (from diarrhea), and anemic (from GI blood loss).

A relapsing and remitting course is the usual pattern of illness; about 50 % of patients with UC have a relapse in any given year.

Symptoms and signs can be formally scored using validated disease activity scores for UC (e.g., Lichtiger score; see Table 14.2).

Table 14.1 Presenting symptoms of ulcerative colitis

Gastrointestinal	Diarrhea usually mixed with blood, with or without mucus
	Frequency
	Constipation in some cases of severe proctitis
	Urgency
	Tenesmus
	Incontinence
	Abdominal pain
Systemic	Tiredness
	Weight loss
	Fever
	Anorexia
Extraintestinal (about 10 % of patients [58])	Related to disease activity
	Arthritis
	Uveitis/iritis
	Deep vein thrombosis
	Erythema nodosum
	Unrelated to disease activity
	Primary sclerosing cholangitis
	Ankylosing spondylitis
	Pyoderma gangrenosum
Complications	Colorectal cancer
	Acute lower gastrointestinal hemorrhage
	Colonic perforation

14.4 Complications

14.4.1 Colorectal Cancer

Colorectal cancer (CRC) is the most common neoplastic complication of UC, with an incidence of 3 per 1,000 person-years of disease and a prevalence of 3–7 % [12]. It is more likely to be multiple, have a higher grade, and be nonpolypoid than sporadic noncolitic cancers.

Particular risk factors for CRC among people with UC are:

- Extensive colitis
- Diagnosis of PSC
- History of colitis for >8 years
- Severity of colitis (particularly the first attack)
- Young age at onset of colitis
- Family history of CRC

Considering all patients with UC, the risk of cancer increases with the duration of the disease:

- Two percent at 10 years
- Ten percent at 20 years
- Twenty percent at 25 years

The risk in the subgroup of those with extensive colitis is significantly greater:

Table 14.2 Activity score for ulcerative colitis (Lichtiger et al.) [59]

Factor	Score	
Diarrhea	0 = 1–2 times/day	3 = 6–9 times/day
	1 = 3–4 times /day	4 = ≥10 times /day
	2 = 5–6 times /day	
Nocturnal bowel movement	0 = No	1 = Yes
Bloody stools	0 = None	2 = ≥50 % of time
	1 = <50 % of the time	3 = Every time
Incontinence/soiling	0 = No	1 = Yes
Abdominal pain	0 = None	
	1 = Mild; minimal interference with daily activity	
	2 = Moderate; interferes with daily activity	
	3 = Severe; incapacitating	
Well-being	0 (Excellent) to 5 (terrible)	
Antidiarrheal or opioid drugs	0 = No	1 = Yes
Abdominal tenderness	0 = None	
	1 = Mild to moderate but localized	
	2 = Mild to moderate but diffuse	
	3 = Severe or evidence of peritonism	

- Five percent at 10 years
- Twenty percent at 20 years
- Forty percent at 25 years

Dysplasia in UC is the most reliable marker of an increased risk of CRC, but it can be difficult to detect. It is divided into four categories:

- Absent
- Indefinite
- Low grade (LGD)
- High grade (HGD)

Dysplasia presents as two main patterns: flat lesions and elevated lesions. Flat dysplasia is often identified incidentally in surveillance biopsies from unremarkable mucosa, although dye-spraying may improve the detection of flat dysplasia. Elevated lesions can be either adenoma-like – essentially sporadic adenomas, as in people without UC – or non-adenoma-like. This latter group is more heterogeneous, the lesions are less demarcated, and the surrounding flat mucosa is more likely to be dysplastic. Hence biopsy of the surrounding mucosa of any elevated lesion in UC is essential. Adenoma-like dysplasia can essentially be treated like any other adenoma if the surrounding mucosa is nondysplastic.

A proctocolectomy with or without ileal pouch formation should be recommended to all patients with the following conditions [13, 14]:

- Cancer
- Any elevated lesion with surrounding flat dysplasia
- A non-adenoma-like elevated lesion
- Flat HGD

It should also be considered in patients with flat LGD. Patients should be told that their risk of CRC is nine times greater than that in patients without LGD, and the risk increases with a more distal location of the cancer in the colon/rectum. A colectomy with ileorectal anastomosis could in exceptional circumstances be considered in colonic cancer/HGD with careful postoperative surveillance (see below Sect. 14.11.2: Colectomy and ileorectal anastomosis). Given these risks in UC, screening for colorectal cancer is obviously important. Screening guidelines have been developed [15]:

- Ideally, screening should be performed when a patient is in remission.
- The first surveillance colonoscopy should be performed after 6–8 years from the onset of symptoms. It is at this colonoscopy that the extent of disease is accurately documented [16].

- The frequency of surveillance is guided by the risk of CRC in any individual and is normally categorized into high risk (yearly colonoscopy), intermediate risk (every 3 years), and low risk (every 5 years) [15]. The risk stratification is based on how extensive the colitis is, the severity of inflammation, the presence of pseudopolyps, and a family history of CRC.
- Ideally, pancolonic dye-spraying should be used with targeted biopsies of abnormal areas. If this is not available, however, two to four random biopsies should be taken every 10 cm along the entire colon and rectum. Additional biopsies should be taken in suspicious areas.
- Patients diagnosed with PSC should have annual colonoscopies irrespective of the state of the liver disease.
- In patients with LGD at one site, colonoscopy should be performed every 6 months until two successive colonoscopies are negative.

14.4.2 Cholangiocarcinoma

The risk of cholangiocarcinoma is increased in patients with UC on account of the relationship between UC and PSC. About 4 % of patients with UC develop PSC during their lifetime, and in this population the lifetime risk of cholangiocarcinoma is about 10 %. The risk of cholangiocarcinoma, like PSC, is not influenced by the disease activity of UC.

14.4.3 Toxic Megacolon

This is a nonobstructive dilatation (>6 cm) of colon in conjunction with extensive colitis (rarely just left-sided disease) and systemic disturbance. The incidence is falling and currently occurs in less than 4 % of patients with UC. Patients are at greatest risk early after diagnosis, especially during the first attack. It often follows a prolonged attack of drug-resistant acute colitis, and hypokalemia, opioid analgesics, drugs causing constipation, anticholinergics, and possibly superadded infections such as *Clostridium difficile* and cytomegalovirus are believed to be precipitants. Examination reveals mild tympanitic distension, but any evidence of localized or generalized peritonism should be an indication for emergency surgery. Medical management of toxic acute UC is permissible at the first instance (see Sect. 14.7.2.1), but any deterioration or failure to improve should again lead to emergency surgery.

The criteria for diagnosis of toxic megacolon are [17]:

- Diagnosis of colitis
- Radiographic evidence of colonic distension >6 cm
- Fever >38 °C
- Heart rate >120 bpm
- Neutrophilia $>10 \times 10^9$
- One of the following:
  - Anemia
  - Dehydration
  - Electrolyte disturbance
  - Hypotension
  - Glasgow Coma Scale score <15

The dilatation is accompanied by and possibly the result of inflammation of the bowel wall extending beyond the mucosa into the muscle. This leaves the bowel prone to perforation, which is why the condition is so dangerous. Perforation of a toxic megacolon carries a mortality of 40 %.

14.4.4 Acute GI Hemorrhage

Severe GI bleeding occurs in less than 5 % of all patients with UC but accounts for about 10 % of the emergency colectomies performed for UC [18]. The risk of significant hemorrhage increases with the extent of the disease.

14.4.5 Benign Strictures

These occur in about 4 % of all patients with UC, predominantly in the left colon. Treatment depends on the degree of symptoms and the extent of disease elsewhere in the colon. Total colectomy is the usual surgical option.

14.5 Diagnosis

UC is diagnosed based on a suggestive history and examination leading to a combination of endoscopic, histological, and microbiological investigation.

14.5.1 Endoscopy

The gold standard for diagnosing colitis is flexible sigmoidoscopy/colonoscopy. This shows acute inflammation starting in the rectum and extending proximally, and allows biopsies to be taken for histology. Care is required because the risk of perforation is high in acute disease, and colonoscopy should be reserved for assessing the extent of disease after the acute attack has been treated. Extent of disease is defined by the Montreal classification (Table 14.3). About 20 % of patients have extensive disease at presentation [19] (Fig. 14.1).

In active disease, the mucosa is erythematous, granular, friable, and demonstrates contact bleeding. Pseudopolyps, which are islands of mucosa within an area of extensive ulceration, may be present in severe disease. In quiescent chronic disease, the mucosa usually shows signs of chronic injury, with loss of the normal vascular pattern, and may appear featureless. Inflammatory polyps may be present.

Biopsies should be taken from multiple sites along the colon (including areas that appear normal), always including the rectum [20]. The contiguous nature of the disease is one of the major features that distinguishes UC from Crohn's colitis, although this is not always apparent macroscopically. However, even when there is variation in the severity of the colitis between different segments of the bowel, which can give a false impression of skip lesions, biopsies from the apparent "skip" area usually show features of chronic inflammation typical of UC, highlighting the importance of multiple biopsies. In chronic disease and in patients who have received topical therapy, the rectum can often appear normal, giving the impression of rectal sparing. Again, biopsy is crucial in the diagnosis. Another area of confusion is near the ileocecal valve, where the "cecal patch" can give the impression that it is a focus of inflammation distant from a more distal area of colitis and therefore a "skip lesion." This can be seen even in normal asymptomatic individuals.

Once colitis is established as a cause of the patient's symptoms, histology and microbiology help confirm the diagnosis of UC.

Table 14.3 Montreal classification

Distribution	Description
Proctitis	Disease limited to the rectum
Left sided	Disease limited to the colorectum distal to the splenic flexure
Extensive	Disease beyond the splenic flexure

14.5.2 Microbiology

All patients with colitis should have stool sent for microbiological assessment to exclude an infectious cause of their colitis. This should include virology, parasitology, and *C. difficile* toxin.

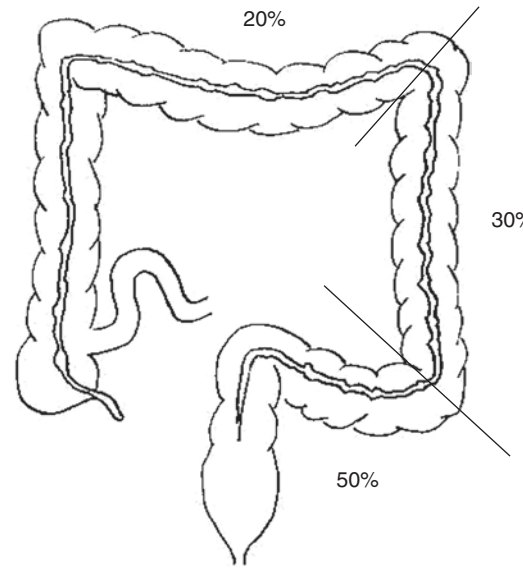


Fig. 14.1 Proportion of people with varying extents of disease at presentation

14.5.3 Histology

UC is confined to the large bowel, although up to 30 cm of terminal ileum can be involved with "backwash ileitis." Reports of biopsies taken during ileocolonoscopy should describe whether the tissue shows features of UC to distinguish it from other common causes of colitis such as Crohn's disease, pseudomembranous colitis, and diverticular disease. They should also comment on disease activity and on any dysplasia seen within the specimen.

The severity of the inflammatory reaction correlates well with the clinical course of the disease. Cardinal features of UC include:

- Inflammation limited to the mucosa and superficial submucosa, although deeper layers can be involved in fulminant colitis
- Diffuse and severe distortion of crypt architecture, although this can take 6 weeks to develop
- Diffuse and severe reduction in crypt density
- Heavy infiltration of inflammatory cells in the lamina propria, especially basal plasmocytosis. Neutrophils are prevalent in active disease, and these can form crypt abscesses, which are a reliable indicator of disease severity.
- Severe mucin depletion
- Superficial ulceration in active disease

14.6 Additional Useful Diagnostic Procedures

Blood tests often show a chronic or acute-on-chronic inflammatory response:

- High C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white cell count
- Low hemoglobin, albumin
- Renal function in all patients presenting with severe acute colitis
- Liver function tests to assess progressive PSC
- Perinuclear anticytoplasmic antibody (pANCA) serology is commonly positive in UC, whereas Crohn's disease is often negative for pANCA but positive for anti–*Saccharomyces cerevisiae* mannan antibodies. Patients who are pANCA positive and anti–*Saccharomyces cerevisiae* mannan antibody negative are far more likely to have UC than Crohn's disease.

Fecal calprotectin is sensitive for GI inflammation.

14.6.1 Imaging

- Plain abdominal radiography is vital in cases of severe acute colitis to exclude toxic dilatation of the colon. If there is any suspicion of toxic megacolon clinically or radiologically, plain abdominal radiography should be repeated daily until the clinical condition improves. Edema of the bowel wall can be seen as "thumbprinting."
- Computed tomography (CT) is useful in assessing the extent of inflammation in UC, although this is nonspecific and does not help in separating the various possible etiologies of the inflammation. CT colonography (virtual colonoscopy) is not a good substitute for colonoscopy in colitis, but it may be used to assess strictures where endoscopy has failed.
- An erect chest radiograph is also useful in cases of suspected perforation.
- Contrast enemas are not commonly used and are reserved for stricture assessment where endoscopy has failed and CT colonography is not available.

14.7 Treatment

UC should be managed jointly by physicians and surgeons.

14.7.1 Conservative Treatment

No evidence that elemental diets or any other treatment other than pharmacological or surgical treatment is of benefit in either the induction or maintenance of remission in UC.

14.7.2 Medical Treatment

The medical treatment of UC is divided into treatment of acute disease, treatment of chronic active disease, and maintenance of remission. Following ileal pouch formation (see Sect. 14.11.4), patients can develop pouchitis. This is discussed here.

14.7.2.1 Acute Colitis

Patients with mild/moderate disease can be managed as outpatients, whereas those with severe disease require inpatient care. Severe attacks are defined by a modernized version of the Truelove and Witts criteria [21] and can be characterized by:

- Stool frequency (>6 per day)
- *Plus* any one of the following:
  - Temperature >37.8 °C
  - Pulse >90 bpm
  - Hemoglobin <10.5 g/dL
  - CRP >30 g/L

Severe Attacks

Specific monitoring and treatment apply are required for patients experiencing severe attacks [22]:

- Frequent clinical evaluation, including stool charts
- Daily blood assessment (full blood count, CRP, electrolytes, albumin)
- Stool culture, including *C. difficile* analysis
- Daily abdominal radiography if any suspicion of colonic dilatation is present
- High-dose intravenous (e.g., hydrocortisone 100 mg four times daily) and topical steroids administered rectally (e.g., hydrocortisone liquid enemas four times daily)
- Intravenous cyclosporine in thiopurine-naïve patients if there is no significant improvement after 3 days, followed by oral cyclosporine when in remission (2 mg/kg intravenously and 4–9 mg/kg orally) [23] or oral azathioprine (1.5–2.5 mg/kg/day). This has been shown to reduce the colectomy rate in patients who do not respond to steroids, although there is a high relapse rate once the cyclosporine is stopped.
- Infliximab may be used as an alternative to cyclosporine [24].
- Intravenous electrolyte-rich fluid with or without blood, as required (maintain hemoglobin >8–10 g/dL)
- Anticoagulation (e.g., subcutaneous low-molecular-weight heparin daily) is essential in UC given the increased risk of deep vein thrombosis in these patients.
- Avoid antidiarrheal drugs (e.g., loperamide, codeine), opioids, anticholinergics, and, if possible, nonsteroidal anti-inflammatory drugs, all of which increase the risk of perforation. Remember that significant pain may indicate perforation.
- Oral 5-aminosalacylic acid (5-ASA) compounds provide no advantage in acute colitis.
- Broad-spectrum antibiotics can be used in those showing signs of septic complications.
- After 3 days of treatment, patients with stool frequency >8/day or a Units of CRP are mg/L >45 are unlikely to improve without a colectomy [25].
- Failure to improve within 7 days of treatment or deterioration within that period indicates that surgery is required.
- Once the clinical condition has improved, patients should convert to oral treatment (as used for mild/moderate acute attacks).
- Patients should be encouraged to eat and drink during severe attacks. A low-fiber diet is usually recommended.

Mild/Moderate Acute Colitis

Specific treatment applies for patients with mild or moderate acute colitis [26]:

- First-line treatment should be with an oral and topical 5-ASA compound (mesalazine). The oral dose should be >2 g daily and the rectal dose, 1 g daily. These can be reduced slowly as symptoms improve.
- When symptoms do not improve within 2 weeks, oral steroids can be administered, with a reducing dose starting at 40 mg prednisolone daily and titrating over 6 weeks until treatment is stopped.
- If symptoms deteriorate during the reducing regimen then the steroids should be increased again until symptoms settle.
- Initially administer oral mesalazine 2–4 g daily, which should be continued after remission is established, and then reduced to half this dose after 2 months (see Sect. 14.7.2.3).

14.7.2.2 Chronic Active Disease

For patients with chronic active disease [27]:

- A 5-ASA such as mesalazine 4 g daily initially, forms the basis of treatment. These are used in conjunction with 5-ASA enemas (e.g., mesalazine 1 g daily) as for mild/moderate acute colitis.
- Failure to wean completely from steroids should lead to the consideration of azathioprine as a steroid-sparing agent (aim for a maintenance dose of 1.5–2.5 mg/kg/day)..
- Anti–tumour necrosis factor (TNF) therapy should be considered in thiopurine-intolerant patients (ACT I and ACT II trials) [28]. Tacrolimus has also been shown to reduce the level of steroid maintenance in refractory disease.
- Appendicectomy may have some effect in the management of ulcerative proctitis, but more studies are needed [29].

14.7.2.3 Maintenance of Remission in Quiescent Disease

The chance of maintaining remission can be maximised by following some key principles [27]:

- Lifelong treatment should be administered, if tolerated by the patient.
- 5-ASA compounds are the mainstay of treatment (e.g., mesalazine 1–2 g/day).
- For distal disease, treatment with topical 5-ASA therapy alone (e.g., mesalazine 500 mg daily) is acceptable if tolerated by the patient.
- For those with frequent relapses despite or for those intolerant to 5-ASA compounds, consider azathioprine 1.5–2.5 mg/kg/day. Anti-TNF therapy is an alternative.
- Appendicectomy has been suggested as a possible adjunct in the maintenance of remission of UC [30].

14.7.2.4 Pouchitis

- Antibiotic therapy is the first-line treatment for pouchitis: commonly metronidazole (400 mg three times daily) or ciprofloxacin (500 mg twice daily) for 2 weeks.
- There is some evidence that combined ciprofloxacin and metronidazole for 4 weeks is superior to either agent alone in reducing remission [31].
- Long-term low-dose antibiotics can be used for those with frequent relapses.
- Topical mesalazine or steroids are used when antibiotics fail to improve the pouchitis.
- Chronic pouchitis is a common cause of pouch failure. Treatment with concentrated preparations of probiotic bacteria (e.g., VSL#3) has had some success both in maintaining remission in chronic pouchitis [32, 33] and as prophylaxis [34]. Budesonide and infliximab have also been used in the treatment of chronic pouchitis.

14.7.3 Surgery

The 2015 European consensus guidelines [14] provide a review of the evidence for surgical decision making in UC. Despite advances in medical treatment, up to 30 % of patients with UC will ultimately require a colectomy. The indications for surgery are:

- Development of complications (e.g., perforation, hemorrhage, dysplasia, cancer)
- Failure of medical treatment
  - Intractable symptoms
  - Frequent relapses or steroid resistance
  - Drug side effects, including steroid dependence

In both situations there are those who require emergency surgery (eg severe acute colitis not responding to medical treatment (Fig. 14.2), colonic perforation) and those who can have their surgery planned electively.

14.7.4 Emergency

Emergency surgery involves total colectomy and end ileostomy as a life-saving procedure. Management of the retained rectum is discussed below. Patients presenting with severe acute colitis as their first attack are the most likely to require colectomy (up to 25 %).

Fig. 14.2 Severe acute colitis (Courtesy of Illustration Services, Cellular Pathology, John Radcliffe Hospital, Oxford, UK)

Following recovery from a total colectomy, the fate of the remaining rectum must be considered, as it can continue to cause bloody anal discharge if the inflammation fails to subside, and it remains a site of potential cancer, although the risk is about 5 % over 20 years. There are four options for the residual rectum:

- Progression to restorative proctocolectomy, if suitable (see Sect. 14.8.1 Completion proctectomy)
- Completion proctectomy (see Sect. 14.8.1 Completion proctectomy)
- Rectal mucosectomy
  - In elderly patients with significant rectal disease in whom the rectum was divided at the level of the levators during emergency surgery, knowing that a pouch or ileorectal anastomosis would never be considered. This technique is rarely used.
- Surveillance only
  - In elderly patients without significant disease

14.7.5 Elective

Three surgical options exist in the elective situation:

- Panproctocolectomy and end ileostomy
- Total colectomy and ileorectal anastomosis
- Panproctocolectomy and ileal pouch–anal anastomosis

The choice of operation depends on the patient's fitness, anal sphincter function, and personal choice.

14.7.5.1 Preoperative Preparation

This is most important in the emergency situation.

- Patients must be adequately hydrated, with a good urine output.
- A hemoglobin concentration >9 g/dL is usually acceptable in an otherwise healthy patient without prior transfusion.
- Renal and hepatic function should be checked and significant electrolyte or clotting abnormalities corrected.

In the elective situation, more attention is directed at choosing the best time for surgery: when nutritional status is optimized and the steroid dose is as low as possible. Preoperative azathioprine does not seem to increase the risk of postoperative complications [35], but the evidence for anti-TNF therapy is less clear.

14.8 Additional Surgical Procedures

14.8.1 Completion Proctectomy

A combined abdominal (laparoscopic or open) and perineal approach is required to remove the rectum in most instances. The perineal part involves a circumanal incision and an intersphincteric dissection of the anus to meet the abdominal dissection, much in the same way as for a panproctocolectomy and end ileostomy (see Sect. 14.11.3). The defect in the perineum is closed in layers.

A solely perineal approach with retrograde proctectomy is a developing technique and uses the technology from transanal endoscopic surgery (transanal minimally invasive surgery) to achieve this.

14.8.2 Closure of Loop Ileostomy

This is usually the third part of a three-stage procedure after restorative proctocolectomy. After checking on a pouchogram that the pouch has healed and that there is no stenosis of the pouch–anal

anastomosis, the loop ileostomy is mobilized around its site in the right iliac fossa, reanastomosed, and the abdomen closed. There is rarely a need to open the midline abdominal wound.

14.9 Differential Diagnosis

See the algorithm in Fig. 14.3 for the investigation of bloody diarrhea. Other causes of colitis must be excluded:

- Crohn's disease: This is the closest differential to ulcerative colitis. The differences are highlighted in Table 14.4. Occasionally, biopsies are not diagnostic of any specific IBD, and these cases are called indeterminate colitis.
- Infective cause
  - Recent contact with an infectious patient
  - Recent antibiotic use for *C. difficile* infection
- Diverticular cause
  - Rectum appears normal in these patients
  - Bleeding diverticulae seen on endoscopy or diverticular disease noted on CT
- Radiation
- Ischemic cause
  - Onset in older people with features of vascular disease elsewhere or recent surgery for an abdominal aneurysm
  - Often associated with significant abdominal pain
- Beçhet enterocolitis
  - Associated history of genital ulceration, arthropathy, and uveitis

These other causes can normally be excluded by a combination of various investigations:

- Clinical history and examination
- Sigmoidoscopy and biopsy
- Histology
- Microbiology

14.10 Prognosis

Surgery is curative in UC, and the morbidity and mortality associated with the disease have improved as a result of better timing of surgery and improved surgical and anesthetic techniques. If quality of life is poor as a result of uncontrolled disease or the side effects of medication, surgery is a sensible option; it is not reserved only for complications of UC. About 30 % of patients will eventually have a colectomy.

When surgery is necessary, the availability of restorative proctocolectomy as an alternative to an end ileostomy also improves quality of life in those for whom a permanent ileostomy is not acceptable [36, 37].

The majority of patients live an unrestricted life and have a normal life expectancy.

14.11 Exemplary Surgical Procedures

We discuss four operations:

1. Emergency colectomy, end ileostomy, and preservation of the rectal stump
2. Colectomy and ileorectal anastomosis
3. Proctocolectomy and end ileostomy
4. Restorative proctocolectomy

All the elective techniques [2–4] are compared in Table 14.5.

All four operations share these common factors:

- All patients having stomas should be seen by a stomatherapy nurse and the site determined preoperatively on the ward, if possible.
- General anesthesia (combined with an epidural in the elective setting)
- Lloyd-Davies position
- Urinary catheter
- Potential for laparoscopic resection in selected individuals. A midline incision is used for open cases. Suggested laparoscopic port placements are shown in Fig. 14.4.

14.11.1 Emergency Colectomy and End Ileostomy

This is the operation of choice for the emergency situation. It can occasionally be used in the elective situation where a patient is undecided about

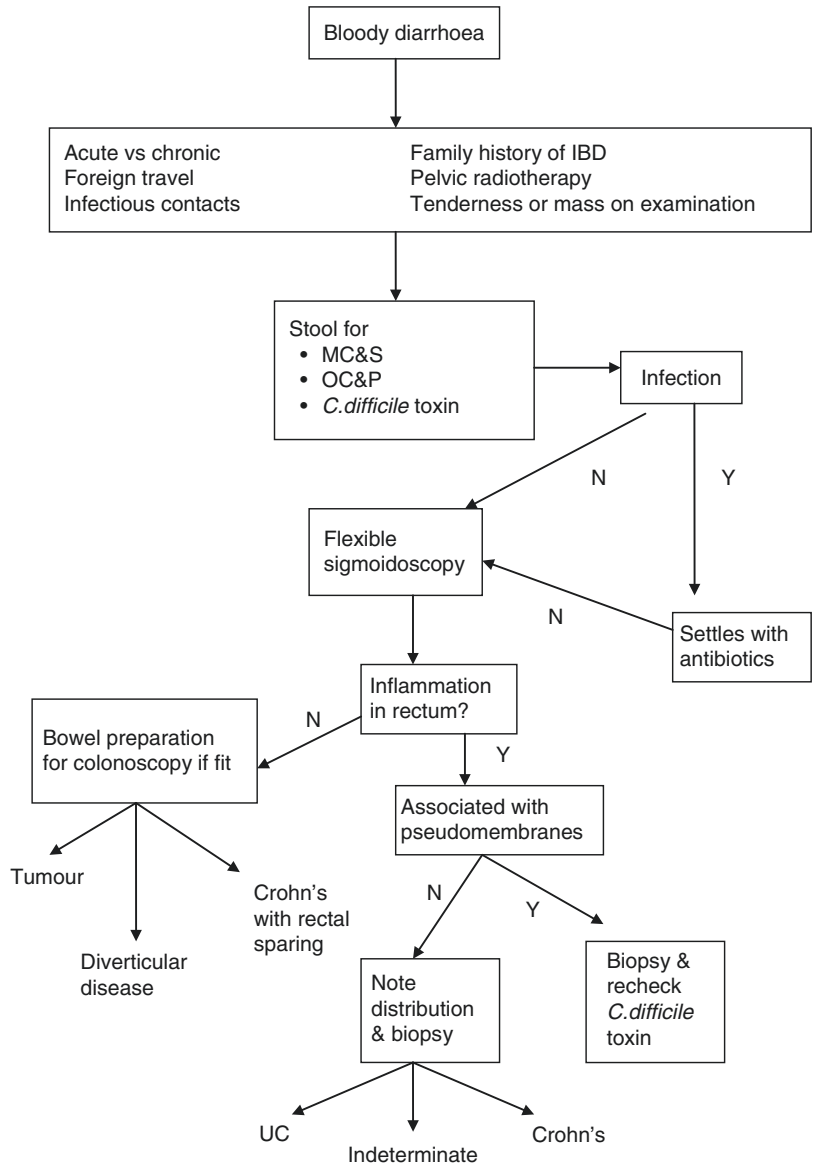


Fig. 14.3 Basic algorithm for the investigation of bloody diarrhea

long-term options; it gives them the invaluable experience of managing a stoma and the quality of life that could be expected with a permanent stoma. It is also used in chronic disease to enable optimal health before a second-stage procedure (e.g., no steroids, improved nutrition).

Indications are given above see Sect. 14.7.3.

14.11.1.1 Technique

- If the rectum is dilated, insert a rigid sigmoidoscope to deflate it before making the incision and leave a rectal catheter postoperatively.
- Mobilize the right colon and ileocecal junction, preserving the ileocolic artery, and divide of ileum just proximal to the ileocecal junction.

Table 14.4 Differences between ulcerative colitis and Crohn's disease

	Ulcerative colitis	Crohn's
Clinical		
Distribution	Continuous	Skip lesions/focality
Small-bowel disease	Not involved	Common
Rectal involvement	Always	Often spared
Anal disease	Rare	Common
Fistulae	Rare	Common
Strictures	Uncommon	Common
Pathological		
Depth of inflammation	Mucosa/submucosa	Full thickness
Fat wrapping	Absent	Present
Pseudopolyps	Common	Uncommon
Mucin depletion	Common	Uncommon
Cobblestone appearance	Absent	Present
Deep fissures	Rare	Present
Crypt abscesses	Frequent	Occasional
Granulomata	Rare	Common
Serological		
Anti–*Saccharomyces cerevisiae* mannan antibodies	15 %	65 %
Perinuclear anticytoplasmic antibodies	70 %	20 %

- Preserve the inferior mesenteric artery. Mobilize and divide the left colon at the level of the distal sigmoid to retain enough length for a mucous fistula (Fig. 14.5). However, it may be necessary to divide the bowel more distally in cases where there is severe bleeding/rectal ulceration. Division below the area of bleeding is obviously necessary in these cases.
- Bring the ileum out through a trephine in the right iliac fossa, which is marked before the surgery.
- Either staple and divide the left colon at the rectosigmoid and leave it within the abdomen, or staple it at the distal sigmoid with enough length to bury it subcutaneously in the midline wound or extraction site in laparoscopic surgery. If the colon is too friable to take sutures or staples, form a formal mucous fistula [38].
- In laparoscopic operations, consider removing the colon either through a separate extraction site (e.g., an extended periumbilical camera port site or an extended suprapubic port site if leaving a buried sigmoid stump) or through the ileostomy site, although this requires widening the ileostomy site and may predispose the patient to parastomal herniation.

14.11.1.2 Possible Complications

These are summarised in Table 14.5

- The intraperitoneal stump leak rate is about 6–12 % [39–41]. Leaving a rectal catheter may reduce this rate. Subcutaneous leaks causing wound infections are more common (10–30 %) [40, 42] but less hazardous than an intraperitoneal leak. However, the longer stump required to bury it in the abdominal wall increases the risk of troublesome symptoms caused by the rectal stump.
- Complications specific to the stoma include high-output stomas, parastomal hernias, stomal prolapse, stricture, retraction, and

Table 14.5 Comparison of three common elective operations for ulcerative colitis

	Proctocolectomy/end ileostomy	Colectomy and ileorectal anastomosis	Restorative proctocolectomy
Advantages	Curative One operation	One operation No risk to sphincter No risk to pelvic nerves	Curative Avoids permanent ileostomy
Disadvantages	Permanent ileostomy	Not curative; may require continuing treatment Require surveillance	10 % Fail Frequency of evacuation Two operations required
Complications	Stoma revision (10–20 %) Perineal wound problems (20 %) Small-bowel obstruction (10–20 %) Minimal bladder or sexual dysfunction	Small-bowel obstruction (10–20 %) Anastomotic leak (5 %)	Pouchitis (40 %) Fistulas to pouch Small-bowel obstruction (10–20 %) Anastomotic leak (5 %) Sexual dysfunction (5 %)
Contraindications	Aversion to stomas	Weak anal sphincters Severe proctitis Rectal dysplasia or cancer	Low rectal cancer or dysplasia Weak anal sphincters

ischemia of the stoma. About 25 % of patient will need revision at 5 years [43].

14.11.2 Colectomy and Ileorectal Anastomosis

This is an uncommon procedure in UC, indicated only in young patients with minimal rectal inflammation, no sphincter dysfunction, good rectal compliance, and no evidence of dysplasia anywhere in the large bowel. It should only be considered in exceptional cases (e.g., for fertility reasons in people who want a ileoanal pouch but also want time to complete a family), occasionally as a bridge to pelvic surgery, and occasionally as a long-term solution.

14.11.2.1 Technique

- The colon is mobilized as in a total colectomy.
- Only the upper rectum is mobilized.
- The bowel is divided at the upper rectum, and a hand-sewn or stapled end-to-end ileorectal anastomosis can be made.
- In the laparoscopic approach, the port placement is the same as that for a total colectomy (Fig. 14.4). The colon is extracted through an extended periumbilical camera port site or an extended suprapubic port site. The anvil of the stapling device is placed into the ileum extracorporeally before returning it to the abdomen and closing the extraction site to enable an anastomosis to be made laparoscopically.

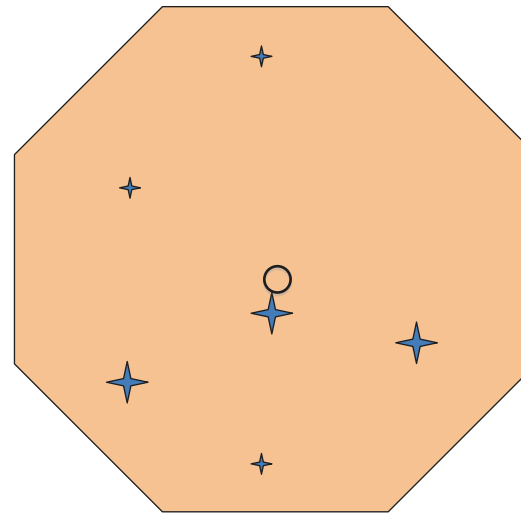


Fig. 14.4 A suggestion for port position in a laparoscopic total colectomy

14.11.2.2 Possible Complications

These are summarised in Table 14.5

- The risk of cancer in the rectum is low but still requires annual surveillance with flexible sigmoidoscopy and biopsy.
- The risks of anastomotic leak and small-bowel obstruction are equivalent to those for restorative proctocolectomy.
- Poor function can result from both an absence of the absorptive capacity of the colon and continuing proctitis. Urgency of defecation is the most common cause of ultimate failure.

14.11.3 Proctocolectomy and End Ileostomy

This procedure is indicated in various circumstances:

- Presence of weak anal sphincters
- Low rectal cancers
- Patients who find the potential complications of restorative proctocolectomy unacceptable
- Patients who want a permanent ileostomy

14.11.3.1 Technique

- Use a purse-string suture to close the anus.
- Some advocate making a trephine for ileostomy before the midline incision to avoid the distortion later created in the abdominal wall by the laparotomy incision [44].
- In non-neoplastic cases, colonic mobilization is as described above for total colectomy.
- In operations for dysplasia or carcinoma, a cancer technique with high ligation and wide clearance should be used.
- The rectum should be mobilized using a technique designed to minimize the risk to the pelvic nerves; some choose a standard mesorectal dissection given that this is the plane with which they are most familiar and thus minimizes the risk of complication (in the region of 2%) [45]. Others choose a close perimuscular dissection, and others still a mixed dissection using the mesorectal plane in areas where the risk to the autonomic nerves is not high and a perimuscular technique in areas of greatest risk. Traditionally, these have a lower risk of injury to the pelvic nerves [46], although the technique is less common. Close rectal dissection seems to be associated with reduced short-term morbidity [47]. In neoplastic cases, however, the mesorectal plane should be used as in other cancer operations.
- Perineal dissection of the lower rectum should take place in the intersphincteric plane to minimize perineal complications, except in cancers close to the dentate line, where the extrasphincteric plane should be used (as for abdominoperineal resection for cancer).
- The empty pelvis is drained with suction drains via the lower abdominal wall.
- The distal ileum is brought out as an end ileostomy and everted to form a spout about 2.5 cm from the anterior abdominal wall.
- In the laparoscopic approach, the port placement is the same as that for a total colectomy (Fig. 14.4). The colon and rectum are extracted via the perineal wound; the ileum is divided intracorporeally to allow this.

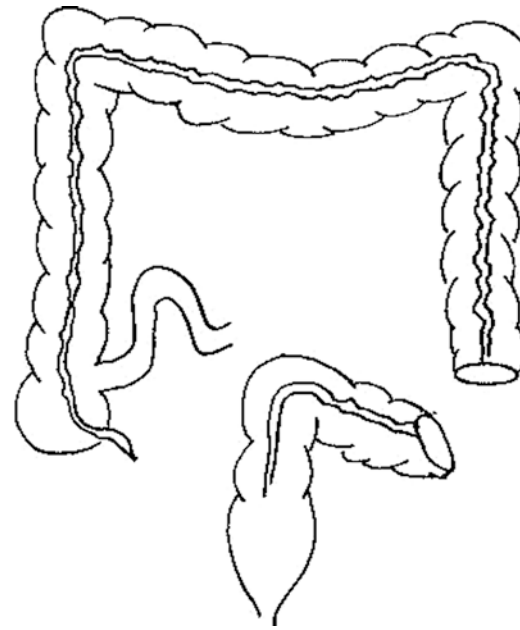


Fig. 14.5 Division of the distal colon in an emergency colectomy, leaving a long distal stump to form a mucous fistula

14.11.3.2 Possible Complications

Postoperative ileus or small-bowel obstruction and pelvic sepsis are the most common postoperative complications (see Table 14.5). Perineal

wound problems are common following proctectomy but are less problematic than after proctectomy for Crohn's disease. Ileostomy complications occur (as mentioned above).

14.11.4 Restorative Proctocolectomy

Before surgery, the following need to be considered:

- Age: Use caution at both extremes. In the elderly, thought needs to be given to anal sphincter function and the added morbidity of undergoing major abdominal surgery. In pediatric patients, the smaller anatomy (especially with respect to the pelvic nerves), future fertility, and the implications of spending the teenage years with a pouch need to be considered.
- Anal sphincter assessment: Endoanal ultrasound and anal manometry should be used to confirm adequate anal sphincter function, especially in parous women.
- Fertility: Men who would consider having children in the future should have a semen specimen taken for storage (sexual dysfunction affects up to 3 % of men following ileal pouch surgery). Women considering having children should be advised that fecundity is reduced following this operation and, if possible, to wait until their family is completed before having pouch surgery [48]. Laparoscopic pelvic dissection may reduce the adverse effects of pelvic dissection on fertility in women [49].
- Pregnancy: Most women should be advised to have a caesarean delivery for future pregnancies, although there is little evidence to support this [50].
- Histology: The slides should be reviewed by an experienced pathologist with a specialist interest in colorectal pathology. Pouch failure rates in indeterminate colitis vary; some suggest comparable outcomes to UC. However, pouch surgery for Crohn's disease has a 30–50 % risk of failure [51, 52] but could be considered in patient with isolated colonic Crohn's disease [53].
- Patients with PSC have a higher incidence of pouchitis and pouch failure and need to be counseled accordingly [54].

14.11.4.1 Technique

- The colon and rectum are mobilized abdominally, as for proctocolectomy and end ileostomy. The ileocolic artery is divided distally to maximize perfusion of the ileum should any vascular division be necessary in the small-bowel mesentery.
- There is no perineal dissection, and the rectum is mobilized to the anorectal junction from above.
- A clamp is placed on the midrectum, and the rectum is washed out via the anus.
- Care is taken to avoid the vagina anteriorly in women.
- A transverse right-angled stapler is applied to the anorectal junction and the bowel is divided, leaving a cuff of rectum as short as possible (<2 cm). The surgeon can check the length by introducing a finger into the rectum and closing the stapler just above the fingertip. There is no clinical advantage in doing a hand-sutured anastomosis with mucosectomy, and the mucosectomy may cause functional problems [55, 56]. There is no increased risk of dysplasia or cancers in stapled compared with hand-sewn pouch–anal anastomoses.
- The ileum is transected just proximal to the ileocecal valve.
- The small-bowel mesentery is mobilized completely to the junction of third and fourth parts of the duodenum.
- Selected mesenteric vessels can be divided to provide extra length if required.
- A *J*-pouch is formed from the terminal 30–40 cm of ileum by folding them into two 15- to 20-cm limbs and using a linear stapler to form a common lumen with a side-to-side anastomosis (Fig. 14.6). The four-limb *W*-pouch is an alternative using 10 cm of ileum for each limb, whereas the *S*-pouch has been largely abandoned because of poor evacuatory function [57].

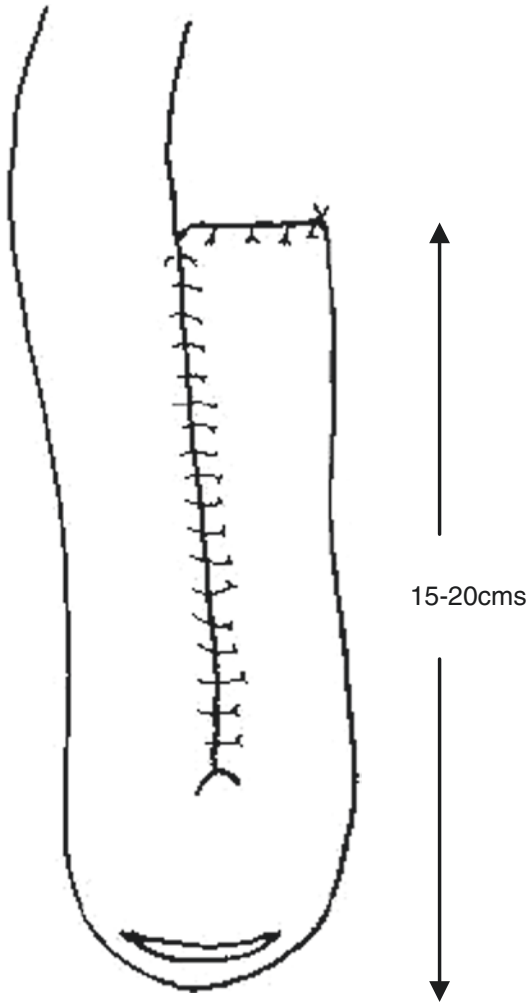


Fig. 14.6 The ileal *J*-pouch construct

- A purse-string suture is placed around the enterotomy used to introduce the linear stapler; this secures the anvil of the stapler.
- A circular stapling device is advanced perianally to the transverse rectal staple line, and the central spike is advanced through the staple line. The circular stapler is united with the anvil and the stapler fired (Fig. 14.7). An alternative is to use a hand-sewn perianal anastomosis with a mucosectomy.
- The excised tissue donuts must be inspected and the anastomosis tested for air leakage.
- A loop ileostomy is constructed through a trephine incision in the right iliac fossa.

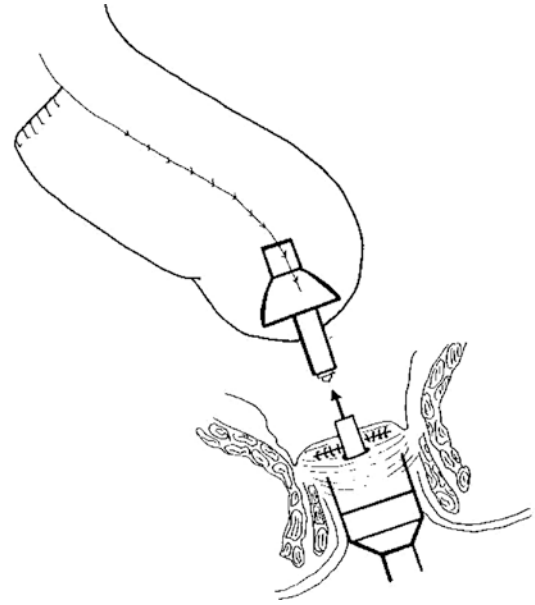


Fig. 14.7 Formation of the stapled ileal pouch–anal anastomosis

- In the laparoscopic approach, the port is placed as for a total colectomy (Fig. 14.4). Division of the anorectal junction is difficult because of the technical difficulty of forming a right-angled staple line on the pelvic floor with laparoscopic equipment. It is best achieved through a suprapubic port. Open right-angled stapling devices can occasionally be used with a modified "glove" port. The colon is extracted as in an ileorectal anastomosis. The ileal pouch is formed and the anvil placed extracorporeally before being returned to the abdomen, as in the ileorectal anastomosis operation.

14.11.4.2 Possible Complications

Overall pouch failure occurs in about 15 % of cases. Common causes of failure include (see Table 14.5):

Pelvic sepsis including fistulae

About one-third of pouches complicated by pelvic sepsis fail. Common reasons include anastomotic leaks or infected hematomas. Subsequent fistulae from the pouch, particularly into vagina or perineum, occur in 7–8 %

Table 14.6 Causes of poor pouch function

Small bowel	Incomplete bowel obstruction
	Bacterial overgrowth
	Irritable bowel
	Dietary sensitivities (e.g., lactose intolerance)
Outlet problems	Anastomotic stricture
	Weak sphincters
Inflammatory	Pouchitis
	Cuffitis
	Crohn's disease
Septic	Chronic pelvic abscess
Pouch structure	Small-volume pouch

of patients and usually require defunctioning followed by further surgery.

Poor function

Good pouch function is considered to be anything up to six bowel motions per day. Frequency, especially associated with urgency and poor gas/liquid discrimination, significantly affects a patient's quality of life. A number of possible causes are listed in Table 14.6.

Pouchitis

Inflammation can develop in the ileal pouch, which can lead to symptoms of stool frequency, urgency, and occasional per rectal (PR) bleeding and pelvic pain. It is diagnosed by positive criteria found in the clinical history, endoscopy, and histology.

Pouchitis is a significant problem, affecting 30–40% of people following ileal pouch surgery, but only 10% will have recurrent attacks. In 1–2% of cases, it is so severe as to require pouch excision or rediversion with a loop ileostomy. The etiology remains unclear, but potential risk factors include extensive UC before colectomy, PSC, no smoking, backwash ileitis, and regular nonsteroidal anti-inflammatory use. Treatment was detailed earlier in the chapter.

References

1. Loftus Jr EV. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. Gastroenterology. 2004;126(6):1504–17.
2. Shivananda S, Lennard-Jones J, Logan R, Fear N, Price A, Carpenter L, et al. Incidence of inflammatory bowel disease across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD). Gut. 1996;39(5):690–7.
3. Ardizzone S, Bianchi Porro G. Inflammatory bowel disease: new insights into pathogenesis and treatment. J Intern Med. 2002;252(6):475–96.
4. Birrenbach T, Bocker U. Inflammatory bowel disease and smoking: a review of epidemiology, pathophysiology, and therapeutic implications. Inflamm Bowel Dis. 2004;10(6):848–59.
5. Andersson RE, Olaison G, Tysk C, Ekbom A. Appendectomy and protection against ulcerative colitis. N Engl J Med. 2001;344(11):808–14.
6. Spehlmann ME, Begun AZ, Burghardt J, Lepage P, Raedler A, Schreiber S. Epidemiology of inflammatory bowel disease in a German twin cohort: results of a nationwide study. Inflamm Bowel Dis. 2008;14:968.
7. Halfvarson J, Bodin L, Tysk C, Lindberg E, Jarnerot G. Inflammatory bowel disease in a Swedish twin cohort: a long-term follow-up of concordance and clinical characteristics. Gastroenterology. 2003;124(7):1767–73.
8. Yang H, McElree C, Roth MP, Shanahan F, Targan SR, Rotter JI. Familial empirical risks for inflammatory bowel disease: differences between Jews and non-Jews. Gut. 1993;34(4):517–24.
9. Satsangi J, Welsh KI, Bunce M, Julier C, Farrant JM, Bell JI, et al. Contribution of genes of the major histocompatibility complex to susceptibility and disease phenotype in inflammatory bowel disease. Lancet. 1996;347(9010):1212–7.
10. Bouma G, Strober W. The immunological and genetic basis of inflammatory bowel disease. Nat Rev Immunol. 2003;3(7):521–33.
11. Cho JH, Weaver CT. The genetics of inflammatory bowel disease. Gastroenterology. 2007;133(4):1327–39.
12. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48(4):526–35.
13. Chambers WM, Warren BF, Jewell DP, Mortensen NJ. Cancer surveillance in ulcerative colitis. Br J Surg. 2005;92(8):928–36.
14. Oresland T, Bemelman WA, Sampietro GM, Spinelli A, Windsor A, Ferrante M, et al. European evidence based consensus on surgery for ulcerative colitis. J Crohns Colitis. 2015;9(1):4–25.
15. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, et al. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2011;60(5):571–607.
16. Van Assche G, Dignass A, Bokemeyer B, Danese S, Gionchetti P, Moser G, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations. J Crohns Colitis. 2013;7(1):1–33.
17. Sheth SG, LaMont JT. Toxic megacolon. Lancet. 1998;351(9101):509–13.
18. Robert JR, Sachar DB, Greenstein AJ. Severe gastrointestinal hemorrhage in Crohn's disease. Ann Surg. 1991;213(3):207–11.

19. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19(Suppl A):5A–36.
20. Eaden JA, Mayberry JF. Guidelines for screening and surveillance of asymptomatic colorectal cancer in patients with inflammatory bowel disease. Gut. 2002;51 Suppl 5:V10–2.
21. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2(4947):1041–8.
22. Jakobovits SL, Travis SP. Management of acute severe colitis. Br Med Bull. 2005;75–76:131–44.
23. Van Assche G, D'Haens G, Noman M, Vermeire S, Hiele M, Asnong K, et al. Randomized, double-blind comparison of 4 mg/kg versus 2 mg/kg intravenous cyclosporine in severe ulcerative colitis. Gastroenterology. 2003;125(4):1025–31.
24. Jarnerot G, Hertervig E, Friis-Liby I, Blomquist L, Karlen P, Granno C, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. Gastroenterology. 2005;128(7):1805–11.
25. Travis SP, Farrant JM, Ricketts C, Nolan DJ, Mortensen NM, Kettlewell MG, et al. Predicting outcome in severe ulcerative colitis. Gut. 1996;38(6):905–10.
26. Dignass A, Lindsay JO, Sturm A, Windsor A, Colombel JF, Allez M, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 2: current management. J Crohns Colitis. 2012;6(10):991–1030.
27. Carter MJ, Lobo AJ, Travis SP. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2004;53 Suppl 5:V1–16.
28. Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005;353(23):2462–76.
29. Bolin TD, Wong S, Crouch R, Engelman JL, Riordan SM. Appendicectomy as a therapy for ulcerative proctitis. Am J Gastroenterol. 2009;104(10):2476–82.
30. Gardenbroek TJ, Eshuis EJ, Ponsioen CI, Ubbink DT, D'Haens GR, Bemelman WA. The effect of appendectomy on the course of ulcerative colitis: a systematic review. Colorectal Dis. 2012;14(5):545–53.
31. Mimura T, Rizzello F, Helwig U, Poggioli G, Schreiber S, Talbot IC, et al. Four-week open-label trial of metronidazole and ciprofloxacin for the treatment of recurrent or refractory pouchitis. Aliment Pharmacol Ther. 2002;16(5):909–17.
32. Mimura T, Rizzello F, Helwig U, Poggioli G, Schreiber S, Talbot IC, et al. Once daily high dose probiotic therapy (VSL#3) for maintaining remission in recurrent or refractory pouchitis. Gut. 2004;53(1):108–14.
33. Gionchetti P, Rizzello F, Venturi A, Brigidi P, Matteuzzi D, Bazzocchi G, et al. Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: a double-blind, placebo-controlled trial. Gastroenterology. 2000;119(2):305–9.
34. Gionchetti P, Rizzello F, Helwig U, Venturi A, Lammers KM, Brigidi P, et al. Prophylaxis of pouchitis onset with probiotic therapy: a double-blind, placebo-controlled trial. Gastroenterology. 2003;124(5):1202–9.
35. Subramanian V, Pollok RC, Kang JY, Kumar D. Systematic review of postoperative complications in patients with inflammatory bowel disease treated with immunomodulators. Br J Surg. 2006;93(7):793–9.
36. Richards DM, Hughes SA, Irving MH, Scott NA. Patient quality of life after successful restorative proctocolectomy is normal. Colorectal Dis. 2001;3(4):223–6.
37. Muir AJ, Edwards LJ, Sanders LL, Bollinger RR, Koruda MJ, Bachwich DR, et al. A prospective evaluation of health-related quality of life after ileal pouch anal anastomosis for ulcerative colitis. Am J Gastroenterol. 2001;96(5):1480–5.
38. Brown SR, Travis SPL, Haboubi N, Hampton J, George B. The management of acute severe colitis: position statement of the Association of Coloproctology of Great Britain & Ireland. 2007.
39. Brady RR, Collie MH, Ho GT, Bartolo DC, Wilson RG, Dunlop MG. Outcomes of the rectal remnant following colectomy for ulcerative colitis. Colorectal Dis. 2008;10(2):144–50.
40. Trickett JP, Tilney HS, Gudgeon AM, Mellor SG, Edwards DP. Management of the rectal stump after emergency sub-total colectomy: which surgical option is associated with the lowest morbidity? Colorectal Dis. 2005;7(5):519–22.
41. Wojdemann M, Wettergren A, Hartvigsen A, Myrhoj T, Svendsen LB, Bulow S. Closure of rectal stump after colectomy for acute colitis. Int J Colorectal Dis. 1995;10(4):197–9.
42. Ng RL, Davies AH, Grace RH, Mortensen NJ. Subcutaneous rectal stump closure after emergency subtotal colectomy. Br J Surg. 1992;79(7):701–3.
43. Phillips RK, Ritchie JK, Hawley PR. Proctocolectomy and ileostomy for ulcerative colitis: the longer term story. J R Soc Med. 1989;82(7):386–7.
44. Nicholls J, Tekkis P. Ulcerative colitis. In: Phillips R, editor. Colorectal surgery. 3rd ed. Philadelphia: Elsevier Ltd; 2005. p. 129–62.
45. Ziv Y, Fazio VW, Sirimarco MT, Lavery IC, Goldblum JR, Petras RE. Incidence, risk factors, and treatment of dysplasia in the anal transitional zone after ileal pouch-anal anastomosis. Dis Colon Rectum. 1994;37(12):1281–5.
46. Berry AR, de Campos R, Lee EC. Perineal and pelvic morbidity following perimuscular excision of the rectum for inflammatory bowel disease. Br J Surg. 1986;73(8):675–7.
47. Bartels SA, Gardenbroek TJ, Aarts M, Ponsioen CY, Tanis PJ, Buskens CJ, et al. Short-term morbidity and quality of life from a randomized clinical trial of close

rectal dissection and total mesorectal excision in ileal pouch-anal anastomosis. Br J Surg. 2015;102(3): 281–7.
48. Olsen KO, Joelsson M, Laurberg S, Oresland T. Fertility after ileal pouch-anal anastomosis in women with ulcerative colitis. Br J Surg. 1999;86(4):493–5.
49. Bartels SA, D'Hoore A, Cuesta MA, Bensdorp AJ, Lucas C, Bemelman WA. Significantly increased pregnancy rates after laparoscopic restorative proctocolectomy: a cross-sectional study. Ann Surg. 2012;256(6):1045–8.
50. Lepisto A, Sarna S, Tiitinen A, Jarvinen HJ. Female fertility and childbirth after ileal pouch-anal anastomosis for ulcerative colitis. Br J Surg. 2007;94(4):478–82.
51. Brown CJ, Maclean AR, Cohen Z, Macrae HM, O'Connor BI, McLeod RS. Crohn's disease and indeterminate colitis and the ileal pouch-anal anastomosis: outcomes and patterns of failure. Dis Colon Rectum. 2005;48(8):1542–9.
52. Tulchinsky H, Hawley PR, Nicholls J. Long-term failure after restorative proctocolectomy for ulcerative colitis. Ann Surg. 2003;238(2):229–34.
53. Melton GB, Fazio VW, Kiran RP, He J, Lavery IC, Shen B, et al. Long-term outcomes with ileal pouch-anal anastomosis and Crohn's disease: pouch retention and implications of delayed diagnosis. Ann Surg. 2008;248(4):608–16.
54. Penna C, Dozois R, Tremaine W, Sandborn W, LaRusso N, Schleck C, et al. Pouchitis after ileal pouch-anal anastomosis for ulcerative colitis occurs with increased frequency in patients with associated primary sclerosing cholangitis. Gut. 1996;38(2): 234–9.
55. Choen S, Tsunoda A, Nicholls RJ. Prospective randomized trial comparing anal function after hand sewn ileoanal anastomosis with mucosectomy versus stapled ileoanal anastomosis without mucosectomy in restorative proctocolectomy. Br J Surg. 1991;78(4): 430–4.
56. Kirat HT, Remzi FH, Kiran RP, Fazio VW. Comparison of outcomes after hand-sewn versus stapled ileal pouch-anal anastomosis in 3,109 patients. Surgery. 2009;146(4):723–9. discussion 9-30.
57. Nicholls RJ, Pezim ME. Restorative proctocolectomy with ileal reservoir for ulcerative colitis and familial adenomatous polyposis: a comparison of three reservoir designs. Br J Surg. 1985;72(6):470–4.
58. Danese S, Semeraro S, Papa A, Roberto I, Scaldaferri F, Fedeli G, et al. Extraintestinal manifestations in inflammatory bowel disease. World J Gastroenterol. 2005;11(46):7227–36.
59. Lichtiger et al. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med 1994; 33:1841–5.

Crohn's Disease

15

Peter Kienle

15.1 Etiology and Epidemiology

Crohn's disease (CD) is a chronic, idiopathic inflammatory bowel disease, and its exact etiology is still debated [1]. Current evidence suggests that the intestinal mucosal barrier is compromised in patients with CD, allowing intestinal bacteria to invade the bowel. Antimicrobial peptides produced in Paneth cells are normally found in the mucus and defend the mucosa against such bacterial invasion, but decreased expression of these peptides (e.g., defensins) has been shown in CD. Moreover, dysfunction of autophagy in affected patients results in defective handling of intracellular and invading bacteria and causes prolonged survival and defective clearance of those microbes. These mechanisms together trigger an uncontrolled immune response, resulting in chronic intestinal inflammation. Therefore the conception of the disease as predominantly a consequence of an inadequate immunological response is only partially correct. An altered microbiome, or "dysbiosis," is probably also relevant over the protracted course of the inflammation. Whether specific infections such as *Mycobacterium avium* subsp *paratuberculosis* play a role remains controversial. A genetic susceptibility (over 160 susceptibility genes have been described; e.g., a *NOD2* mutation results in an up to 60-fold higher incidence) and environmental factors are both of importance because there is a higher incidence in developed countries and a distinct north-to-south gradient. Smoking is a proven risk factor and also increases the risk of relapse after surgery. Other factors such as status after appendectomy, perinatal infections, and oral contraceptives remain controversial. Psychosocial factors probably are not of etiological relevance, but they do seem to influence symptom manifestation and the course of the disease. Together, this evdicence shows that the etiology of Crohn's disease is probably multifactorial, but several aspects remain unclear. The incidence of the disease is around 5–8 per 100,000 per year in most Western countries, with a major peak between the second and fourth decades and a smaller peak between the fifth and seventh decades of life. Fifteen to 20 % of patients are younger than 20 years. The overall prevalence amounts to about 120–200 per 100,000.

15.2 Pathology

Macroscopic features:

- Segmental, discontinuous inflammation ("skip lesions") with strictures, stenosis, and wall thickening
- "Fat wrapping" or "creeping fat" (Fig. 15.1), serositis, bowel wall adhesions

P. Kienle
Department of Surgery, University Medicine Mannheim, Mannheim, Germany
e-mail: peter.kienle@umm.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_15

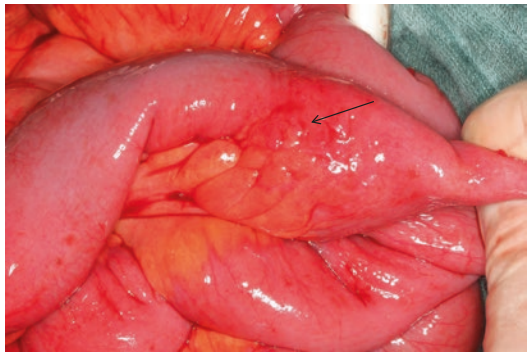


Fig. 15.1 "Fat creeping" phenomenon (*arrow*) in the small bowel in a patient with Crohn's disease

- Aphthoid lesions, fissural ulcerations, cobblestone pattern
- Fistula
- Rectum is typically spared
- Perianal lesions

Microscopic features:

- Transmural chronic inflammation with lymphoid aggregates
- Widening of the submucosa with edema, lymphangiectasia, and submucosal fibrosis
- Neuronal hyperplasia, ganglionitis
- Transmural fissures and fistula
- Noncaseating epithelioid granulomas (high specificity but low sensitivity for diagnosis of Crohn's disease, are found in 20 % of biopsies and >60 % of resected bowel specimens)
- Granulomatous lymphadenitis

15.3 Clinical Manifestations and Symptoms

CD can affect the entire gastrointestinal tract, from the mouth to the anus (see Table 15.1 for a distribution of CD). The most commonly affected part of the bowel is the ileocecal region (60–70 %). Segmental or general colitis and anorectal disease occur in 20–30 % of patients, often in combination.

The clinical symptoms depend on the affected bowel and the phenotype. Because the inflammation is typically segmental and may affect

Table 15.1 Distribution of disease according to the Montreal classification [2]

Terminal ileum	40–50 %
Ileocolon	~20 %
Colon	~30 %
Upper gastrointestinal tract	~5 %
Anorectal disease	20–30 %

the entire gastrointestinal tract, symptoms are predominantly determined by the part of bowel or organ involved. Three phenotypes, which determine clinical behavior, can be differentiated according to the Montreal classification: without stricture formation, nonpenetrating (B1); stricturing (B2); or penetrating (B3). Category B3 includes a subcategory of perianally penetrating (B3p). Most patients initially present with a B1 phenotype, and about half of patients progress to a more aggressive phenotype within 20 years after the initial diagnosis. However, the data and clinical experience seem to question this rigid differentiation, as there is a considerable overlap between these phenotypes: patients often present with both a stricture and a fistula, where the latter is the potential cause of the stenosis or in turn occurs as a consequence of a more distal stenosis. Interenteric fistulas and luminal stenosis are often combined, especially in conglomerate tumors of primarily inflamed bowel and secondary affected adherent bowel.

Stenosis typically presents as acute fibrotic stenosis, which is potentially reversible after medical treatment, or as chronic fibrotic stenosis. In both cases patients suffer from abdominal cramps, especially after eating; pain; and abdominal distension, potentially progressing to subileal obstruction or complete bowel obstruction. Patients also often present with diarrhea – the most common clinical symptom in CD – as a result of either bacterial overgrowth before a stenosis, malabsorption (bile acids in the terminal ileum), or the inflammation itself. This situation, sometimes in combination with occult bleeding, can result in anemia. Furthermore, patients are often malnourished and anorectic. When the transmural inflammation progresses into neighboring tissue, fistulas can occur (Table 15.2, Fig. 15.2). These in turn can trigger abscesses, which may present as pain

Table 15.2 Types of fistula in Crohn's disease

Type	Clinical symptoms	Indication for surgery
Interenteric	Often asymptomatic	Relative or no indication (except for a high fistula with functional short-bowel syndrome)
	Short-bowel syndrome (e.g., jejunocolic fistula)	
	Part of a "conglomerate tumor"	
Enterocutaneous	Oligosymptomatic	Depends on symptoms
	Painful, skin irritation	Absolute
Retroperitoneal ("blind ending") (Fig. 15.5a, b)	Asymptomatic	
	Ureteral stenosis	
	Sepsis (smoldering)	
	Bone affected (septic spondylitis or arthritis)	
Enterovesical	Urinary tract infections	Absolute
	Pneumaturia	
Enterovaginal	Often oligosymptomatic	Depends on symptoms, relative
	Vaginal passage of gas, stool, or pus	
	Vaginal discharge	
	Recurrent vaginal or urinary tract infections	
Perianal	Oligosymptomatic	Depends on symptoms, relative
	Pain	
	Secretion	

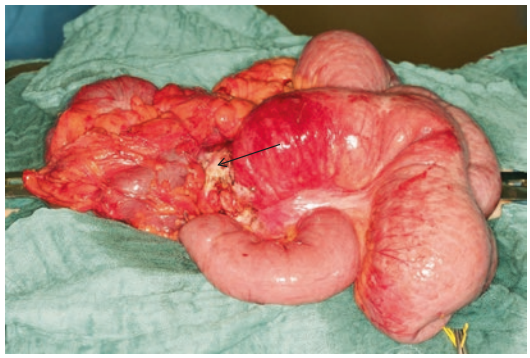


Fig. 15.2 Ileocolic fistula (*arrow*) in Crohn's disease of the ileocecal region

(mostly dull, noncolicky), fever, or even full-blown sepsis. Conglomerate inflammatory tumors may be palpable as a mass.

15.3.1 Extraintestinal Manifestations

Extraintestinal manifestations and associated diseases occur in about 20–40 % of patients and depend on the activity of the CD (Table 15.3). Therefore treatment of the underlying disease should primarily be intensified. Anemia is the most commonly associated disease, mostly because of an iron deficiency caused by chronic inflammation, and less frequent as a result of intestinal bleeding or a lack of vitamin B_{12} (ileal inflammation/stenosis or loss of ileum after resection). The second most commonly afflicted tissues are the joints, where peripheral and axial arthropathy are generally differentiated. Eyes are involved in 2–13 % and the skin in 2–15 %. Sclerosing cholangitis usually only occurs in patients with Crohn's colitis. Pancreatitis develops in up to 4 % of patients, but this is often a result of the side effects of medication (azathioprine in 3–5 %) and cholecystolithiasis than from direct inflammation of the duodenum and papilla of Vater or the pancreatic parenchyma.

15.3.1.1 Disease Activity and Classification

Disease pattern, activity, and severity are classified several ways, and these are worthwhile in studies [3]. But in clinical routine these classifications, such as the Crohn's Disease Activity Index (CDAI) or the pediatric CDAI (PCDAI) are generally too complex. The CDAI is a validated composite score grading the severity of CD based

Table 15.3 Extraintestinal manifestations and associated diseases in Crohn's disease

Location	Type
Blood	Anemia
	Thrombophilia
Joints	Sakroiliitis
	Peripheral arthritis
	Ankylosing spondylitis
Eyes	Uveitis
	Episcleritis
Bones	Osteoporosis/osteopenia
Skin	Erythema nodosum
	Pyoderma gangrenosum
Thorax	Pleuritis
	Myocarditis
Kidneys	Amyloidosis
	Nephrolithiasis
Pancreas	Pancreatitis
Hepatobiliary tract	Cholecystolithiasis
	Primary sclerosing cholangitis
	Cholangiocarcinoma
	Autoimmune hepatitis

Table 15.4 Grading of disease activity in Crohn's disease (European Crohn's and Colitis Organisation guidelines, version 4)

Mild	Moderate	Severe
Equivalent to a CDAI of 150–220	Equivalent to a CDAI of 220–450	Equivalent to a CDAI >450
Patient is ambulatory, eating and drinking, and has <10 % weight loss	Intermittent vomiting or weight loss >10 %	Cachexia (body mass index 18 kg/m^2) or evidence of obstruction or abscess
No features of obstruction, fever, dehydration, abdominal mass, or tenderness	No overt obstruction	Persistent symptoms despite intensive treatment
CRP is usually higher than the upper limit of normal	Treatment for mild disease is ineffective or there is a tender mass	CRP increased
	CRP is higher than the upper limit of normal	

CDAI Crohn's Disease Activity Index, *CRP* C-reactive protein

on the following clinical parameters measured over 7 days: number of soft or liquid stools, use of antidiarrheal medication (0 or 1), abdominal pain (0–3), general well-being (0–4), number of extraintestinal manifestations, abdominal mass (0, 2, or 5), hematocrit (percentage decrease from expected), and body weight (percentage decrease from expected). The scores achieved for each parameter are multiplied by a predefined factor and summarized to provide a final score, which ranges from 0 to approximately 600. A CDAI score below 150 is generally considered to mean quiescent disease, whereas a score above 450 generally signifies very severe disease.

The Harvey-Bradshaw index is a simplified disease activity index. It consists only of clinical parameters, but it has also not really been implemented in clinical practice.

Clinical disease activity can be categorized as mild, moderate, or severe (Table 15.4), although these groups are not precisely defined entities. Most studies consider moderate disease activity (CDAI >220 in adults and PCDAI ≥30 in children) as a prerequisite for inclusion in trials. But because of the high remission rate in the placebo groups in recent studies, a C-reactive protein concentration >10 mg/L is now often also required.

The following classification into remission, response, and relapse is of value in studies:

- Remission: reduction of the CDAI to <150 points, or, in children, of the PCDAI to ≤10 points.
- Relapse: reduction of the CDAI by at least 100 points; in children, of the PCDAI by at least 12.5 points.
- Recurrence: reoccurrence of symptoms after a remission with a >70-point increase in the CDAI (PCDAI, ≥12.5 points) and an overall CDAI >150, given there was a remission beforehand, with a CDAI of <150 points.

Furthermore, guidelines distinguish between localized and extensive disease:

- Localized disease: intestinal CD affecting <30 cm, usually in an ileocecal location (but also may include more proximal small or large bowel)

- Extensive disease: intestinal CD affecting >100 cm, whatever the location. This applies to all inflammation in discontinuous segments.

  Obviously, there is a wide area between 30 and 100 cm, but these somewhat pragmatic definitions are of value for medical and especially surgical decision making (roughly, the more bowel affected, the higher the threshold to operate).

15.3.1.2 Diagnostics

There is no single gold standard method to diagnose CD. The diagnosis is based on the clinical picture, the course of the disease, and the combination of diagnostic modalities, including laboratory workup, endoscopy, histology, and radiology.

15.3.2 Differential Diagnosis

In acute lower-quadrant pain, acute appendicitis and yersiniosis are the most important differential diagnoses. Granulomatous chronic intestinal inflammations can also be caused by sarcoidosis or tuberculosis, especially outside Western Europe. Malignant lymphomas and small-bowel cancers occasionally are the reason for small-bowel stenosis and a "conglomerate." The major differential diagnoses in Crohn's colitis are ulcerative colitis, infectious colitis (including pseudomembranous colitis), and irritable bowel syndrome.

15.3.3 Laboratory

Initial laboratory testing, apart from a standard workup (e.g., full blood count, urea) should include markers of inflammation (C-reactive protein). Fecal calprotectin and lactoferrin can be used to differentiate inflammation from functional complaints, as they are very sensitive markers for bowel inflammation. Calprotectin, for example, has a positive predictive value of 85–90 % in distinguishing inflammatory bowel disease from irritable bowel syndrome. However, these tests are not very specific for CD and are therefore mostly useful during patient follow-up. Albumin is a valuable parameter for nutritional status, especially preoperatively, since a low concentration is correlated with a higher risk of complications [5].

15.3.4 Endoscopy

Ileocolonoscopy and random biopsies from the terminal ileum and each colonic segment should be done to look for microscopic evidence of CD to establish the diagnosis (Fig. 15.3). Moreover, the upper gastrointestinal tract also needs to be investigated by endoscopy to rule out Crohn's lesions there or other diagnoses. Endoscopy is of importance in monitoring treatment and also postoperatively, as newer studies imply a better outcome in patients treated early and aggressively on the basis of early mucosal changes on endoscopy [6].

15.3.5 Imaging

High-resolution ultrasound has an important role in the acute setting, especially to detect fistulas, stenosis, and abscesses. It is also useful to monitor bowel inflammation during treatment.

A plain radiograph is of value in emergency situations, such as bowel obstruction and perforation.

High-resolution magnetic resonance imaging (MRI) or computed tomography (CT) enterography or enteroclysis have the highest diagnostic accuracy for detecting intestinal involvement in CD and especially extramural complications such as fistulas and abscesses. MRI and CT and should be performed during the primary workup of patients with a high suspicion of CD. As MRI has no risk of radiation exposure, it should be preferred whenever possible (Figs. 15.4 and 15.5). CT is generally preferred when an intervention is likely (e.g., abscess drainage; Fig. 15.6).

In rare cases where the standard imaging techniques are negative but there still is a high clinical suspicion of CD, small-bowel capsule endoscopy

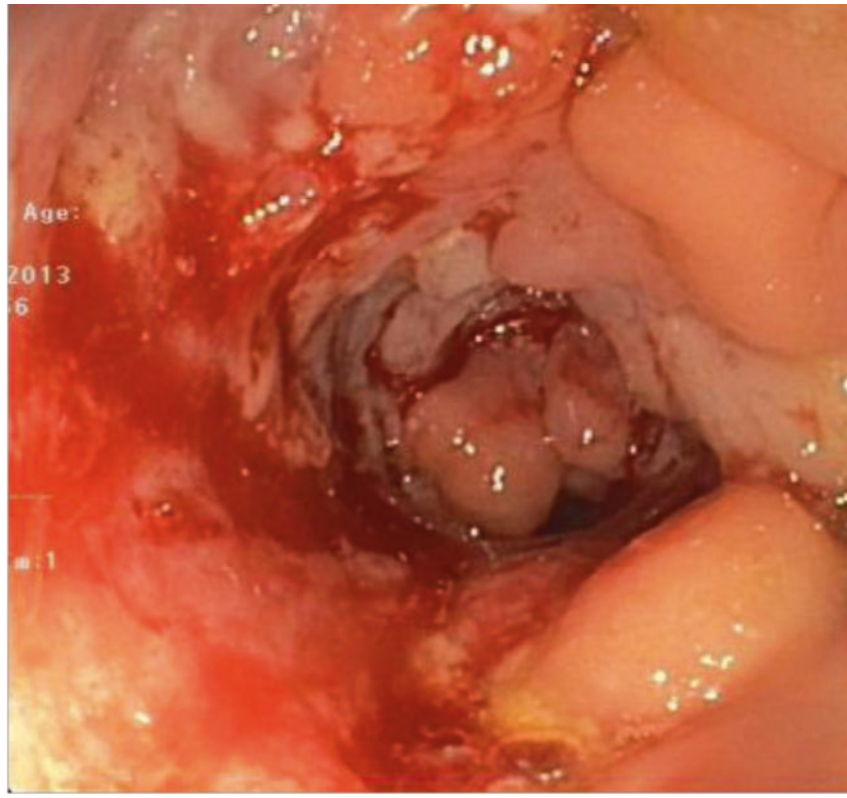


Fig. 15.3 Endoscopic view of a stenosis with a cobblestone appearance in the distal ileum of a patient with Crohn's disease

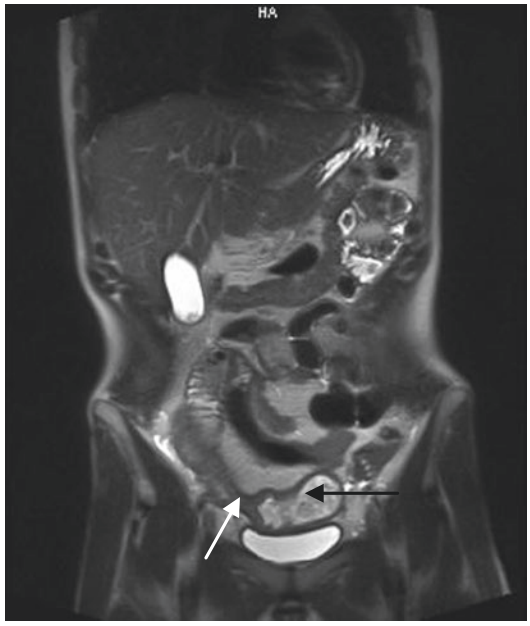


Fig. 15.4 Inflammatory stenosis in the distal ileum (wall thickening; *white arrow*) with prestenotic dilatation (*black arrow*)

can be used to clarify the diagnosis. Double-balloon enteroscopy is only indicated in cases where biopsies (e.g., to exclude malignancy) or therapeutic procedures (e.g., dilatation of a stenosis) are warranted.

In perianal disease, MRI is the imaging modality of choice because it is very accurate. Endosonography is an alternative and is probably as good as MRI if performed by an experienced examiner. But its use is limited because of access (anal stenosis) and pain issues, especially in severe perianal disease.

15.3.5.1 Therapy

Treatment in CD is primarily conservative [7, 8]. However, there are special situations where surgery can be considered (e.g., isolated short-segment ileocecal inflammation) or must be implemented (emergencies) as the primary treatment. The choice of drug in conservative treatment greatly depends on disease activity, site, and accompanying complications (e.g., stenosis,

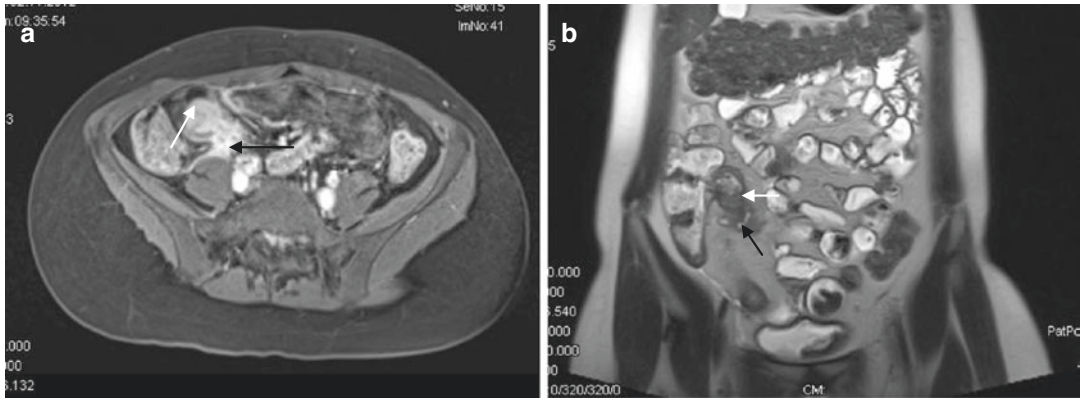


Fig. 15.5 (**a**, **b**) Inflammatory stenosis in the distal ileum (wall thickening; *white arrow*) with a blind-ending fistula to the retroperitoneum (*black arrow*) (**a** axial image, **b** coronal image)

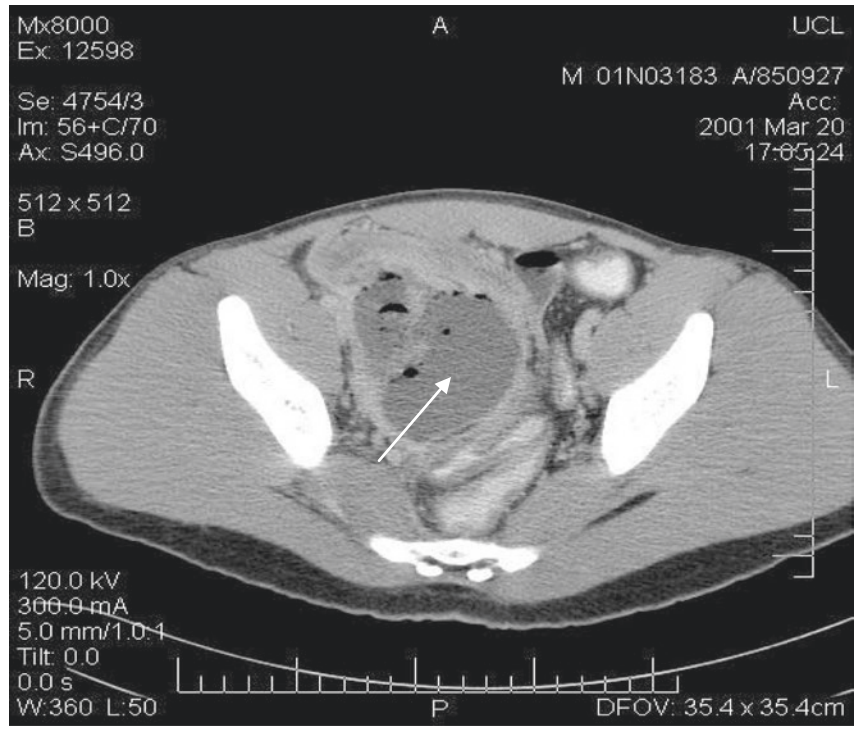


Fig. 15.6 Large pelvic abscess in ileocecal Crohn's disease (*arrow*)

abscess). Obviously, patients need to be counseled with regard to the immense harm of smoking in CD. (Smoking cessation is more effective than any medication to prevent postoperative recurrence!)

Steroids should not be given over a longer period of time because of their side effects and because they are not effective in maintaining remission.

15.4 First-Line Treatment

15.4.1 Ileocecal CD

15.4.1.1 Mildly Active

Budenoside 9 mg/day is the treatment of choice, and about 50–70 % of patients will go into remission within 8–12 weeks. Mesalazine is considerably less effective but can be used. Merely

symptomatic therapy is also viable as between 20 % and up to 40 % of patients go into spontaneous remission.

15.4.1.2 Moderately Active

Budenoside 9 mg/day or systemic steroids (1 mg/kg/day), with the addition of antibiotics if needed (septic complications), is the treatment of choice. This is effective in up to 90 % of patients within 6 weeks.

15.4.1.3 Severely Active

Patients should be primarily treated with systemic steroids.

15.4.2 Crohn's Colitis

15.4.2.1 Mildly and Moderately Active

Sulfasalazine or systemic steroids are first-line options. In distal colitis, suppositories or enemas (mesalazine) can also be used.

15.4.2.2 Highly Active

Patients should be primarily treated by systemic steroids.

15.4.3 Extensive Small-Bowel Disease

Patients should be primarily treated by systemic steroids. Early immunosuppression should be considered.

15.4.4 Oesophageal and Gastroduodenal Disease

Patients should be primarily treated by systemic steroids in combination with proton pump inhibitors.

15.4.5 Perianal Disease

Antibiotics are a good initial option (metronidazol, ciprofloxacin). Longer treatment with metronidazol is problematic because of its side effects (peripheral neuropathy, metallic taste, nausea). Immune modulators or anti–tumor necrosis factor (TNF) (sometimes in combination) are the treatment of choice in severe cases. There is no evidence that standard treatment (5-aminosalicylic acid and steroids) is effective in perianal disease. All treatments are probably not very successful in actually healing fistulas, but secretion and inflammation are reduced and quality of life is thereby significantly improved.

15.5 Treatment Escalation

Surgical options should always be considered before an immunosuppressive therapy is implemented. Contraindications need to be considered; for example, tuberculosis and severe infections including undrained abscesses are absolute contraindications for treating patients with anti-TNF.

Steroid-refractory disease should primarily be treated with anti-TNF with or without azathioprine (2–2.5 mg/kg/day) or 6-mercaptopurine (1–1.5 mg/kg/day). Therapy with anti-TNF achieves an improvement or remission in up to 70 % of patients in this setting and, compared with the above-mentioned thiopurines, acts more quickly. Methotrexate is an alternative (25 mg/week, intramuscularly) in special situations (e.g. when other treatments cannot be continued due to side-effects). Vedolizumab, a bowel-selective integrin antagonist, is another option; it has been proven effective in patients with CD, with similar remission rates as anti-TNF.

When immunosuppressive therapy fails, dosage and application intervals should be optimized before changing to another drug.

15.6 Surgery

15.6.1 Indications for Surgery

The majority of patients with CD (80–90 %) will have to be operated on at some time over the course of their disease, and although medical therapy has become more aggressive, this rate does not seem to have gone down significantly in

the past 20 years. About 50 % will have to be operated on a second time within another 5–10 years. Newer studies suggest that this reoperation rate may have gone down to around 25 % but data are conflicting.

Surgery is generally only indicated when complications occur, or when the symptoms are not adequately controlled by medication or the medication causes side effects, resulting in a deterioration of quality of life. Isolated symptomatic ileocecal CD is the one entity (other than emergencies or cancer) where primary resection is regarded as equivalent to the escalation of medical treatment (i.e., immunosuppression), as most of these patients will have to be operated on in the near future anyway, the operation has a low morbidity, symptoms are relieved quickly, and, most important, more than 50 % of patients will not require further treatment postoperatively or another operation for a long time (≥10 years). Therefore, guidelines recommend that patients with isolated ileocecal CD be counseled in regard to surgery as a viable primary alternative to medical treatment.

Only around 5 % of patients have to be operated on as an emergency, the most common reason being complete bowel obstruction, toxic megacolon, perforations (Fig. 15.7), and, rarely, bleeding.

Indications for surgery:

- Stenosis
- Fistula
- Abscess
- Dysplasia
- Cancer (small bowel or colonic)
- Emergency
  - Bowel obstruction
  - Perforation
  - Bleeding
  - Toxic megacolon

In CD, the line between absolute and relative indications for surgery is sometimes indefinite. Obviously, cancer, high-grade dysplasia, and emergencies are absolute indications, but in all other situations, indications for surgery may not be so clear and may change depending on the clinical situation. For example, a patient may present with manifest bowel obstruction, but after bowel rest, parenteral nutrition, and anti-inflammatory treatment (e.g., steroids), this may completely resolve; after adequate medical treatment, this patient may not need an operation for a long time. Or, after draining an abscess interventionally (guided by ultrasound or CT) and antibiotic treatment patients may recover so well that an operation is not immediately necessary. Whether an operation is indicated at all after successful drainage is controversial. Most guidelines recommend resection (with a low level of evidence) in an elective setting, arguing that the abscess will recur in around 50 % of patients.

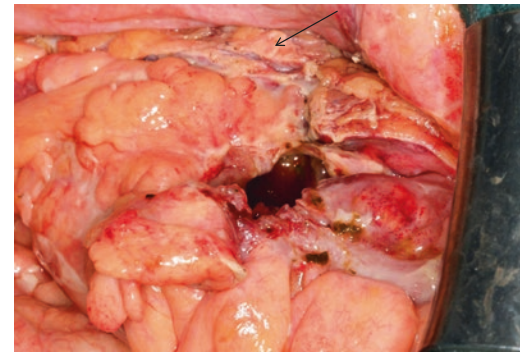


Fig. 15.7 Sigmoid perforation in severe Crohn's colitis ("fat creeping"; *arrow*) with fecal peritonitis

With regard to fistulas, the principle is that asymptomatic fistulas generally do not require surgery, whereas early surgery should be considered for symptomatic fistulas. Enterovesical and blind-ending retroperitoneal fistulas are absolute indications for surgery.

Enterocutaneous and high interenteric fistulas may also present as absolute indications for surgery if they result in the loss of a large amount of fluid, severely affected skin, or a functional short-bowel syndrome (Fig. 15.8, Table 15.2).

As a general rule, stenoses are an indication for invasive treatment if they are indeed symptomatic and do not respond to medical therapy. Short stenoses (up to 5 cm long) can be treated by dilatation if they are accessible by endoscopy. Although results after surgical treatment with regard to morbidity and restenosis rates are comparable with those after endoscopic dilatation, there is growing consensus that a short stenosis

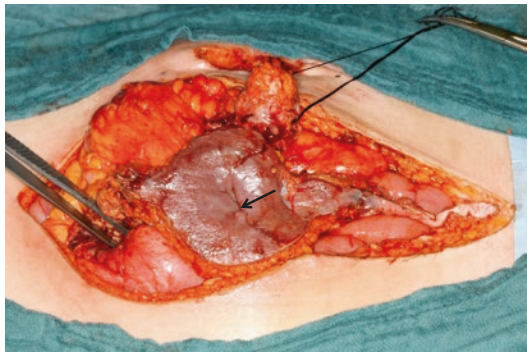


Fig. 15.8 High-flow enterocutaneous fistula (*arrow* at the cutaneous opening) with severely affected skin (intraoperative view after excision of the fistula, including the affected skin; forceps were placed in one of the fistulas among a whole system of fistulas arising from the small bowel)

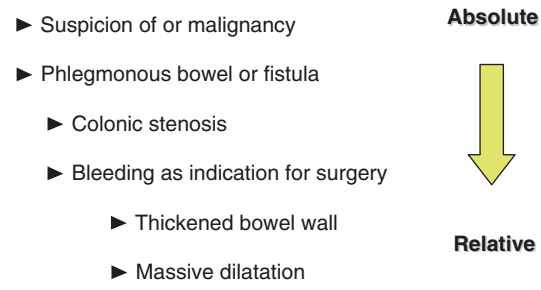


Fig. 15.9 Contraindications for strictureplasty

should probably be treated first by endoscopy (the exception is isolated short ileocecal stenosis as discussed before) [9].

15.6.2 Surgical Principles

There is ample level-I evidence that extensive resection has no benefit over limited resection with regard to recurrence. Therefore, to reduce the risk of short-bowel syndrome, only the affected bowel should be resected, without the relevant safety margins of unaffected tissues. However, anastomosis should not be performed in inflamed tissue because it may increase the risk of leakage. If there is extensive disease, however, the portion of the affected bowel not responsible for the patient's symptoms may sometimes have to be left in situ.

Stenosis can be treated by strictureplasty or resection; the recurrence rates in the available low-evidence studies (nonrandomized with a high selection bias) are not significantly different between the two groups (reoperation rates of around 50% within 10 years). Strictureplasty should be the preferred choice because no bowel is resected, but it can be contraindicated or is often not technically feasible because of severe inflammatory thickening of the wall or fistulas in the affected bowel (Fig. 15.9).

Generally, classical strictureplasty is recommended only for a stenosis with a maximal length of 10–15 cm. The most commonly used strictureplasty according to Heinicke-Mikulicz, as an example, is generally restricted to stenoses of up to 10 cm (Fig. 15.10a, b). With newer techniques such as the side-to-side isoperistaltic strictureplasty according to Michaelassi, much longer stenosis (≥50 cm) can be treated (Fig. 15.11a, b) [10].

Treatment of colonic stenoses with strictureplasty is generally not recommended because there is always a concern of malignancy. Technically, however, this can be done and is justified in selected cases where a resection may contribute greatly to an already poor functional result (e.g., larger parts of the colon were previously resected).

In several small-bowel stenoses following each other ("skip lesions"), treatment greatly depends on the length of unaffected bowel in between each lesion and the remaining bowel length. It makes little sense to perform several strictureplasties within a small distance if the lesions could be resected completely in a small segment of bowel with a single anastomosis. The same applies to resections; here also several anastomoses within a short distance, only make sense if the patient has a relevant risk of short-bowel syndrome. If the clinical significance of a stenosis remains unclear intraoperatively, a Foley catheter can be passed through a small enterotomy to evaluate the inner bowel diameter or, alternatively, intraoperative endoscopy can be done.

In the case of a fistula, the strategy depends on whether the fistula arises from an inflamed bowel

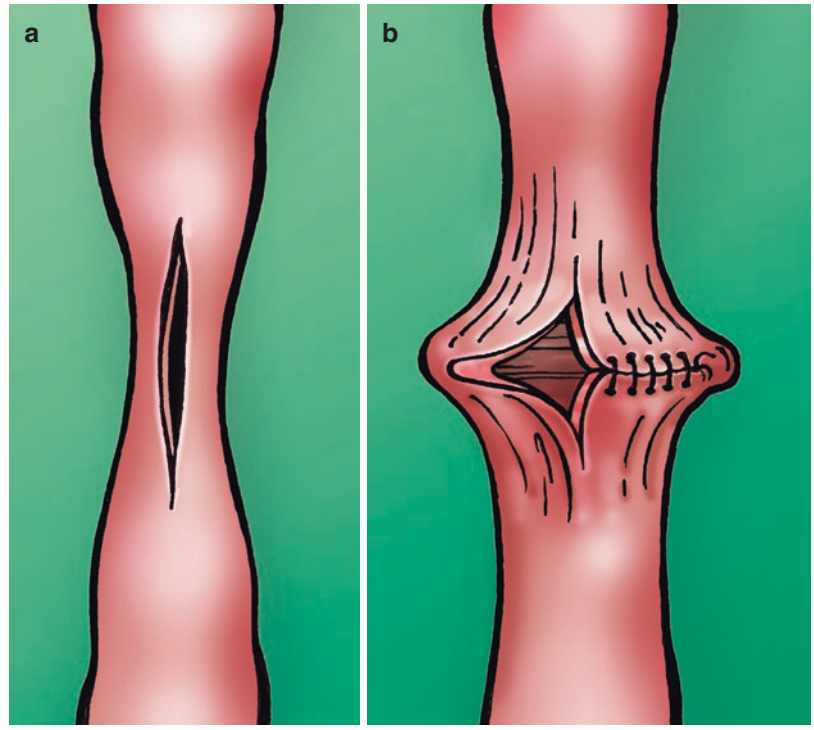


Fig. 15.10 (**a**, **b**) Schematic illustration of strictureplasty according to Heinicke-Mikulicz (**a** longitudinal incision, **b** vertical closure)

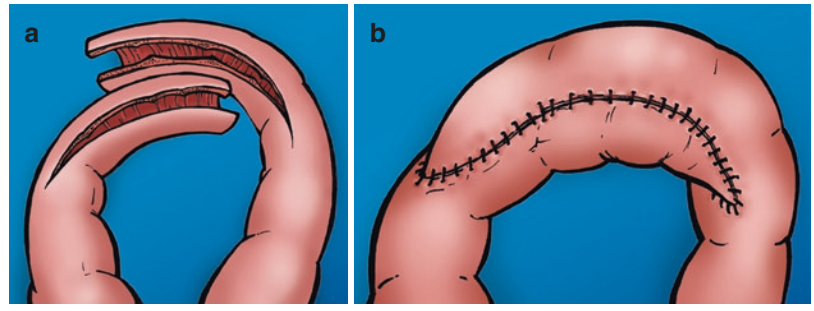


Fig. 15.11 (**a**, **b**) Schematic illustration of strictureplasty according to Michaelassi (**a** longitudinal incision after transverse dissection, **b** side-to-sideanastomosis)

or merely penetrates the bowel secondarily, without the bowel being affected by CD. The latter type of fistula can be excised and closed using sutures; a fistula originating from inflamed bowel needs to be treated with resection of the bowel including the fistula.

The technique used to fashion an anastomosis remains controversial. Previous small, case-control studies suggested that a stapled, wide side-to-side anastomosis may result in less restenosis and also has a lower leak rate. A large randomized controlled trial, however, did not show any differences [11]. Therefore, no specific method of performing anastomosis can be recommended; the surgeon can choose freely. If the bowel parts to be anastomosed have a large difference in diameter, an end-to-side or side-to-side construction seems advantageous (Fig. 15.12a–c). Newer, innovative techniques such as the Kono anastomosis, which is essentially the combination of a strictureplasty with an end-to-end-anastomosis, need to be tested in controlled studies in order to judge their efficacy [12].

In localized colonic stenosis, segmental resection with narrow margins to the unaffected bowel

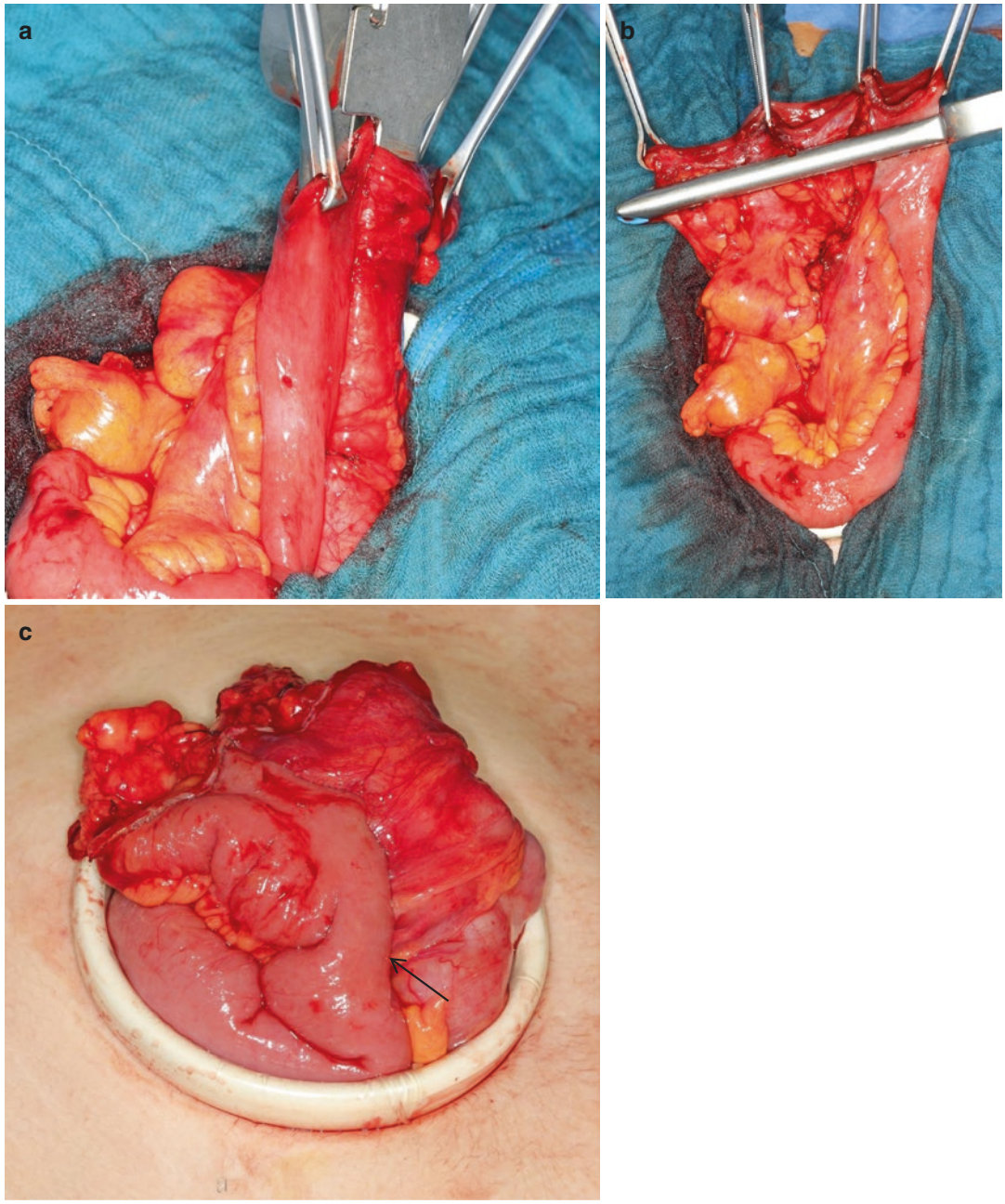


Fig. 15.12 Side-to-side stapled anastomosis (ileocecal anastomosis) with an ILA-100. (**a**) Longitudinal stapling. (**b**) Transverse stapling. (**c**) Completed anastomosis after stapling before sewing over the *transverse staple line* (inverted running suture) and securing the *bottom staple line* (*arrow*) with two interrupted sutures

is the procedure of choice. The use of more radical resections such as subtotal colectomy to reduce recurrence rates has not been shown to be significantly advantageous, especially when considering quality of life [13]. In extensive Crohn's colitis, the type of procedure greatly depends on the distribution of the disease. If the rectum is spared, as often is the case in CD, subtotal colectomy with ileorectostomy may be an option. But here again, quality of life depends on whether

perianal disease is present and on sphincter function. In the case of Crohn's colitis without perianal disease and without an affected small bowel, which is rare, restorative proctocolectomy can be discussed, but pouch failure is significantly more common here than in ulcerative and indeterminate colitis.

In the case of dysplasia (which needs to be confirmed by a second pathologist) or cancer of the small bowel, oncological radical resection of the affected segment is mandatory. There is controversy over whether oncological segmental resection of the colorectum (hemicolectomy, sigmoid or rectal resection) is indeed appropriate. Especially in long-standing Crohn's colitis, the pathogenesis of malignancy is comparable to that in ulcerative colitis, and here oncological proctocolectomy is recommended. On the other hand, whereas in ulcerative colitis with cancer or dysplasia a permanent stoma can often be avoided by performing an ileoanal pouch, this option is normally not possible in CD (see above). Patients are generally reluctant to accept a lifelong end-ileostomy. Guidelines have left this issue unresolved. In our practice, if high-grade dysplasia or cancer is confirmed in different locations of the colon and rectum, and if no contraindication for an ileoanal pouch is present, we recommend oncological proctocolectomy as a restorative procedure.

15.6.3 Risk Factors and Surgical Strategy

Because of the growing spectrum of medications for treating CD, surgery is often only regarded as a last resort. This results in patients often coming to surgery in a poor nutritional status and immunocompromised. In these cases, adequate preparation and more conservative surgery can reduce perioperative complications. Serum albumin concentrations as a surrogate marker for nutritional status have been shown to adequately predict complications, the cutoff being between somewhere between 30 and 35 mg% [5]. In our owen practice this cutoff point is 30 mg%. Supplemental enteral (e.g., protein shakes) and possibly also parenteral nutrition should be given for at least 1 week (often a considerably longer period is necessary) before surgery to improve nutritional status. Steroids should be weaned, ideally to less than 10 mg Decortin (prednisone). There remains controversy about immunosuppressants: stopping azathioprine is generally not recommended, but evidence is poor. Nonetheless, the most valid case-control study looking at a homogenous group of patients indeed showed a significant effect of azathioprine on perioperative local septic complications [14]. However, as effective drug concentrations persist for a long time, interruption of this treatment is probably not of any value. The data on biologicals are conflicting; however, the majority of recently published meta-analyses (five of six published between 2012 and 2014) indeed showed an association of perioperative complications with anti-TNF use [15]. Therefore, it seems prudent to operate at the end of the treatment interval (a minimum of 3 weeks after the last application, preferably 4 weeks) or, if possible, even to interrupt treatment. In our experience, the overwhelming majority of operations can be postponed so that nutritional status can be improved, steroids can be weaned, and an adequate interval to the last application of biological treatment can be achieved. This concept has also been successful in other hands [16]. If this is not possible (emergency) or the patient's poor condition persists, surgery should be adapted to the situation. Primary anastomoses should either be protected by diversion (protective stoma) or not done at all; in the latter a resectional stoma after bowel resection is a good option (instead of a Hartmann procedure).

15.6.4 Minimally Invasive Surgery

Virtually all abdominal procedures in CD can be performed laparoscopically. There is level-I evidence supporting the laparoscopic approach for ileocecal resection, since patients recover more quickly and complications are not increased and are possibly fewer compared with conventional surgery [17]. Obviously, patients operated on

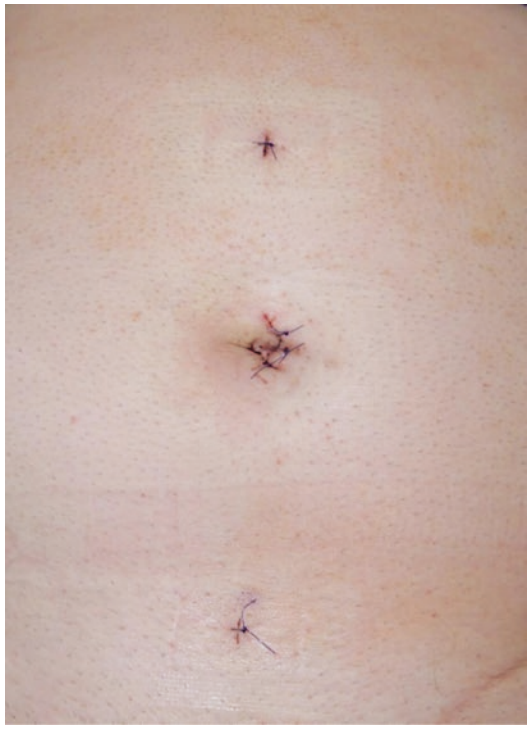


Fig. 15.13 Cosmetic result 3 days after laparoscopic ileocecal resection (bowel was harvested through an umbilical incision)

Table 15.5 Relative contraindications to performing laparoscopic procedures in Crohn's disease (listed from more relevant to less relevant)

Extensive previous abdominal surgery
Conglomerate tumor
Extensive intra-abdominal fistulization
Malignancy
Poor general condition

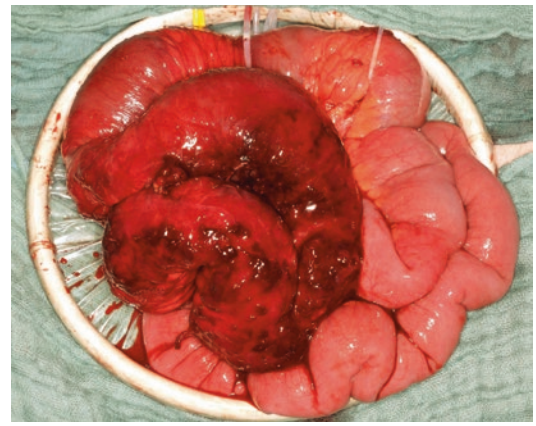


Fig. 15.14 Bulky small-bowel conglomerate in Crohn's disease

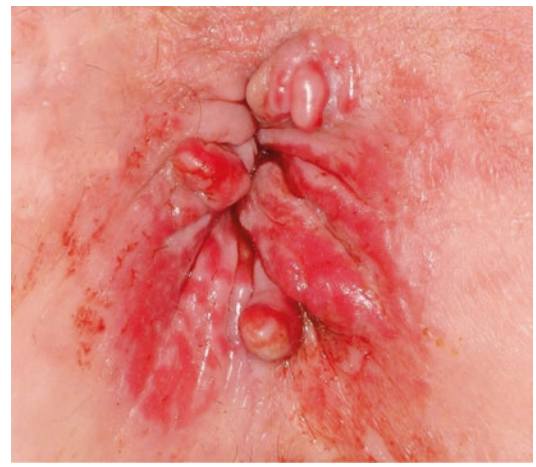


Fig. 15.15 Anal inflammation in Crohn's disease with skin tags

laparoscopically have a better cosmetic result (Fig. 15.13), but the duration of the procedure is significantly longer. There is a relevant conversion rate of around 5–20 %, which depends on patient selection and surgical expertise. There are no longer any absolute contraindications to laparoscopy, but there are several relative contraindications that need to be considered (Table 15.5). It is obviously not sensible to do a difficult dissection through a minimally invasive procedure to then make a large incision to extract a bulky conglomerate (Fig. 15.14) 15.5.

15.6.5 Perianal Disease

Around 25–35 % of patients with CD develop perianal disease. This includes abscesses, fistulas, fissures, ulcerations, and skin tags (Fig. 15.15).

Perianal disease is diagnosed on the basis of inspection, digital rectal examination, and proctoscopy; the latter often has to be done under anesthesia because it is painful. Other useful investigations are endosonography (in case of fistulas, abscesses or sphincter defects, but not always possible, especially when there is a stenosis) and MRI. Fistulography is now considered

obsolete. CT still has a limited role in diagnosing abscesses, especially when MRI is not available. Anorectal manometry may be of some use in patients with incontinence, although differentiation of clinically continent and incontinent patients on the basis of manometry values is only moderate.

Several classifications can be used to categorize perianal disease and especially fistulas. The Perianal Disease Activity Index assesses the clinical activity of perianal disease in CD [18] and includes the evaluation of five aspects: fistula discharge, pain and restriction of activities, restriction of sexual activity, type of perianal disease, degree of induration.

The most commonly used classification of fistulas is undoubtedly the Parks classification, which categorizes fistulas according to their anatomic localization with regard to the anal sphincter complex: intersphincteric, transsphincteric, suprasphincteric, or extrasphincteric (Fig. 15.16). However, because fistulas in CD are often difficult to classify, a simpler classification by the American Gastroenterological Association differentiates between "simple" and "complex" fistulas [19] (Table 15.6).

Simple fistulas are low, with no further manifestation of the disease (especially no relevant proctitis), and do not affect larger portions of the sphincter, therefore allowing a simple excision or "laying open" surgical technique. Obviously, these fistulas have a low rate of recurrence: around 20% within 5 years after surgery. Complex fistulas are high, occurring above the dentate line (intersphincteric, transsphincteric, extrasphincteric, suprasphincteric), with many external openings (Fig. 15.17), and may be associated with perianal abscesses, rectal stricture, proctitis, or connection with the bladder or vagina.

The fistula drainage assessment has been proposed to quantify fistula healing and has been used to standardize the clinical assessment of perianal disease in clinical trials. The presence of purulent drainage after gentle compression using a finger is considered as an index of activity; on the other hand, the absence of drainage is defined

Table 15.6 Simple versus complex perianal fistulas in Crohn's disease

Simple	Complex
► Single opening	► several openings
► low fistula	► high fistula
► no other perianal manifestation	► other perianal manifestations

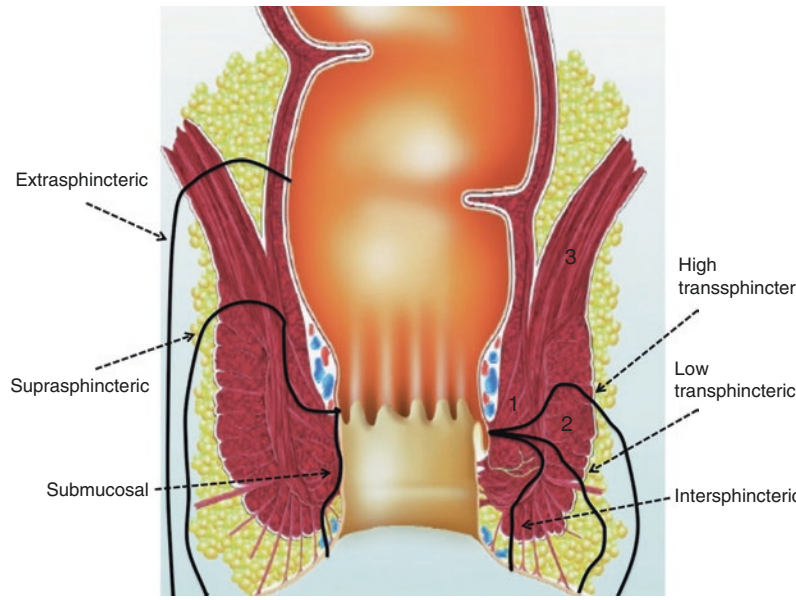


Fig. 15.16 Parks classification of perianal fistula: intersphincteric, transsphincteric, suprasphincteric, extrasphincteric (*1* internal sphincter, *2* external sphincter, *3* puborectal sling)

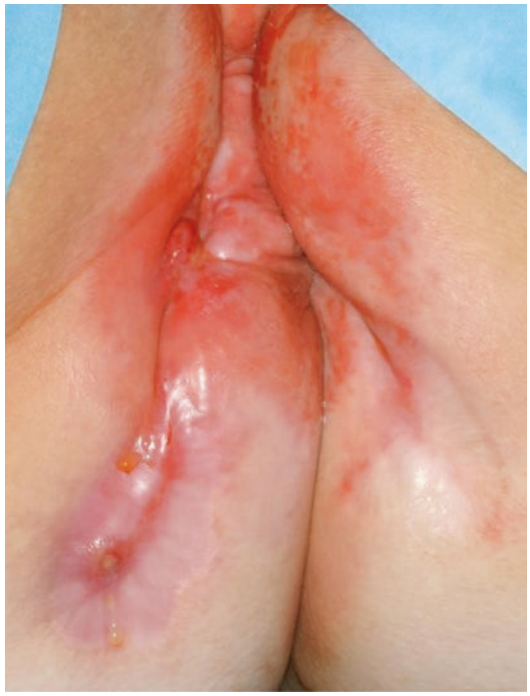


Fig. 15.17 Complex fistula in Crohn's disease

as remission. Clinical response is defined as a reduction of 50 % or more in the number of draining tracts. Finally, if no pus drains after compression, the fistula is considered closed [20].

An algorithm for how to proceed in patients with perianal fistulas in CD is given in Fig. 15.18. Perianal fistulas have to be drained, as in patients without CD. Only submucosal, subcutaneous, low intersphincteric, and low transsphincteric fistulas can be laid open. High transsphincteric and complex fistulas should primarily be treated with (noncutting) setons. Any surgery more extensive than seton placement needs to be weighed carefully against the failure rate and against the risk of iatrogenic sphincter injury with concomitant stool incontinence. Patients with CD often fare well with setons, showing few symptoms and good quality of life.

Any reconstructive surgery only makes sense if there is little or no proctitis. Initial studies with the fistula plug suggested high healing rates, but newer studies show disappointing closure rates. Nonetheless, because continence is usually not compromised by the procedure, it is a potential option. Flaps (especially a mucosal flap) are generally considered as primary options to close higher fistulas. Graciloplasty has proven successful in about 80 % of patients with rectovaginal fistulas with a large defect or patients with recurrent rectovaginal fistulas. For all reconstructive procedures in complex fistulas, however, patients have to be counseled that only about half of the fistulas will indeed remain healed over a long period of time (5 years) [21]. Adequate medical treatment is therefore mandatory in patients with severe perianal disease.

If closure of a complex fistula is intended, a defunctioning stoma can, in our experience, be of value, especially in cases where previous repairs have already failed. However, evidence for this is low. The choice of stoma depends on the distribution of the disease. Functionally, a sigmoidostomy is obviously the best option. But in the case of inflammation of the large bowel, complications such as stoma fistulas or stenosis are likely, and then an ileostomy is the better option. If a defunctioning stoma is constructed, we prefer to close the efferent limb directly under the abdominal wall, creating an end stoma to completely prevent the passage of stool into the anal region. This also has the advantage of lower rates of stoma herniation or prolapse compared with loop stomas. Many patients with complex perianal disease try to avoid a stoma at all costs. It is easier to convince patients to have a temporary stoma constructed; then, when they realize the advantages of a stoma (e.g., often improved quality of life), many want to keep the stoma or even agree to the construction of a permanent stoma.

Proctectomy may be indicated as a final solution in severe perianal disease. In such cases a partially sphincter-preserving procedure (in the same plane as intersphincteric resection, but including sphincterotomy to warrant adequate postoperative drainage) with excision of the fistulas and omentoplasty seems advantageous compared with abdominoperineal resection. Not only is the outward anatomy preserved, which is undoubtedly an advantage in these often young patients, but usually there is no large perineal defect that may result in a nonhealing sinus.

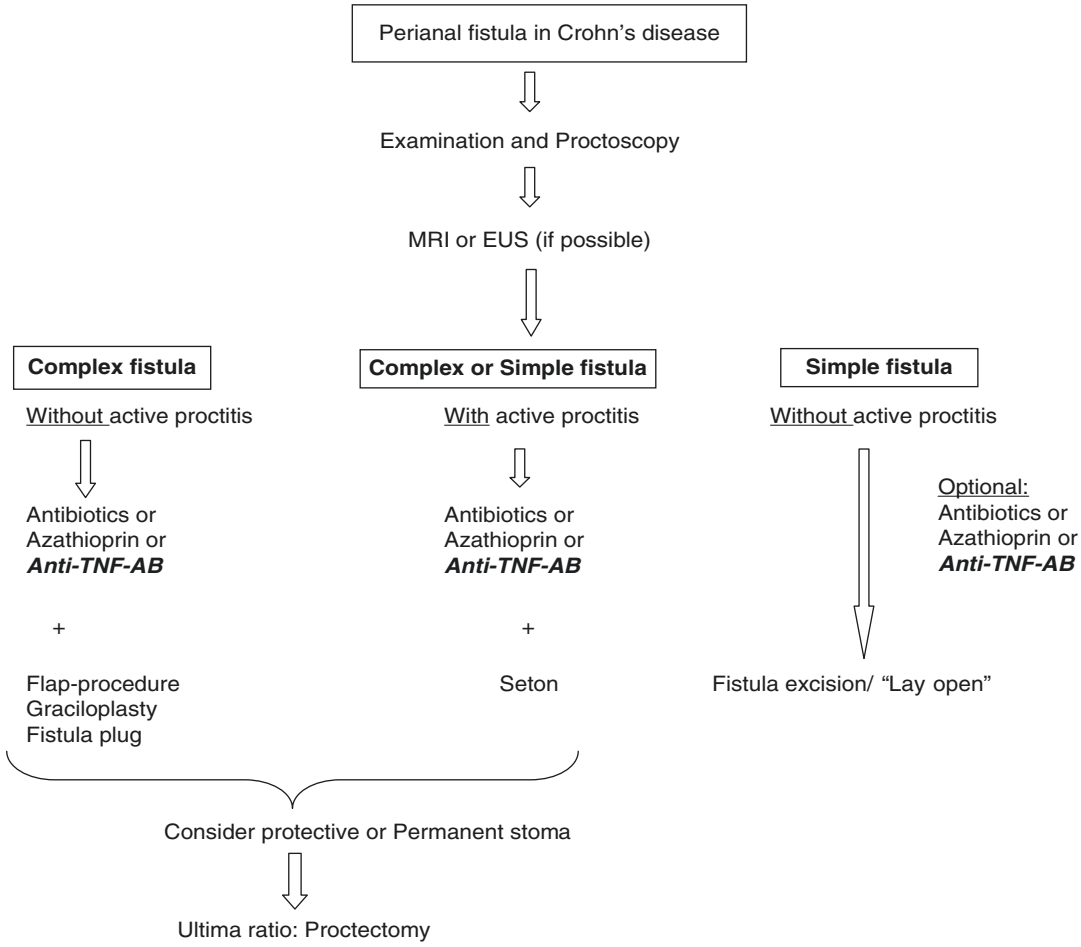


Fig. 15.18 Modified American Gastroenterological Association algorithm to treat perianal fistulas in Crohn's disease (abscesses have to be adequately drained before implementation) [19]

In conclusion, complex fistulas in CD are difficult to treat and healing rates are moderate. Therefore, these complex cases should be treated in specialist centers if reconstructive procedures are planned.

15.6.6 Special Aspects

15.6.6.1 Volume Aspect/Specialist Institution

Several studies have shown that patients with CD benefit from interdisciplinary teams. There is now also increasing evidence that outcomes with regard to morbidity and mortality are significantly better if patients undergoing surgery for CD are treated at a high-volume hospital [22]. Therefore, especially complex cases should preferably be treated in specialist centers.

15.6.6.2 Cancer

The risk for small-bowel cancer is tremendously increased in CD, but it is still a rare event. Because symptoms are very similar to those of an inflammatory or fibrotic stenosis, the diagnosis is often made late, which is probably the major reason why the prognosis is poor [23]. However, because of the rarity of small-bowel cancer, specific surveillance measures are not indicated. In the case of a Hartmann's situation, bypassed bowel (a situation which should be strictly avoided in the surgery of Crohn's disease), or

long blind limbs, treating physicians should be aware that cancer can also arise here. If in doubt, endoscopy with biopsies (if the region is accessible) or MRI/CT are options to investigate potential malignancy.

The risk of colorectal cancer in Crohn's colitis is probably nearly equal to or as high as that in ulcerative colitis, and the prognosis in most series is poorer. Therefore, it is sensible to adhere to the guidelines recommended for ulcerative colitis, for example, yearly colonoscopies with random biopsies or, alternatively, chromoendoscopy-guided biopsies in patients with long-standing Crohn's colitis (from the 15th year of diagnosis) or pancolitis (from the 8th year) [7]. In patients with sclerosing cholangitis, endoscopic surveillance should be started directly after diagnosis.

Anal adenocarcinoma (often associated with a fistula) and squamous cell anal cancer are more common among patients with CD than the normal population but overall are rare events [24]. Again, the prognosis for both entities is poor, and early radical excision with abdominoperineal excision and flap coverage (we prefer a rectus abdominis flap) is the procedure of choice. Neoadjuvant or adjuvant treatment may be indicated, depending on the stage. If long-standing fistulas persist, regular biopsies are mandatory to rule out cancer.

15.6.6.3 Pregnancy and Fertility

Patients wanting to become pregnant should be in clinical remission, as active disease reduces fertility and increases the risk for premature birth and miscarriage. If patients have active disease while trying to become pregnant, the active disease will persist or the status may even deteriorate in around two-thirds of patients. As a consequence, current guidelines do not support the cessation of medical therapy in patients wanting to become pregnant except for methotrexate, which has been proven to be teratogenic and to have embryotoxic effects [25]. All other treatments (azathioprine, biologicals, steroids, mesalazine) should be continued during pregnancy because disease relapse is considered more harmful to the pregnancy and the unborn child than the potential effects of the medication.

For men wishing to father a child, sulfasalazine should be discontinued and, if necessary, switched to another drug because it can cause reversible infertility by lowering sperm quality.

During breastfeeding, mesalazine and steroids can be continued safely under supervision. All other drugs, such as azathioprine and biologicals, the situation is somewhat unclear; these drugs go into the breast milk and may harm the baby. Whether to discontinue treatment or cease breastfeeding must be weighed carefully with regard to the advantages and disadvantages of each.

References

1. Baumgart DC, Sandborn WJ. Crohn's disease. Lancet. 2012;380:1590–650.
2. Silverberg MS, Satsangi J, Ahmad T, et al. Towards an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a working party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19(Suppl A):5–36.
3. Laass MW, Roggenbuck D, Conrad K. Diagnosis and classification of Crohn's disease. Autoimmun Rev. 2014;13(4–5):467–71.
4. Van Assche G, Dignass A, Panes J, Beaugerie L, Karagiannis J, Allez M, Ochsenkühn T, Orchard T, Rogler G, Louis E, Kupcinskas L, Mantzaris G, Travis S, Stange E, European Crohn's and Colitis Organisation (ECCO). The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohns Colitis. 2010;4(1):7–27.
5. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. Dis Colon Rectum. 2000;43:1141–5.
6. Peter De Cruz, Michael A Kamm, Amy L Hamilton, Kathryn J Ritchie, Efrosinia O Krejany, Alexandra Gorelik, Danny Liew, Lani Prideaux, Ian C Lawrance, Jane M Andrews, Peter A Bampton, Peter R Gibson, Miles Sparrow, Rupert W Leong, Timothy H Florin, Richard B Gearry, Graham Radford-Smith, Finlay A Macrae, Henry Debinski, Warwick Selby, Ian Kronborg, Michael J Johnston, Rodney Woods, P Ross Elliott, Sally J Bell, Steven J Brown, William R Connell, Paul V Desmond. Crohn's disease management after intestinal resection: a randomised trial. Lancet. 2014. pii: S0140-6736(14)61908-5.
7. Preiß JC, Bokemeyer B, Buhr HJ, Dignaß A, Häuser W, Hartmann F, Herrlinger KR, Kaltz B, Kienle P, Kruis W, Kucharzik T, Langhorst J, Schreiber S, Siegmund B, Stallmach A, Stange EF, Stein J, Hoffmann JC. Updated German clinical practice

guideline on "Diagnosis and treatment of Crohn's disease" 2014. Z Gastroenterol. 2014;52(12):1431–84.
8. Dignass A, Van Assche G, Lindsay JO, Lémann M, Söderholm J, Colombel JF, Danese S, D'Hoore A, Gassull M, Gomollón F, Hommes DW, Michetti P, O'Morain C, Oresland T, Windsor A, Stange EF, Travis SP. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: current management. J Crohns Colitis. 2010;4(1):28–62.
9. Bhalme M, Sarkar S, Lal S, Bodger K, Baker R, Willert R. Endoscopic balloon dilatation of Crohn's disease strictures: results from a large United kingdom series. Inflamm Bowel Dis. 2014;20(2):265–70.
10. Campbell L, Ambe R, Weaver J, Marcus SM, Cagir B. Comparison of conventional and nonconventional strictureplasties in Crohn's disease: a systematic review and meta-analysis. Dis Colon Rectum. 2012;55(6):714–26.
11. McLeod RS, Wolff BG, Ross S, Parkes R, McKenzie M, Investigators of the CAST Trial. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. Dis Colon Rectum. 2009;52(5):919–27.
12. Kono T, Ashida T, Ebisawa Y, Chisato N, Okamoto K, Katsuno H, et al. A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease. Dis Colon Rectum. 2011;54:586–92.
13. Tekkis PP, Purkayastha S, Lanitis S, Athanasiou T, Heriot AG, Orchard TR, Nicholls RJ, Darzi AW. A comparison of segmental vs subtotal/total colectomy for colonic Crohn's disease: a meta-analysis. Colorectal Dis. 2006;8(2):82–90.
14. Myrelid P, Olaison G, Sjödahl R, Nyström PO, Almer S, Andersson P. Thiopurine therapy is associated with postoperative intra-abdominal septic complications in abdominal surgery for Crohn's disease. Dis Colon Rectum. 2009;52(8):1387–94.
15. Yang ZP, Hong L, Wu Q, Wu KC, Fan DM. Preoperative infliximab use and postoperative complications in Crohn's disease: a systematic review and meta-analysis. Int J Surg. 2014;12(3):224–30.
16. Zerbib P, Koriche D, Truant S, Bouras AF, Vernier-Massouille G, Seguy D, Pruvot FR, Cortot A, Colombel JF. Pre-operative management is associated with low rate of post-operative morbidity in penetrating Crohn's disease. Aliment Pharmacol Ther. 2010;32(3):459–65.
17. Tilney HS, Constantinides VA, Heriot AG, Nicolaou M, Athanasiou T, Ziprin P, Darzi AW, Tekkis PP. Comparison of laparoscopic and open ileocecal resection for Crohn's disease: a metaanalysis. Surg Endosc. 2006;20(7):1036–44.
18. Irvine EJ. Usual therapy improves perianal Crohn's disease as measured by a new disease activity index. McMaster IBD Study Group. J Clin Gastroenterol. 1995;20:27–32.
19. Sandborn WJ, Fazio VW, Feagan BG, Hanauer SB. AGA technical review on perianal Crohn's disease. Gastroenterology. 2003;125:1508–30.
20. Sandborn WJ, Feagan BG, Hanauer SB, Lochs H, Löfberg R, Modigliani R, Present DH, Rutgeerts P, Schölmerich J, Stange EF, Sutherland LR. A review of activity indices and efficacy endpoints for clinical trials of medical therapy in adults with Crohn's disease. Gastroenterology. 2002;122(2):512–30.
21. Löffler T, Welsch T, Mühl S, Hinz U, Schmidt J, Kienle P. Long-term success rate after surgical treatment of anorectal and rectovaginal fistulas in Crohn's disease. Int J Colorectal Dis. 2009;24(5):521–6.
22. Ananthakrishnan AN, McGinley EL, Binion DG. Does it matter where you are hospitalized for inflammatory bowel disease? A nationwide analysis of hospital volume. Am J Gastroenterol. 2008;103(11):2789–98.
23. Elriz K, Carrat F, Carbonnel F, Marthey L, Bouvier AM, Beaugerie L, CESAME study group. Incidence, presentation, and prognosis of small bowel adenocarcinoma in patients with small bowel Crohn's disease: a prospective observational study. Inflamm Bowel Dis. 2013;19(9):1823–6.
24. Thomas M, Bienkowski R, Vandermeer TJ, Trostle D, Cagir B. Malignant transformation in perianal fistulas of Crohn's disease: a systematic review of literature. J Gastrointest Surg. 2010;14(1):66–73.
25. van der Woude CJ, Kolacek S, Dotan I, Oresland T, Vermeire S, Munkholm P, Mahadevan U, Mackillop L, Dignass A, European Crohn's Colitis Organisation (ECCO). European evidenced-based consensus on reproduction in inflammatory bowel disease. J Crohns Colitis. 2010;4(5):493–510.

Indeterminate Colitis

16

Tom Øresland

The term *indeterminate colitis* first appeared in 1970 when Kent et al. [1] retrospectively studied the clinical features and microscopic appearance of colectomy specimens from 222 patients, most of whom underwent surgery for chronic colitis. They found that 14 cases could not be properly diagnosed according to the classical morphological criteria and had overlapping features of both diagnoses; these were labeled as "indeterminate colitis." Some years later, in 1978, the occurrence of indeterminate cases was confirmed in another study looking at surgical resection specimens [2]. The main reason for this uncertainty was that some specimens had transmural inflammation and deep ulcers and fissures extending into the muscularis propria, but they did not show granulomata and the lymphoid hyperplasia associated with Crohn's disease. The existence of this diagnostic dilemma was generally accepted but had limited implications in terms of its influence on treatment options. Pharmacological treatment was not that advanced and was mainly based on sulfasalazine and steroids. With the general introduction of colonoscopy with biopsies for the diagnosis of inflammatory bowel disease (IBD)–related colitis, pathologists have agreed that histological changes in mucosal biopsies alone are insufficient for a diagnosis of an indeterminate colitis. The term *IBD unclassified* has been agreed on for use in patients not yet operated on and for whom a definite diagnosis cannot be established [3, 4]. Pharmacological treatments have recently become more advanced and diverse, but patients with IBD colitis have all been treated in much the same way; there has not been a need for special treatment algorithms for patients with indeterminate colitis.

Since the early 1970s, the surgical treatment of IBD colitis has evolved toward continence-preserving operations, initially with the continent ileostomy. The type of colitis is not a major concern as long as patients do not demonstrate disease activity in the small bowel [5]. There has, however, been particular concern regarding restorative proctocolectomy in patients with a diagnosis of indeterminate colitis because not only might Crohn's colitis extend into the small bowel, thus risking the loss of a substantial length of bowel (including that used for the pouch), but also the risk of perianal disease with fistula formation, especially with Crohn's disease located in the rectum. Fistulating Crohn's disease in patients with an ileal pouch is most debilitating because continence is often at a borderline level [6], and adding perianal sepsis often leads to pouch failure.

T. Øresland
Faculty of Medicine, University of Oslo,
Oslo, Norway

Department of GI Surgery, Akershus University
Hospital, 1438 Lørenskog, Norway
e-mail: tom.oresland@medisin.uio.no

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology,* European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_16

16.1 What Is the Etiology of Indeterminate Colitis?

The etiology of IBD is still unknown, although the understanding of the disease's mechanisms is increasing. The phenotypes of Crohn's disease are many, and there is a debate over whether there are several Crohn's disease genotypes. Disease distribution can change over time, and early onset (during childhood) Crohn's disease may progresses differently and more aggressively compared with late-onset disease [7, 8]. For ulcerative colitis, the extent and progression of inflammation differs widely between individuals, and there are also special cases with only left-sided colitis in combination with localized inflammation of the appendix or cecum. There are microscopic colitis types with collagen or lymphocyte infiltration of the submucosa. In some patients the diagnosis shifts between most of these diagnoses, in whom the long-term course is unpredictable.

It is generally accepted that IBD results from negative interplay involving the gut immune system;, the mucosal barrier, including the mucus layer; the environment represented by the gut bacteria and ingested nutrients; and finally the genome [9]. Notwithstanding the overwhelming volume of research in genetics during the past three decades, in clinical practice there has been few benefits for patients. Genome-wide array studies have identified more than 200 genes associated with IBD, the majority related to Crohn's disease but a good proportion also in ulcerative colitis; abnormalities in some genes are seen in both diseases [10, 11]. There are as yet no absolute connections between gene mutation and disease expression in an individual. The most obvious example of this is the *NOD2/Card15* gene in Crohn's disease; although it was initially thought to be highly associated with the disease, later studies showed that certain populations (e.g., in Scotland and Scandinavia) almost totally lack this gene [9, 12]. Thus it is no surprise that some patients have colitis with morphological findings that do not fit into current classification systems.

16.2 Can We Improve on Defining a Diagnosis?

The differential diagnosis for IBD is based not only on morphology – although the pathologist mostly has the last word. Clinical features, clinical course, macroscopic distribution on endoscopy, and the surgical specimen all have a bearing on the final diagnosis. Tables 16.1 and 16.2 summarize the clinical and morphological differences

Table 16.1 Macroscopic features used for the diagnosis of inflammatory bowel disease

	Ulcerative colitis	Crohn's disease
Localization within gastrointestinal tract	Especially colon and rectum	Whole gastrointestinal tract
Ileum	Not except in backwash ileitis	Often involved
Colon	Left > right	Right > left
Rectum	Commonly involved	Typically spared
Distribution within gastrointestinal tract	Diffuse (continuous)	Segmental (discontinuous)
Ulcers	Superficial ulcers	Aphthous ulcers; confluent, deep, linear ulcers
Pseudopolyps	Common	Uncommon
Skip lesions	Absent	Present
Cobblestone pattern	Absent	Present
Deep fissures	Absent, except in fulminant colitis	Present
Fistulae	Absent, except in fulminant colitis	Present
Mucosal atrophy	Marked	Minimal
Thickness of the wall	Normal	Increased
Fat wrapping	Absent	Present
Strictures	Uncommon	Present

From Ref. [13], reproduced with permission from Elsevier

Table 16.2 Microscopic features used for the diagnosis of inflammatory bowel disease

	Ulcerative colitis	Crohn's disease
Crypt architectural irregularity	Diffuse (continuous)	Focal (discontinuous)
Chronic inflammation	Diffuse (continuous); decreases proximally	Focal (discontinuous); variable
Patchiness	Uncommon	Common
Localization	Superficial Transmucosal Sometimes in submucosa	Transmural
Serositis	Absent, except in fulminant colitis	Present
Lymphoid aggregates	Frequent in mucosa, submucosa	Common, transmural
Granulomas	Absent, except with ruptured cysts	Present
Acute inflammation	Diffuse (continuous)	Focal (discontinuous)
Crypt epithelial polymorphs	Diffuse (continuous)	Diffuse (continuous)
Crypt abscesses	Common	Uncommon
Mucin depletion	Present, pronounced	Uncommon, mild
Neuronal hyperplasia	Rare	Common
Muscular hypertrophy	Absent	Present
Paneth cell metaplasia	Present	Uncommon
Pyloric gland metaplasia	Rare	Present

From Ref. [13], reproduced with permission from Elsevier

between a clear-cut diagnosis of ulcerative colitis and Crohn's colitis [13].

These tables illustrate that differentiating between ulcerative colitis and Crohn's disease is not always easy. It is obvious that few patients will fit exactly into this classification system, and there is no consensus on the number of features needed for one diagnosis or the other. Some pathologists also tend to subdivide indeterminate colitis into that which is more like ulcerative colitis and that which is more like Crohn's disease [14]. It is also recognized that indeterminate colitis more frequently occurs among children than adults [7, 15].

There has been some expectation that biological markers will aid in differentiating between the two diagnoses. Perinuclear antineutrophil cytoplasmic antibody is a marker for ulcerative colitis but is only present in approximately 60 % of cases and is not considered to be of value in the differential diagnosis. Other biological markers (e.g., anti–*Saccaromyces cerevisiae* antibody) are no better, and just as with genome studies they are not widely used clinical practice [16–18]. However, positive serology preoperatively may identify patients who are likely to develop pouchitis after an ileal pouch–anal anastomosis (IPAA) [19]. Good endoscopy with multiple biopsies from all levels of the colon and rectum, and the opinion of a skilled, dedicated IBD pathologist, is currently the best means of accurate diagnosis. This results in a small percentage of patients with indeterminate colitis; however, most eventually behave as having ulcerative colitis and only a few develop overt Crohn's disease [20]. A better understanding will determine whether indeterminate colitis is a separate pathological entity or simply a stage in the progression toward one of the classical IBD diagnoses.

16.3 Surgery in a Patients with Indeterminate Colitis

Several large series of restorative pouch surgery indicate that a diagnosis of indeterminate colitis is compatible with successful IPAA [21]. The risk of pouch failure is not substantially increased, but a tendency for more complications has been noted in some studies but not others [22]. A group from the Mayo Clinic initially reported a slightly higher

failure rate in patients with indeterminate colitis [23]; however, data from the Cleveland Clinic show no differences with respect to functional outcomes or complication rates [24]. The St. Mark's Hospital experience is that as long as indeterminate colitis does not have features favoring Crohn's disease, there are no differences in failure rates or functional outcomes [14]. Today, most surgeons would agree that – notwithstanding a slight uncertainty regarding an increased risk of pouch failure –advising patients with indeterminate colitis to consider having IPAA is justified [25]. In terms of risks for developing pouchitis and cancer, there seem to be no major differences compared with ulcerative colitis [26].

Yet a dilemma remains: operating on patients with IBD unclassified does not automatically infer that the pathologist's report will conclude a diagnosis of indeterminate colitis. The preoperative diagnosis is based on mucosal biopsies, whereas the colectomy specimen provides full-thickness material, and the diagnosis may turn out to be Crohn's disease. With this in mind, most surgeons recommend a staged procedure, with a colectomy and end ileostomy as the first step. This has the advantage of giving the pathologist a better basis for a definitive diagnosis. In the case of Crohn's colitis and a patient wishing for a restorative option, the indication for performing an ileorectal anastomosis is stronger, provided the rectum is reasonably healthy. Other alternatives include proctectomy and ileostomy, a continent ileostomy, and expectant, keeping the rectum under surveillance.

In indeterminate colitis the options of an ileorectal anastomosis or an IPAA must be thoroughly discussed with the patient based on several factors, which must be weighed against each other. The pathologist might be inclined toward one or another diagnosis. The rectum itself must be assessed as early as possible after colectomy; waiting too long often results in a diversion (exclusion) proctitis that can be difficult to distinguish from ongoing IBD. Proctitis of some severity, especially with signs of reduced rectal compliance, makes ileorectal anastomosis a less attractive or even impossible alternative. My practice is to recommend treatment with local rectal 5-aminosalicylic acid after colectomy – at least until a definite decision on a next step has been made. In ulcerative colitis, and hence more so in indeterminate colitis, an ileorectal anastomosis is an alternative to proctectomy and a pelvic pouch in select cases. The most obvious is female patients with a strong wish for childbearing; ileorectal anastomosis avoids pelvic dissection to minimize the risk of adhesions affecting the fallopian tubes [27, 28]. Some male patients also absolutely cannot accept even a minute risk of iatrogenic sexual dysfunction. In the elderly, the reduced overall surgical risk involved in an ileorectal anastomosis and the possible worse functional outcome after IPAA might lead patients to choose the rectum-sparing alternative.

The downside of ileorectal anastomosis is the need for continuous cancer surveillance and prophylactic medical treatment to minimize the risk of dysplasia and recurrent or worsening disease. This risk for patients with ulcerative colitis is estimated at a 50 % chance of retaining the rectum 10 years [29–31]. There are no such estimates for indeterminate colitis, but one might think that the prognosis is not worse. With IPAA, the risk of pouchitis is high, but it mostly responds well to treatment and is seldom a cause for pouch failure. There are no good data on the risk of pouchitis in those with indeterminate colitis.

The functional outcome after IPAA does not differ significantly from that of ileorectal anastomosis. The life-time failure rate for IPAA is about 15 %. The advantage is a cure for the disease and, in the absence of primary sclerosing cholangitis (PSC) and a history of dysplasia/cancer, there is no need for surveillance of a patient with an otherwise well-functioning pouch. Knowing that the risk of complications may be increased in patients with indeterminate colitis, the above-mentioned aspects should be discussed with each patient, who of course has the final say in this choice. However, the way information is presented to the patient has a tremendous impact on this decision, so the burden lies heavily on the surgeon to give up-to-date and unbiased information.

Another situation may represent a diagnostic dilemma: when the outcome of pouch surgery is

not as good as expected, with pelvic and/or perianal septic complications ending in difficult-to-treat fistulas and failure. In these situations, irrespective of whether the working diagnosis was ulcerative colitis or indeterminate colitis, there is a tendency to convert the diagnosis to Crohn's disease [32]. When something goes wrong, a surgeon wishes for an explanation – preferably something other than surgical failure. In a patient with a diagnosis of indeterminate colitis who then develops perianal disease, there is a tendency to amend the diagnosis to Crohn's disease; this is often readily supported by the pathologist. This may well be motivated and often correct; however, one should be aware of this potential bias because it may incorrectly increase the failure statistics for patients with IPAA and a final diagnosis of Crohn's disease, since many patients with similar disease features may not have complications and thus do not have their diagnosis reassigned as Crohn's disease.

References

1. Kent TH, Ammon RK, DenBesten L. Differentiation of ulcerative colitis and regional enteritis of colon. Arch Pathol. 1970;89(1):20–9.
2. Price AB. Overlap in the spectrum of non-specific inflammatory bowel disease – 'colitis indeterminate'. J Clin Pathol. 1978;31(6):567–77.
3. Geboes K, Colombel JF, Greenstein A, Jewell DP, Sandborn WJ, Vatn MH, et al. Indeterminate colitis: a review of the concept – what's in a name? Inflamm Bowel Dis. 2008;14(6):850–7.
4. Geboes K, Van Eyken P. Inflammatory bowel disease unclassified and indeterminate colitis: the role of the pathologist. J Clin Pathol. 2009;62(3):201–5.
5. Kock NG. Intra-abdominal "reservoir" in patients with permanent ileostomy. Preliminary observations on a procedure resulting in fecal "continence" in five ileostomy patients. Arch Surg. 1969;99(2):223–31.
6. Oresland T, Fasth S, Nordgren S, Hulten L. The clinical and functional outcome after restorative proctocolectomy. A prospective study in 100 patients. Int J Colorectal Dis. 1989;4(1):50–6.
7. Prenzel F, Uhlig HH. Frequency of indeterminate colitis in children and adults with IBD – a meta analysis. J Crohns Colitis. 2009;3(4):277–81.
8. Turner D, Travis SP, Griffiths AM, Ruemmele FM, Levine A, Benchimol EI, et al. Consensus for managing acute severe ulcerative colitis in children: a systematic review and joint statement from ECCO, ESPGHAN, and the Porto IBD Working Group of ESPGHAN. Am J Gastroenterol. 2011;106(4):574–88.
9. Cummings JR, Cooney RM, Clarke G, Beckly J, Geremia A, Pathan S, et al. The genetics of NOD-like receptors in Crohn's disease. Tissue Antigens. 2010;76(1):48–56.
10. Parkes M. The genetics universe of Crohn's disease and ulcerative colitis. Dig Dis. 2012;30 Suppl 1:78–81.
11. Doecke JD, Simms LA, Zhao ZZ, Huang N, Hanigan K, Krishnaprasad K, et al. Genetic susceptibility in IBD: overlap between ulcerative colitis and Crohn's disease. Inflamm Bowel Dis. 2013;19(2):240–5.
12. Van Limbergen J, Wilson DC, Satsangi J. The genetics of Crohn's disease. Annu Rev Genomics Hum Genet. 2009;10:89–116.
13. Magro F, Langner C, Driessen A, Ensari A, Geboes K, Mantzaris GJ, et al. European consensus on the histopathology of inflammatory bowel disease. J Crohns Colitis. 2013;7(10):827–51.
14. Tekkis PP, Heriot AG, Smith O, Smith JJ, Windsor AC, Nicholls RJ. Long-term outcomes of restorative proctocolectomy for Crohn's disease and indeterminate colitis. Colorectal Dis. 2005;7(3):218–23.
15. Romano C, Famiani A, Gallizzi R, Comito D, Ferrau V, Rossi P. Indeterminate colitis: a distinctive clinical pattern of inflammatory bowel disease in children. Pediatrics. 2008;122(6):e1278–81.
16. Mitchell PJ, Rabau MY, Haboubi NY. Indeterminate colitis. Tech Coloproctol. 2007;11(2):91–6.
17. Castillo S, Ramaiah B, Blum S, Remy P. The value of serologic markers in indeterminate colitis: a prospective follow-up study. Gastroenterology. 2003;125(3):999; author reply -1000.
18. Tremaine WJ. Is indeterminate colitis determinable? Curr Gastroenterol Rep. 2012;14(2):162–5.
19. Hui T, Landers C, Vasiliauskas E, Abreu M, Dubinsky M, Papadakis KA, et al. Serologic responses in indeterminate colitis patients before ileal pouch-anal anastomosis may determine those at risk for continuous pouch inflammation. Dis Colon Rectum. 2005;48(6):1254–62.
20. Burakoff R. Indeterminate colitis: clinical spectrum of disease. J Clin Gastroenterol. 2004;38(5 Suppl 1):S41–3.
21. Oresland T, Bemelman W, Sampietro G, Spinelli A, Windsor A, Tiret E, et al. European evidence based consensus on surgery for ulcerative colitis. J Crohn's Colitis. 2015;9(1):4–25.
22. Murrell ZA, Melmed GY, Ippoliti A, Vasiliauskas EA, Dubinsky M, Targan SR, et al. A prospective evaluation of the long-term outcome of ileal pouch-anal anastomosis in patients with inflammatory bowel disease-unclassified and indeterminate colitis. Dis Colon Rectum. 2009;52(5):872–8.
23. Yu CS, Pemberton JH, Larson D. Ileal pouch-anal anastomosis in patients with indeterminate colitis: long-term results. Dis Colon Rectum. 2000;43(11):1487–96.
24. Fazio VW, Kiran RP, Remzi FH, Coffey JC, Heneghan HM, Kirat HT, et al. Ileal pouch anal anastomosis:

analysis of outcome and quality of life in 3,707 patients. Ann Surg. 2013;257(4):679–85.
25. Wolff BG. Is ileoanal the proper operation for indeterminate colitis: the case for. Inflamm Bowel Dis. 2002;8(5):362–5; discussion 8–9.
26. Stewenius J, Adnerhill I, Anderson H, Ekelund GR, Floren CH, Fork FT, et al. Incidence of colorectal cancer and all cause mortality in non-selected patients with ulcerative colitis and indeterminate colitis in Malmo Sweden. Int J Colorectal Dis. 1995;10(2):117–22.
27. Oresland T, Palmblad S, Ellstrom M, Berndtsson I, Crona N, Hulten L. Gynaecological and sexual function related to anatomical changes in the female pelvis after restorative proctocolectomy. Int J Colorectal Dis. 1994;9(2):77–81.
28. Olsen KO, Juul S, Bulow S, Jarvinen HJ, Bakka A, Bjork J, et al. Female fecundity before and after operation for familial adenomatous polyposis. Br J Surg. 2003;90(2):227–31.
29. Leijonmarck CE, Lofberg R, Ost A, Hellers G. Long-term results of ileorectal anastomosis in ulcerative colitis in Stockholm County. Dis Colon Rectum. 1990;33(3):195–200.
30. Andersson P, Norblad R, Soderholm JD, Myrelid P. Ileorectal anastomosis in comparison with ileal pouch anal anastomosis in reconstructive surgery for ulcerative colitis – a single institution experience. J Crohns Colitis. 2014;8(7):582–9.
31. Borjesson L, Lundstam U, Oresland T, Brevinge H, Hulten L. The place for colectomy and ileorectal anastomosis: a valid surgical option for ulcerative colitis? Tech Coloproctol. 2006;10(3):237–41; discussion 41.
32. Delaney CP, Remzi FH, Gramlich T, Dadvand B, Fazio VW. Equivalent function, quality of life and pouch survival rates after ileal pouch-anal anastomosis for indeterminate and ulcerative colitis. Ann Surg. 2002;236(1):43–8.

Diverticular Disease

17

Christoph Holmer and Martin E. Kreis

17.1 Etiology

Common theories with respect to the development of diverticulosis focus on three areas: structural abnormalities of the colonic wall, disordered motility, and the role of dietary fiber. The colonic wall is weakest between the mesenteric and antimesenteric teniae, where the vasa recta penetrate the muscle. Microscopic studies have revealed muscle atrophy at these sites, which are naturally susceptible to herniation [1]. Diverticula often form at these areas of weakness, bulging through the circular muscle but rarely through the teniae.

In addition to structural changes in the colonic wall, altered colonic motility has been implicated in the development of diverticular disease. Contraction of the bowel wall subsequently causes locally increased intracolonic pressure, resulting in a functional obstruction. This segmentation creates a driving force that causes visible distension of the local diverticula [2]. The high pressures resulting from segmentation in turn lead to focal muscular atrophy and subsequent mucosal herniation [3]. Pulsion diverticula occur most frequently in the sigmoid colon because the lumen of the colon is the narrowest there, resulting in the generation of the highest pressures.

Diverticular disease has been considered a disease of Western civilization; a large body of evidence supports the role of diet, particularly low fiber content, in the pathogenesis of diverticular disease [4]. It has been proposed that such diets result in decreased fecal bulk; a narrowing of the colon and an increase in intraluminal pressure also occur in order to move the smaller fecal mass. By contrast, a high-fiber diet results in increased fecal bulk and is associated with improved intestinal transit time, which is an important element of healthy bowel function [4].

Additional factors such as physical activity, smoking, genetics, and nonsteroidal anti-inflammatory medications have also been linked to diverticular disease. The amount of physical activity and the risk of developing symptomatic diverticular disease are inversely related [4]. A relationship between smoking and the development of diverticular disease could not be demonstrated [5]. However, once patients develop diverticular disease, evidence suggests that smoking results in a higher susceptibility to complications [6].

The presence of diverticula in children and young adults with Marfan syndrome or Ehlers-Danlos syndrome, and the strong relationship

C. Holmer • M.E. Kreis (✉)
Department of General, Visceral and Vascular Surgery, Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12200 Berlin, Germany
e-mail: christoph.holmer@charite.de; martin.kreis@charite.de

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_17

between polycystic kidney disease and diverticular perforation, suggest a possible genetic relationship [7]. Evidence suggests that chronic use of nonsteroidal anti-inflammatory medications is almost twice as common among patients with diverticular disease as it is in healthy controls with no known colonic disease [8]. Nonsteroidal anti-inflammatory drug use may also increase the risk of complications of diverticulitis [9]. However, it has been shown that none of these factors alone can explain the development of diverticular disease [16].

- The common theories with respect to the development of diverticulosis focus on three areas: structural abnormalities of the colonic wall, disordered motility, and the role of dietary fiber.

17.2 Epidemiology

The incidence of colonic diverticular disease is remarkably dependent on a patient's age and nationality. Diverticular disease of the colon is common in developed nations; the highest prevalence is seen in the United States, Europe, and Australia [10]. The disorder is rare in rural Africa and Asia. Furthermore, westernized nations have high prevalences of left-sided diverticulosis. Right-sided diverticulosis, although rare among Western populations, is more common in Asia, where overall rates of diverticula are much lower. The presence of right-sided diverticula is considered a distinctly different disease from left-sided diverticulosis, and is thought to be largely the result of genetic predisposition.

Industrialization and development have been shown to increase rates of diverticulosis [16]. Within a given country, the incidence of colonic diverticula can vary among ethnic groups. Among Chinese inhabitants of Singapore, incidence was reported to be 0.14 cases per 1 million population per year, versus 5.41 cases among Europeans [11]. Urbanization within a country over time can also lead to an increase in the prevalence of diverticulosis. Results of series studying symptomatic diverticular disease in Africa showed a growing incidence in increasingly urbanized communities [12].

Rates of diverticulitis are also increasing. In Finland the incidence of diverticulitis has risen 50 % in the past two decades, largely because of reduced dietary fiber intake and an aging population [13].

The prevalence of diverticula in the colon increases substantially with age. Among those younger than age 30, only 1–2 % of patients have diverticulosis [14]. In early autopsy studies from the 1920s to the 1940s, the overall prevalence was reported as 2–10 % [15]. Prevalence increases to 50 % or even 66 % among patients older than 80 years [1]. Approximately 10–25 % of patients with diverticulosis will develop diverticulitis [16]. The prevalence is similar in both sexes.

- The incidence of colonic diverticular disease increases substantially with age.
- Westernized nations have high prevalences of left-sided diverticulosis, whereas right-sided diverticulosis is more common in Asia, where overall rates of diverticula are much lower.

17.3 Classification

Diverticular disease can be classified as asymptomatic diverticulosis, uncomplicated diverticulitis, complicated diverticulitis, recurrent symptomatic disease, and diverticular hemorrhage. Most patients with anatomic diverticulosis – around 75–80 % – will remain asymptomatic throughout their lifetime. Of the few who develop complications, diverticulitis – and its sequelae such as abscesses, fistulas, or obstruction – is the most usual manifestation, followed by diverticular hemorrhage. Treatment recommendations include conservative approaches with observation and dietary modifications, along with antibiotic treatment, abscess drainage, and surgery [17]. A differentiated treatment depends on disease stage. An exact, comprehensive, and applicable classification of the disease is a prerequisite before treatment. Despite its prevalence, a classification system for diverticular disease has yet to be

universally adopted. Since the traditional classification for perforated diverticulitis was put forward by Hinchey et al. [18] in 1978 (Table 17.1), several modifications and new grading systems have been presented to display a more contemporary overview of the disease. In the German literature, the Hansen and Stock classification has been mainly used since 1998. This classification accounts for asymptomatic diverticulosis and complicated diverticulitis in different stages, depending on the severity of the complications [19] (Table 17.2). These aspects make it probably the most useful classification in clinical practice. However, it has rarely been adopted in the international literature. The wide use of computed tomography (CT) initiated modifications to the Hinchey classification, but several new radiological classifications for diverticular disease were also developed. A publications on the role of CT in diverticular disease by Ambrosetti et al. [20] allocates diverticulitis into severe or moderate disease (Table 17.3). In this approach, CT guides physicians in the treatment of acute complications.

Unfortunately, these different classifications of diverticular disease have led to conflicting terminology in the current literature. Moreover, none of the classifications seem to sufficiently embrace the entire spectrum of the clinical presentation of the disease. A new classification of sigmoid diverticulitis corresponding to the German guidelines for diverticular disease classification (GGDDC) [17] (Table 17.4) was proposed at the end of 2013. This modern classification seems to form a sound basis for developing appropriate strategies to evaluate differentiated treatment.

Table 17.1 Hinchey classification

Stage	Description
I	Pericolic abscess or phlegmon
II	Pelvic, intra-abdominal, or retroperitoneal abscess
III	Generalized purulent peritonitis
IV	Generalized fecal peritonitis

Table 17.2 Hansen and Stock classification [19]

Stage	Description
0	Diverticulosis
I	Acute uncomplicated diverticulitis
II	Complicated diverticulitis
IIa	Peridiverticulitis, phlegmonous diverticulitis
IIb	Abscess diverticulitis, covered perforation, fistulation
IIc	Free perforation
III	Chronic recurrent diverticulitis

Table 17.3 Ambrosetti et al. classification [20]

Stage	CT findings
Moderate diverticulitis	Localized sigmoid wall thickening (<5 mm), pericolic fat stranding
Severe diverticulitis	Abscess, extraluminal air, extraluminal contrast

17.3.1 Asymptomatic Diverticulosis

Asymptomatic diverticular disease is frequently an incidental finding during the assessment of a patient for other reasons, such as routine screening

Table 17.4 German guidelines diverticular disease classification

Stage	Description
Typ 0	Asymptomatic diverticulosis
Typ 1	Uncomplicated diverticulitis
Typ 1a	Diverticulitis without peridiverticulitis
Typ 1b	Diverticulitis with phlegmone
Typ 2	Complicated diverticulitis
Typ 2a	Microabscess (<1 cm)
Typ 2b	Macroabscess
Typ 2c1	Purulent peritonitis
Typ 2c2	Fecal peritonitis
Typ 3	Chronic diverticular disease
Typ 3a	Symptomatic uncomplicated diverticular disease
Typ 3b	Recurrent diverticulitis without complications
Typ 3c	Recurrent diverticulitis with complications (stenosis, fistula)
Typ 4	Diverticular hemorrhage

for colon cancer. No treatment or follow-up needs to be offered to this large population.

17.3.2 Uncomplicated Diverticulitis

Acute diverticulitis is usually associated with signs and symptoms of active inflammation. Patients present with abdominal pain in the left lower quadrant or suprapubic region. Pain is generally exacerbated by eating and diminished upon defecation or the release of flatus, which suggests colonic wall tension caused by higher-than-normal intraluminal pressure. Assessment can indicate fullness or mild tenderness in the left lower quadrant. Laboratory findings show increased infection values (C-reactive protein, leukocytes). The morphologic correlate CT is bowel wall thickening (Fig. 17.1) or inflammatory infiltration of pericolic fat (Fig. 17.2). Patients with uncomplicated diverticulitis can usually be treated conservatively. Few patients develop subsequent attacks or complications that necessitate surgery [21, 22].

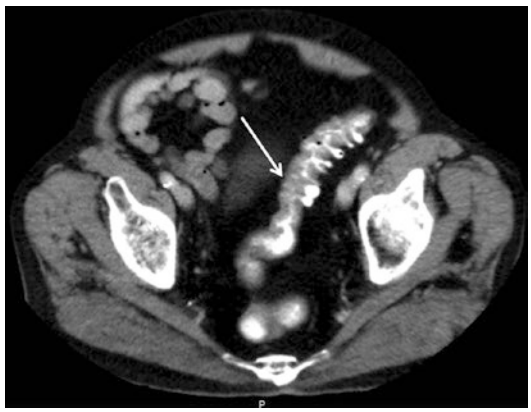


Fig. 17.1 Uncomplicated diverticulitis: bowel wall thickening (→)

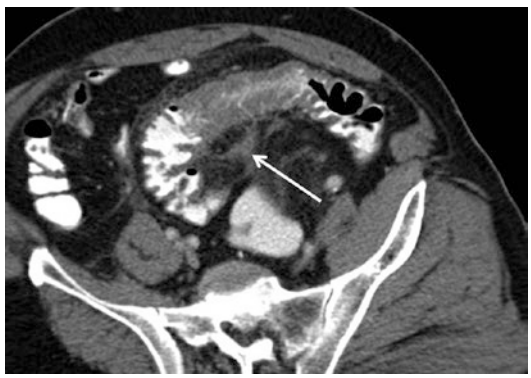


Fig. 17.2 Peridiverticulitis/Phlegmon (→)

17.3.3 Complicated Diverticulitis

In addition to the symptoms of uncomplicated diverticulitis, flank rebound or guarding may be detectable in patients with complicated diverticulitis. Generalized tenderness suggests a free colon perforation and peritonitis. Bacteria may breach the mucosa and extend the process through the full wall thickness, ultimately leading to perforation. The extent and localization of the perforation establish its clinical course. Microperforations can remain contained by pericolic fat and mesentery and may cause small pericolic abscesses. Large perforations can result in an extensive abscess, which could continue around the bowel wall and form a large inflammatory mass or extend to other organs. Free perforation into the peritoneum, causing frank peritonitis, can be life-threatening, but it is rare. The morphologic correlates on CT are mesocolic or retroperitoneal abscess (Fig. 17.3) or an abscess in the minor pelvis, or free air (Fig. 17.4) and/or fluid. Complicated diverticulitis usually requires elective surgical intervention. Patients who present with diffuse peritonitis or free perforation require emergency surgery.

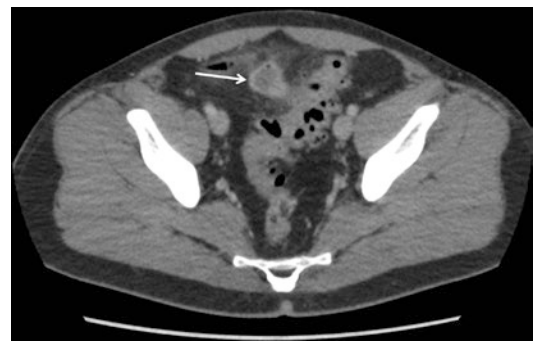


Fig. 17.3 Complicated diverticulitis with abscess (→)

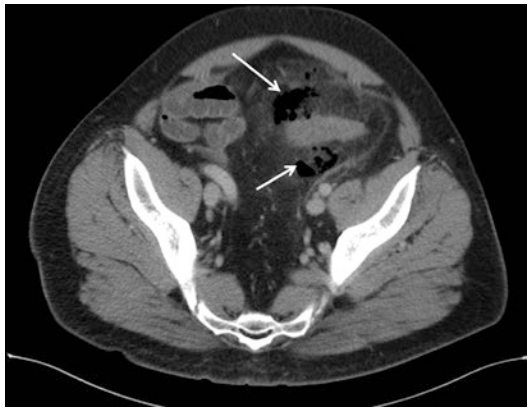


Fig. 17.4 Complicated diverticulitis with perforation (free air →)

17.3.4 Chronic Diverticular Disease

The clinical presentation of recurrent diverticular disease varies between mild and severe symptoms. The typical sign of chronic inflammation on CT is bowel wall thickening, sometimes with colonic stenoses or fistulas. However, multiple episodes of diverticulitis are not associated with increased mortality or an increased risk of complicated diverticulitis [21–23]. The potential risk of free perforation decreases with each previous episode of diverticulitis [23]. Therefore, recommending colectomy after the first episode of complicated diverticulitis is not justifiable based solely on the potential risk of free perforation. Greater consideration should be given to the clinical course, symptoms (e.g., pain), the risk of recurrence, and the patient's basic risk. The indications for operative intervention should be determined individually and with reference to the patient's respective characteristics (age, general condition, and number/frequency of episodes of diverticulitis). In the case of recurrent diverticulitis with complications, such as stenoses (Fig. 17.5) or fistulas (Fig. 17.6), a surgical treatment is usually necessary.

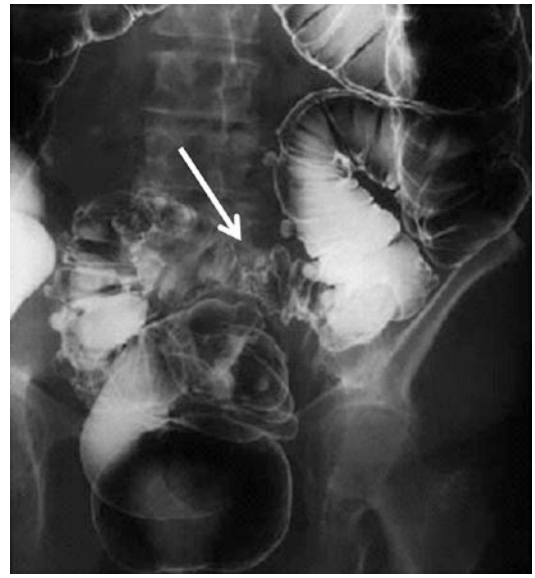


Fig. 17.5 Chronic recurrent diverticulitis with stenosis

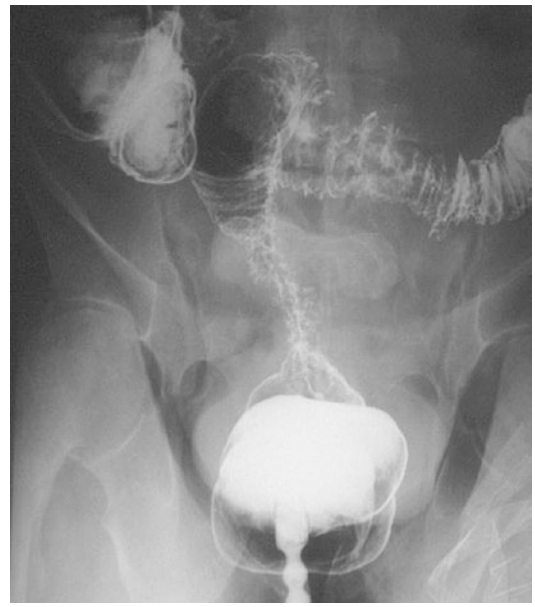


Fig. 17.6 Chronic recurrent diverticulitis with colovesical fistula

17.3.5 Diverticular Hemorrhage

Important lower gastrointestinal bleeding can be caused by diverticula, vascular ectasias, colitis, or neoplasms [24–26]. Diverticular sources have been reported to be the most typically identified cause, accounting for more than 40% of lower gastrointestinal bleeding episodes [27, 28]. Severe hemorrhage can occur in 3–5% of patients with diverticulosis [29, 30]. Despite the fact that most diverticula are in the left colon in individuals from

Western countries, the site of bleeding may more often be located in the proximal colon [31–34]. The clinical presentation of diverticular hemorrhage is usually one of an abrupt, painless onset. Hemorrhage ceases spontaneously in 70–80% of patients, and rebleeding rates range from 22 to 38% [29, 30]. The chance of a third bleeding episode can be as high as 50%, resulting in the frequent recommendation of surgical resection after a second bleeding episode [35]. The recommended initial diagnostic test is colonoscopy. If the bleeding source is identified by colonoscopy, endoscopic therapeutic maneuvers can be performed. If the bleeding source is not identified, further assessment with noninvasive (nuclear scintigraphy) or invasive (angiography) techniques can be undertaken in an attempt to localize and treat the bleeding source. Surgery in lower gastrointestinal bleeding is usually reserved until endoscopic or angiographic treatments fail. Segmental resection is most usually considered if the bleeding site is clearly identified from a therapeutically unsuccessful angiographic or endoscopic procedure. Subtotal colectomy may be required in patients with persistent bleeding and no angiographic or endoscopic identification of a definite bleeding site.

- Diverticular disease can be classified as asymptomatic diverticulosis, uncomplicated diverticulitis, complicated diverticulitis, recurrent symptomatic disease, and diverticular hemorrhage.
- Treatment recommendations include conservative approaches with observation and dietary modifications, as well as antibiotic treatment, abscess drainage, and surgery. A differentiated treatment depends on disease stage.
- A new classification of sigmoid diverticulitis corresponding to the GGDDC seems to sufficiently embrace the entire spectrum of the clinical presentation of the disease.

17.4 Diagnostics

17.4.1 Radiological Imaging

Radiological imaging techniques that are used in the diagnosis of acute diverticulitis are soluble contrast enemas, ultrasound, CT, and magnetic resonance imaging (MRI). Today, soluble contrast enemas are obsolete for diagnosing acute diverticulitis because of their low accuracy and the inability to determine the extent and complications of diverticular disease. The primary disadvantage of contrast enema examination in the evaluation of diverticulitis is that the inflammatory process is predominantly extramucosal. Therefore a contrast enema is often unsuccessful in delineating complications of acute diverticulitis and may underestimate the extent of pericolonic disease. Finally, and perhaps most important, a contrast enema has absolutely no role in the therapeutic intervention for diverticulitis.

Ultrasound is a real-time dynamic examination with wide availability and easy accessibility. Similar to CT, ultrasound is capable of evaluating the transmural involvement of diverticular disease using a ‚quick noninvasive technique that eliminates the need for intravenous or intraluminal contrast. In some European countries, ultrasound is routinely used as the initial imaging technique in patients clinically suspected of having acute colonic diverticulitis [36, 37]. However, the use of CT in the evaluation of patients with acute diverticular disease has greatly increased. CT has the advantage of delineating the extent of the extraluminal disease process, provides an unlimited view, and may also direct therapeutic intervention in the case of complicated disease (e.g., CT-guided percutaneous drainage of intra-abdominal abscesses).

The most widely used diagnostic criteria to determine acute diverticulitis with ultrasound and CT are increased thickness of the colonic wall, pericolic fat stranding, and the presence of inflamed diverticula. A high diagnostic sensitivity and specificity are reported for both ultrasound (92 and 90%, respectively) and CT (94 and 99%, respectively) [38, 39]. However, abdominal ultrasound is often limited by overlying gas that obscures the diseased segment and may produce false-negative results. This problem is accentuated by obesity and acute diverticulitis, where inflammation may cause a localized ileus in neighboring small-bowel segments. Disease in the distal sigmoid colon is also more difficult to assess because it can be poorly accessible to the ultrasound as a result of interference from the bladder and other

pelvic structures. Its main limitation lies in the operator variability inherent in ultrasonography compared with CT, in which subjective interpretation is much less problematic.

MRI has the advantage that no ionizing radiation or intravenous contrast medium is needed to achieve a higher soft-tissue contrast than CT. MRI produces quality images with subtle details superior to those from both CT and ultrasound [40, 41]. MRI does not require the intravenous, oral, and rectal contrast necessary for optimal CT scans. In addition, MRI is not limited by poor visualization caused by overlying gas and fat. However, the high cost and current limited availability of MRI do not make it feasible for routine use at this time. Furthermore, MRI takes significantly longer than CT and may not be acceptable for use in critically ill patients [40, 41].

In conclusion, CT should be the standard radiologic imaging technique for diagnosing acute diverticulitis. CT may be substituted by ultrasound under favorable conditions.

17.4.2 Colonoscopy

Colonoscopy is not recommended in the acute phase to diagnose acute diverticulitis because of the potential risk of converting a sealed perforation to a free perforation by insufflation of air [42, 43]. Colonoscopy should usually be done 4–6 weeks after an episode of acute diverticulitis in order to exclude a colonic malignancy.

- CT of the abdomen and pelvis is the most appropriate initial imaging modality in the assessment of suspected diverticulitis. It may be substituted by ultrasound under favorable conditions.
- Colonoscopy is not recommended in the acute phase to diagnose acute diverticulitis because of the potential risk of converting a sealed perforation to a free perforation by insufflation of air.

17.5 Treatment

Treatment recommendations include conservative approaches with observation and dietary modifications, as well as antibiotic treatment, abscess drainage, and surgery [17]. However, scientific evidence is scarce for some aspects of diverticulitis treatment, leading to treatment often being guided by a surgeon's personal preference. Many guidelines for the treatment of diverticular disease were developed to expand the evidence base for treatment, but no general guidelines exist. In addition to the above-mentioned GGDDC from 2013 [44], the 2014 practice parameters for the treatment of sigmoid diverticulitis from the American Society of Colon and Rectal Surgeons [45] should also be mentioned as recent guidelines. Their purpose is to provide information that decisions can be based on, rather than dictate a specific form of treatment. These guidelines should not be deemed inclusive of all proper methods of care or exclusive of methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of all the circumstances of the individual patient.

17.5.1 Medical Treatment

In the absence of complications and systemic signs and symptoms, patients with mild abdominal tenderness may be treated conservatively. Conservative treatment typically includes dietary modification and oral or intravenous antibiotics. This has been shown to be successful in 70–100 % of patients [46]. Uncomplicated diverticulitis may be managed in the outpatient setting with dietary modification and oral antibiotics for those without fever, excessive vomiting, or marked peritonitis, as long as follow-up is ensured. If these conditions are not met or the patient fails to improve with outpatient therapy, hospital admission is required. Antibiotics should be selected based on appropriate coverage for gram-negative and anaerobic bacteria [47]. Conservative treatment resolves acute diverticulitis in 85 % of patients [15]. After recovery from the first episode, fiber intake prevents recurrence in more than 70 % of patients [48]. Immunosuppressed or immunocompromised patients are more likely to present with perforation and fail medical treatment [49]. Approximately 15 % of patients

develop pericolonic or intramesenteric abscess [50]. Abscesses smaller than 2 cm in diameter may resolve with antibiotic treatment without any further intervention, whereas larger abscesses may require percutaneous drainage. This may prevent an emergency operation and multistaged surgeries involving the creation and closure of a stoma [50].

17.5.2 Surgical Treatment

Surgical treatment of the disease can be emergent or elective, depending on the stage of the disease and the clinical presentation. Intraoperative surgical options are based on the patient's status and the severity of intra-abdominal contamination [18] (Table 17.1). The desired surgical option is resection of the diseased segment with primary anastomosis, with or without intraoperative lavage or resection, and anastomosis with a temporary diverting ileostomy. In advanced stages of peritonitis, the Hartmann procedure (sigmoid colectomy, end colostomy, and closure of the rectal stump) is often performed, but it has been shown that the closure operation (Hartmann reversal) is not only technically challenging but also may be associated with significant postoperative morbidity and mortality [51]. Therefore, in an emergency situation because of free perforation, a primary anastomosis with a defunctioning ileostomy should be favored because the stoma reversal rate after primary anastomosis is higher than after the Hartmann procedure. The Hartmann procedure should be reserved for patients with perforated diverticulitis with severe septic complications. However, the final treatment decision – primary anastomosis or the Hartmann procedure – should depend on the patient's situation. It is also important that the decision be based not only on intraoperative findings or the extent of peritonitis, but rather on the patient's overall condition. Anastomotic healing may not occur in an unfit patient, even with mild inflammation, whereas patients with no or few comorbidities may fare well with primary anastomosis despite severe peritonitis [52].

A number of recent publications have discussed the use of laparoscopic peritoneal lavage and drainage for perforated sigmoid diverticulitis, as an alternative to resection [53, 54]. In the case of no localized diverticular bleeding, a subtotal colectomy should be performed if the diverticular bleeding site cannot be localized.

In this context, two prospective randomized studies from the Netherlands and Scandinavia are currently investigating the role of laparoscopic lavage with drainage for purulent and fecal peritonitis (Hinchey III and IV) compared with resection [55, 56]. Pending the results of these studies, laparoscopic lavage with drainage should be critically reviewed and subject to strict indications. According to the available datam the presence of fecal peritonitis or visible perforation is considered a contraindication for this procedure. Classical resection with abdominal lavage should also be performed if immunosuppression or septic disease is present.

The decision for elective colectomy after recovery from acute diverticulitis should be determined individually and with reference to the patient's characteristics (age, general condition, severity of diverticulitis, and number/frequency of episodes of diverticulitis). In the case of recurrent diverticulitis with complications, such as stenoses or fistulas, surgical treatment is usually necessary.

There are several important points regarding surgical technique. From a technical standpoint, the proximal margin of resection should be in an area of pliable colon without hypertrophy or inflammation. Resection of the diseased colon along with removal of the entire thickened colonic segment is the desired goal. With respect to the extent of resection required, according to current data it is not necessary to remove the entire colonic segment bearing diverticula because such a strategy does not reduce the recurrence rate. The splenic flexure should be mobilized when necessary to perform adequate resection and anastomosis.

- Depending on the severity of the inflammation, acute diverticulitis is treated conservatively or surgically.
- Laparoscopic sigmoid resection with restoration of continuity has been the prevailing modality for treating acute and recurrent sigmoid diverticulitis.
- The Hartmann procedure should be reserved

for perforated diverticulitis with severe septic complications.
- In the case of diverticular bleeding, a subtotal colectomy should be performed if the site of the diverticular bleeding cannot be localized.

17.6 Access

Laparoscopic sigmoid resection with restoration of continuity has been the prevailing modality for treating acute and recurrent sigmoid diverticulitis. The laparoscopic approach has advantages over open laparotomy, including less pain, smaller incisions, and shorter recovery. There is no increase in early and late complications [57, 58], and cost and outcome are comparable with those of open resection [59].

- The laparoscopic approach has advantages over open laparotomy, without increased complications.

17.7 Complications

17.7.1 Fistulas

When a diverticular phlegmon or abscess extends or ruptures into an adjacent organ, fistulas can arise, the most typical being colovesicular fistulas [60]. The incidence of colovesical fistulas in diverticular disease has been reported to range between 2 and 23 % [61, 62]. Such fistulas have a two-to-one male predominance, attributable to protection of the bladder by the uterus, and a 50 % rate of hysterectomy in female patients with colovesical fistulas. The underlying mechanism is the direct extension of a ruptured diverticulum or erosion of a peridiverticular abscess into the bladder. While sigmoid diverticulitis accounts for the underlying pathology in approximately two-thirds of patients, colovesical fistula has also been reported as a result of cancer of the colon or bladder, radiation therapy, or Crohn's disease [61, 63]. To date the diagnosis of colovesical fistula due to sigmoid diverticulitis remains a challenge, without a gold standard of treatment. Recurrent or persistent urinary tract infections, urinary frequency, dysuria, and hematuria are the most frequent clinical findings. These symptoms are unspecific, however, and thus diagnosis of colovesical fistula may be delayed. Pneumaturia and fecaluria are considered pathognomonic for colovesical fistulas, but these symptoms are not always present. Diagnostic procedures for colovesical fistulas are conducted to prove the existence of the fistula and to delineate the underlying etiology, as this determines further therapeutic strategy. Diagnostic tests and procedures range from the simple poppy seed test to the chromium nuclear study and the Bourne test to abdominal CT and MRI, cystoscopy, and colonoscopy [64–66]. Different from advanced cancer resection for colovesical fistula because of sigmoid diverticulitis, sigmoid segment resection and closure of the bladder defect is required for colovescial fistulas. In view of a spontaneous closure rate of only 2 % for colovesical fistulas [67, 68], and inflammatory complications in up to three-quarters of patients [69, 70], the existence of colovesical fistulas should be seen as an indication for surgery. Conservative or endoscopic procedures remain reserved for individual cases.

17.7.2 Stenosis

During an episode of acute diverticulitis, partial colonic stenosis can happen because of relative luminal narrowing from pericolic inflammation or compression from abscess formation. Colonic pseudo-obstruction can also occur. Acute diverticulitis might cause small-bowel obstruction or ileus if a loop of small intestine becomes incorporated into the inflammatory mass. These presentations usually improve as inflammation subsides with effective treatment; failure to do so should prompt surgical consultation.

Recurrent episodes of diverticulitis, sometimes subclinical, can initiate progressive fibrosis and colonic wall stricture without persisting inflammation. Ultimately, high-grade or complete stenosis can happen, requiring surgery. An insidious presentation with nonspecific symptoms is typical. The important issue is to distinguish between a

diverticular stricture and a stenosing neoplasm. A colonoscopy with biopsy should be done to make this differentiation, but this procedure is not always possible [71]. Stenoses in which malignant disease cannot be excluded should undergo surgical en bloc resection. Interventional and endoscopic procedures have had no significant importance in the treatment of inflammatory sigmoid stenosis [72].

17.7.3 Abscess

After perforation of a diverticulum, a localized phlegmon can develop; further spread may lead to the formation of large local or distant abscesses. When an abscess is suspected, CT is the best modality to ensure the diagnosis and to monitor the course of the disease. Small pericolic abscesses can generally be treated conservatively with continued antibiotics and bowel rest [73]. The size of the abscess seems to be an important indicator for the success of nonoperative management, especially when antibiotics alone are considered as the first-line treatment. An abscess diameter approximately 3–4 cm or less usually could be successfully managed by antibiotic treatment [74, 75]. For patients with distant or unresolving abscesses, drainage is indicated. Surgery used to be the main treatment option, but CT-guided percutaneous drainage of abdominal abscesses is now preferred when feasible. If feasible, percutaneous drainage of the abscess is successful in up to 90 % of patients.

- Ddiverticulitis can lead to serious complications such as fistula, stenosis, and abscess. In these cases, surgery is usually indicated.

17.8 Special Considerations

17.8.1 Diverticulitis in Young Patients

The indication for surgery in younger patients, generally defined as those who are 50 years old or younger, has been the subject of controversy. It has been reported that younger patients more frequently require surgery for diverticulitis [76] or are more prone to recurrent disease [77] than older patients. Based on the presumed association between younger age and more virulent disease, elective surgery has been recommended in patients younger than 50 years old after their first attack of uncomplicated diverticulitis [78]. However, other retrospective series did not confirm a correlation between younger age and more severe disease [79]. In addition, prospective data do not support an aggressive surgical approach for younger patients [80]. After stratification for the severity of disease, however, age was no longer a significant factor [81]. Based on current data, there is no sufficient justification to recommend elective surgery after one attack of sigmoid diverticulitis in younger patients; rather, the disease should be treated similarly in both younger and older patients, depending on its severity and inclination for recurrence.

- Diverticulitis should be treated similarly in both younger and older patients, depending on its severity and inclination to recurrence.

17.8.2 Diverticulitis in Immunocompromised Patients

Conditions that represent an immunocompromised state include severe infection, steroids, diabetes mellitus, renal failure, malignancy, cirrhosis, and chemotherapy or immunosuppressive therapy. Chronic use of steroids is also associated with increased postoperative mortality after surgery for diverticulitis [49]. Although the incidence of diverticulitis does not seem to be increased in this population, the complications and sequelae of the diverticulitis are more severe. This group of patients may lack a normal inflammatory response and present with minimal or subtle signs and symptoms, which may delay diagnosis and treatment. There is an increased rate of free perforation, increased need for surgery, and increased postoperative mortality [82, 83]. Therefore, it is generally recommended that surgery be offered to transplant

patients, immunocompromised patients, and patients under immunosuppression after their first documented episode of diverticulitis. The studies supporting this practice are generally retrospective, with small sample sizes [84]. On the other hand, there are no data presenting evidence against this practice.

- Surgery should generally be offered to immunocompromised patients after their first documented episode of diverticulitis because of an increased rate of morbidity and mortality.

17.8.3 Recurrent Diverticulitis After Resection

Recurrent diverticulitis after surgical treatment is rare, with an incidence ranging from 1 to 10 %. In general, the progression of diverticular disease in the remaining colon is approximately 15 % [85]. In such cases, the previous diagnosis and treatment can be questioned and investigated. An important factor to be considered in terms of surgery is the adequacy of resection, meaning the degree of proximal resection and the level of distal anastomosis [83, 86]. If the anastomosis is positioned in the rectum, the rate of recurrence is lower, than an anastomosis positioned above the rectum. Care also must be taken to exclude other components of differential diagnosis, especially irritable bowel syndrome, inflammatory bowel disease, and ischemic colitis.

- Recurrent diverticulitis after surgical treatment is rare. Care should be taken to exclude other components of differential diagnosis, especially irritable bowel syndrome, inflammatory bowel disease, and ischemic colitis.

17.8.4 Right-Sided Diverticulitis

Diverticulosis in Asia predominantly occurs on the right side. Diverticula of the right colon may be singular or multiple. In contrast to Asian populations, right-sided diverticulitis is a rare disease in Western countries. Right-sided diverticulitis occurs in approximately 1–3.6 % of all patients suffering from colonic diverticular disease [87, 88]. It presents with symptoms similar to those of acute appendicitis. Thus right-sided diverticulitis remains a diagnostic dilemma. An abdominal mass is usually found in 26–88 % of cases [89, 90]. Analogous to the surgical treatment of left-sided diverticulitis, complicated stages (abscess, phlegmone, perforation) are treated surgically, and primary resection should be given preference over limited operations without resection of the inflamed segment.

- In contrast to Asian populations, right-sided diverticulitis is a rare disease in Western countries.
- Analogous to the surgical treatment of left-sided diverticulitis, complicated stages of right-sided diverticulitis (abscess, phlegmone, perforation) are treated surgically.

References

1. Hughes LE. Postmortem survey of divericular disease of the colon. Gut. 1969;10:336.
2. Morson BC. The muscle abnormality in diverticular disease of the colon. Proc R Soc Med. 1963;56:798–800.
3. Chia JG, Wilde CC, Ngoi SS, Goh PM, Ong CL. Trends of diverticular disease of the large bowel in a newly developed country. Dis Colon Rectum. 1991;34:498–501.
4. Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Trichopoulos DV, Willett WC. A prospective study of diet and the risk of symptomatic diverticular disease in men. Am J Clin Nutr. 1994;60(5):757–64.
5. Aldoori WH, Giovannuci EL, Rimm EB, Wing AL, Trichopoulos DV, Willett WC. A prospective study of alcohol, smoking, caffeine and the risk of symptomatic diverticular disease in men. Ann Epidemiol. 1995;5:221–8.
6. Papagrigoriadis S, Macey L, Bourantas N, Rennie JA. Smoking may be associated with complications in diverticular disease. Br J Surg. 1999;86:923–6.
7. Sharp CK, Zeligman BE, Johnson AM, Duley I, Gabow PA. Evaluation of colonic diverticular disease in autosomal dominant polycystic kidney disease without end-stage renal disease. Am J Kidney Dis. 1999;34(5):863–8.
8. Goh H, Bourne R. Non-steroidal anti-inflammatory drugs and perforated diverticular disease: a case-control study. Ann R Coll Surg Engl. 2002;84:93–6.
9. Wilson RG, Smith AN, Macintyre IM. Complications of diverticular disease and non-steroidal anti-inflammatory drugs: a prospective study. Br J Surg. 1990;77:1103–4.

10. Painter NS, Burkitt DP. Diverticular disease of the colon: a deficiency disease of Western civilization. BMJ. 1971;2:450–4.
11. Kyle J, Adesola A, Tinckler L, de Beaux J. Incidence of diverticulitis. Scand J Gastroenterol. 1967;2:77–80.
12. Ogunbiyi OA. Diverticular disease of the colon in Ibadan, Nigeria. Afr J Med Med Sci. 1989;18:241–4.
13. Makela J, Kiviniemi H, Laitinen S. Prevalence of perforated sigmoid diverticulitis is increasing. Dis Colon Rectum. 2002;45(7):955–61.
14. Parks TG. Natural history of diverticular disease of the colon. A review of 521 cases. BMJ. 1969;4(5684):639–42.
15. Stollman N, Raskin JB. Diverticular disease of the colon. Lancet. 2004;363(9409):631–9.
16. Hobson KG, Roberts PL. Etiology and pathophysiology of diverticular disease. Clin Colon Rectal Surg. 2004;17:147–53.
17. Lembcke B. Diverticular disease – diagnosis and classification. Chirurg. 2014;85:289–98.
18. Hinchey EJ, Schaal PG, Richards GK. Treatment of perforated diverticular disease of the colon. Adv Surg. 1978;12:85–109.
19. Hansen O, Graupe F, Stock W. Prognostic factors in perforating diverticulitis of the large intestine. Chirurg. 1998;69:443–9.
20. Ambrosetti P, Becker C, Terrier F. Colonic diverticulitis: impact of imaging on surgical management – a prospective study of 542 patients. Eur Radiol. 2002;12:1145–9.
21. Mueller MH, Glatzle J, Kasparek MS, Becker HD, Jehle EC, Zittel TT, Kreis ME. Long-term outcome of conservative treatment in patients with diverticulitis of the sigmoid colon. Eur J Gastroenterol Hepatol. 2005;17(6):649–54.
22. Holmer C, Lehmann KS, Engelmann S, Gröne J, Buhr HJ, Ritz JP. Long-term outcome after conservative and surgical treatment of acute sigmoid diverticulitis. Langenbecks Arch Surg. 2011;396(6):825–32.
23. Ritz JP, Lehmann KS, Frericks B, Stroux A, Buhr HJ, Holmer C. Outcome of patients with acute sigmoid diverticulitis: multivariate analysis of risk factors for free perforation. Surgery. 2011;149(5):606–13.
24. Potter GD, Sellin JH. Lower gastrointestinal bleeding. Gastroenterol Clin N Am. 1988;17:341–56.
25. Boley SJ, DiBiase A, Brandt LJ, Sammartano RJ. Lower intestinal bleeding in the elderly. Am J Surg. 1979;137:57–64.
26. Gostout CJ, Wang KK, Ahlquist DA, et al. Acute gastrointestinal bleeding: experience of a specialized management team. J Clin Gastroenterol. 1992;14:260–7.
27. Peura DA, Lanza FL, Gostout CJ, Foutch PG. The American College of Gastroenterology bleeding registry: preliminary findings. Am J Gastroenterol. 1997;92:924–8.
28. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92:419–24.
29. McGuire Jr HH, Haynes Jr BW. Massive hemorrhage for diverticulosis of the colon: guidelines for therapy based on bleeding patterns observed in fifty cases. Ann Surg. 1972;175:847–55.
30. Zuckerman GR, Prakash C. Acute lower intestinal bleeding: part II – etiology, therapy, and outcomes. Gastrointest Endosc. 1999;49:228–38.
31. Meyers MA, Alonso DR, Gray GF, Baer JW. Pathogenesis of bleeding colonic diverticulosis. Gastroenterology. 1976;71:577–83.
32. Casarella WJ, Kanter IE, Seaman WB. Right-sided colonic diverticula as a cause of acute rectal hemorrhage. N Engl J Med. 1972;286:450–3.
33. McGuire Jr HH. Bleeding colonic diverticula: a reappraisal of natural history and management. Ann Surg. 1994;220:653–6.
34. Wong SK, Ho YH, Leong AP, Seow-Choen F. Clinical behavior of complicated right-sided and left-sided diverticulosis. Dis Colon Rectum. 1997;40:344–8.
35. Stollman NH, Raskin JB. Diagnosis and management of diverticular disease of the colon in adults: ad hoc practice parameters committee of the American College of Gastroenterology. Am J Gastroenterol. 1999;94:3110–21.
36. Schwerk WB, Schwarz S, Rothmund M. Sonography in acute colonic diverticulitis. A prospective study. Dis Colon Rectum. 1992;35(11):1077–84.
37. Hollerweger A, Rettenbacher T, Macheiner P, Brunner W, Gritzmann N. Sigmoid diverticulitis: value of transrectal sonography in addition to transabdominal sonography. AJR Am J Roentgenol. 2000;175:1155–60.
38. Laméris W, van Randen A, Bipat S, Bossuyt PM, Boermeester MA, Stoker J. Graded compression ultrasonography and computed tomography in acute colonic diverticulitis: meta-analysis of test accuracy. Eur Radiol. 2008;18:2498–511.
39. Liljegren G, Chabok A, Wickbom M, Smedh K, Nilsson K. Acute colonic diverticulitis: a systematic review of diagnostic accuracy. Colorectal Dis. 2007;9:480–8.
40. Sarma D, Longo WE, NDSG. Diagnostic imaging for diverticulitis. J Clin Gastroenterol. 2008;42(10):1139–41.
41. Heverhagen JT, Sitter H, Zielke A, Klose KJ. Prospective evaluation of the value of magnetic resonance imaging in suspected acute sigmoid diverticulitis. Dis Colon Rectum. 2008;51(12):1810–5.
42. Hale WB, NDSG. Colonoscopy in the diagnosis and management of diverticular disease. J Clin Gastroenterol. 2008;42:1142–4.
43. Crispin A, Birkner B, Munte A, Nusko G, Mansmann U. Process quality and incidence of acute complications in a series of more than 230,000 outpatient colonoscopies. Endoscopy. 2009;41:1018–25.
44. Kruis W, Germer CT, Leifeld L. Diverticular disease: guidelines of the German society for gastroenterology, digestive and metabolic diseases and the German society for general and visceral surgery. Digestion. 2014;90(3):190–207.
45. Feingold D, Steele SR, Lee S, Kaiser A, Boushey R, Buie WD, Rafferty JF. Practice parameters for the

treatment of sigmoid diverticulitis. Dis Colon Rectum. 2014;57(3):284–94.
46. Janes S, Meagher A, Frizelle A. Elective surgery after diverticulitis. Br J Surg. 2005;92:133–42.
47. Ambrosetti P, Jenny A, Becker C, et al. Acute left colonic diverticulitis – compared performance of computed tomography and water-soluble contrast enema: prospective evaluation of 420 patients. Dis Colon Rectum. 2000;43:1363–7.
48. Painter NS. Diverticular disease of the colon. The first of the Western diseases shown to be due to deficiency of dietary fiber. S Afr Med J. 1982;61:1016–20.
49. Chapman J, Davies M, Wolff B, et al. Complicated diverticulitis: is it time to rethink the rules? Ann Surg. 2005;242:576–83.
50. Ambrosetti P, Chautems P, Soravia C, et al. Long-term outcome of mesocolic and pelvic diverticular abscesses of the left colon: a prospective study of 73 cases. Dis Colon Rectum. 2005;48:787–91.
51. Aydin HN, Remzi FH, Tekkis PP, et al. Hartmann's reversal is associated with high postoperative adverse events. Dis Colon Rectum. 2005;48:2117–26.
52. Mueller MH, Karpitschka M, Renz B, Kleespies A, Kasparek MS, Jauch KW, Kreis ME. Co-morbidity and postsurgical outcome in patients with perforated sigmoid diverticulitis. Int J Colorectal Dis. 2011; 26(2):227–34.
53. Myers E, Hurley M, O'Sullivan GC, Kavanagh D, Wilson I, Winter DC. Laparoscopic peritoneal lavage for generalized peritonitis due to perforated diverticulitis. Br J Surg. 2008;95(1):97–101.
54. Toorenvliet B, Swank H, Schoones JW, Hamming JF, Bemelman WA. Laparoscopic peritoneal lavage for perforated colonic diverticulitis: a systematic review. Colorectal Dis. 2010;12:862–7.
55. Swank HA, Vermeulen J, Lange JF, et al. The LADIES trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with primary anastomosis for purulent or faecal peritonitis in perforated diverticulitis (NTR2037). BMC Surg. 2010;10:29.
56. Thornell A, Angenete E, Gonzales E, Heath J, Jess P, Lackberg Z, Ovesen H, Rosenberg J, Skullman S, Haglind E, Scandinavian Surgical Outcomes Research Group, SSORG. Treatment of acute diverticulitis laparoscopic lavage vs. resection (DILALA): study protocol for a randomised controlled trial. Trials. 2011;12:186.
57. Klarenbeek BR, Veenhof AA, Bergamaschi R, van der Peet DL, van den Broek WT, de Lange ES, Bemelman WA, Heres P, Lacy AM, Engel AF, Cuesta MA. Laparoscopic sigmoid resection for diverticulitis decreases major morbidity rates: a randomized control trial: short-term results of the Sigma trial. Ann Surg. 2009;249(1):39–44.
58. Gervaz P, Inan I, Perneger T, Schiffer E, Morel P. A prospective, randomized, single-blind comparison of laparoscopic versus open sigmoid colectomy for diverticulitis. Ann Surg. 2010;252(1):3–8.
59. Dwivedi A, Chahin F, Agrwal S, et al. Laparoscopic colectomy vs. open colectomy for sigmoid diverticular disease. Dis Colon Rectum. 2002;45:1309–14.
60. Woods RJ, Lavery IC, Fazio VW, Jagelman DG, Weakley FL. Internal fistulas in diverticular disease. Dis Colon Rectum. 1988;31:591–6.
61. Najjar SF, Jamal MK, Savas JF, et al. The spectrum of colovesical fistula and diagnostic paradigm. Am J Surg. 2004;188:617.
62. Solkar MH, Forshaw MJ, Sankararajah D, et al. Colovesical fistula – is a surgical approach always justified? Colorectal Dis. 2005;7:467.
63. Gruner JS, Sehon JK, Johnson LW. Diagnosis and management of enterovesical fistulas in patients with Crohn's disease. Am Surg. 2002;68:714–9.
64. Amendola MA, Agha FP, Dent TL, Amendola BE, Shirazi KK. Detection of occult colovesical fistula by the Bourne test. AJR Am J Roentgenol. 1984; 142:715–8.
65. Kwon EO, Armenakas NA, Scharf SC, Panagopoulos G, Fracchia JA. The poppy seed test for colovesical fistula: big bang, little bucks! J Urol. 2008; 179:1425–7.
66. Lippert MC, Teates CD, Howards SS. Detection of enteric-urinary fistulas with a noninvasive quantitative method. J Urol. 1984;132:1134–6.
67. Daniels IR, Bekdash B, Scott HJ, Marks CG, Donaldson DR. Diagnostic lessons learnt from a series of enterovesical fistulae. Colorectal Dis. 2002;4:459–62.
68. Hsieh JH, Chen WS, Jiang JK, Lin TC, Lin JK, Hsu H. Enterovesical fistula: 10 years experience. Clin Med J. 1997;59:283–8.
69. Kirsh GM, Hampel N, Shuck JM, Resnick MI. Diagnosis and management of vesicoenteric fistulas. Surg Gynecol Obstet. 1991;173:91–7.
70. Amin M, Nallinger R, Polk Jr HC. Conservative treatment of selected patients with colovesical fistula due to diverticulitis. Surg Gynecol Obstet. 1984;159:442–4.
71. Forde KA, Treat MR. Colonoscopy in the evaluation of strictures. Dis Colon Rectum. 1985;28:699–701.
72. Bertram P, Truong S, Schumpelick V. Sigmoid diverticulitis. Emergency intervention in abscess, hemorrhage and stenosis. Chirurg. 2002;73(7):675–80.
73. Wong WD, Wexner SD, Lowry A, et al. Practice parameters for the treatment of sigmoid diverticulitis: supporting documentation. Dis Colon Rectum. 2000;43:290–7.
74. Kumar RR, Kim JT, Haukoos JS, Macias LH, Dixon MR, Stamos MJ, Konyalian VR. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Dis Colon Rectum. 2006;49:183–9.
75. Siewert B, Tye G, Kruskal J, Sosna J, Opelka F, Raptopoulos V, Goldberg SN. Impact of CT-guided drainage in the treatment of diverticular abscesses: size matters. AJR Am J Roentgenol. 2006;186:680–6.
76. Pautrat K, Bretagnol F, Huten N, de Calan L. Acute diverticulitis in very young patients: a frequent surgical management. Dis Colon Rectum. 2007;50:472–7.

77. Lahat A, Menachem Y, Avidan B, Yanai H, Sakhnini E, Bardan E, Bar-Meir S. Diverticulitis in the young patient – is it different? World J Gastroenterol. 2006;12:2932–5.
78. Cunningham MA, Davis JW, Kaups KL. Medical versus surgical management of diverticulitis in patients under age 40. Am J Surg. 1997;174:733–5. discussion 735–736.
79. Ritz JP, Lehmann KS, Stroux A, Buhr HJ, Holmer C. Sigmoid diverticulitis in young patients – a more aggressive disease than in older patients? J Gastrointest Surg. 2011;15(4):667–74.
80. Guzzo J, Hyman N. Diverticulitis in young patients: is resection after a single attack always warranted? Dis Colon Rectum. 2004;47:1187–90.
81. Chautems RC, Ambrosetti P, Ludwig A, Mermillod B, Morel P, Soravia C. Long-term follow-up after first acute episode of sigmoid diverticulitis: is surgery mandatory?: a prospective study of 118 patients. Dis Colon Rectum. 2002;45:962–6.
82. Perkins JD, Shield CF, Chang FC, Farha GJ. Acute diverticulitis. Comparison of treatment in immunocompromised and nonimmunocompromised patients. Am J Surg. 1984;148:745–8.
83. Patient Care Committee of the Society for Surgery of the Alimentary Tract (SSAT). Surgical treatment of diverticulitis. J Gastrointest Surg. 1999;3:212–3.
84. Qasabian RA, Meagher AP, Lee R, Dore GJ, Keogh A. Severe diverticulitis after heart, lung, and heart-lung transplantation. J Heart Lung Transplant. 2004;23:845–9.
85. Thaler K, Baig MK, Berho M, et al. Determinants of recurrence after sigmoid resection for uncomplicated diverticulitis. Dis Colon Rectum. 2003;46:385–8.
86. Lo CY, Chu KW. Acute diverticulitis of the right colon. Am J Surg. 1996;171:244–6.
87. Flückiger R, Styger S, Huber A. Diverticulitis of the cecum and ascending colon. Chirurg. 1998;69:174–9.
88. Hildebrand P, Birth M, Bruch HP, Schwandner O. Surgical management of right-sided diverticulitis. Zent Bl Chir. 2005;130:123–7.
89. Eggimann T, Kung C, Klaiber C. Right-sided diverticulitis: new diagnostic and therapeutic aspects. Schweiz Med Wochenschr. 1997;127:1474–81.
90. Markham NI, Li AK. Diverticulitis of the right colon – experience from Hong Kong. Gut. 1992;33:547–9.

Other Colitides

18

Adam Dziki

18.1 Necrotizing Enterocolitis

18.1.1 Definition

Necrotizing enterocolitis (NEC) represents a significant clinical problem. Ischemic and necrotic alterations in the intestinal wall more frequently occur in the terminal ileum than in the cecum and ascending colon. The necrosis begins in the mucous layer and then may involve the full thickness of the bowel wall, resulting in perforation [1, 2].

18.1.2 Epidemiology/Etiology

NEC is the most common gastrointestinal emergency occurring in neonates (predominantly in preterm infants). About 8 % of babies with birth weights from 750 to 1,500 g show symptoms of NEC, but less than 10 % of neonates with the disease are born full term. The symptoms occur in episodic epidemics, and approximately 80 % of them occur within the first month of life – though almost never during the first days of life.

The real etiology of the condition is still unknown and is regarded as multifactorial. Only some predisposing factors have been established [3–5]. Prematurity is considered to be the most important risk factor, but hyaline membrane syndrome, infection, hyperosmolar formula feeding, a lack of breast milk, ischemia, and reperfusion injury also play essential roles. Non-breastfed newborns develop signs of NEC six times more frequently than babies naturally fed.

18.1.3 Symptoms

The clinical manifestations of NEC may be nonspecific. Symptoms develop after 10 days of life, in relation to the onset of artificial formula feeding. Initial symptoms include:

- Temperature instability
- Feeding intolerance, vomiting
- Abdominal distension and tenderness
- Decreased bowel movements and ileus

Symptoms in advanced stages include:

- Blood-streaked stools
- Abdominal wall erythema

As NEC progresses, systemic signs may develop: apnea, lethargy, and low peripheral perfusion with hypoxia, coagulopathy, and cardiorespiratory deterioration resulting in septic shock.

A. Dziki
Department of General and Colorectal Surgery,
University Hospital, Lodz, Poland
e-mail: adziki@wp.pl

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_18

Nonspecific laboratory test abnormalities include:

- Leukopenia or leukocytosis with a shift to the left
- Low platelet count
- Hypoglycemia
- Prolonged prothrombin time and activated partial thromboplastin time
- Decreased fibrinogen
- Severe metabolic acidosis

18.1.4 Complications

NEC can lead to death as a consequence of systemic septic shock. The survival rate is estimated at approximately 75 %, whereas 50 % of survivors may reveal long-term complications mainly as:

- Intestinal strictures (25–33 % incidence), the main location of which is the left side of the colon. Symptoms occur 2–3 weeks after recovery from the initial disease.
- Short-bowel syndrome, which is the result of surgical resections of excessive portions of absorption-related small bowel. Short-bowel syndrome can also lead to malnutrition.

18.1.5 Diagnosis

NEC is obviously diagnosed based on clinical manifestations, laboratory test results, and radiological findings:

- Abdominal radiography is the essential diagnostic imaging technique for neonates with signs of suspected NEC. An anteroposterior radiograph and left lateral decubitus image should be reviewed for all visible signs of the condition. Serial radiographs performed at 8-h intervals may help assess progression of the disease.
- Pneumatosis intestinalis is a pathognomonic marker of NEC. It comprises a characteristic layer of hydrogen gas corresponding with the submucosal layer of the bowel wall. Gas is generated by bacterial fermentation.
- Free intraperitoneal air is a sign of bowel perforation and is an obvious indication for emergency surgical intervention.

Radiography may reveal other signs of NEC, such as fixed and dilated loops, ascites, and portal vein gas [1].

Abdominal ultrasound also seems to be an effective and useful tool in assessing the progression of NEC. Ascites and portal vein gas can be easily observed in ultrasonograms.

18.1.6 Therapy

Conservative Treatment

If the diagnosis of NEC is well established, conservative treatment should be applied initially with nasogastric tube decompression, intravenous fluids, and adequate oxygenation. The administration of broad-spectrum antibiotic therapy is started, changing to more specific antibiotics according to bacteriological findings. Medical therapy is associated with an approximately 50 % success rate after about a week of continuous treatment.

Surgery

The absolute and obvious indication for surgery is intestinal perforation in the course of NEC, with free air on plain abdominal radiograph and full-thickness necrotic alterations of the bowel wall. The relative indications for surgery include worsened clinical manifestations, a decreased white blood cell count, and signs such as persistent fixed loops seem on repeated abdominal radiographs. Surgical procedures are also necessary when medical management fails. The essential concern in the surgical treatment of NEC is the preservation of as much of the intestine as possible.

18.1.7 Surgical Procedures

Procedure I

- The resection of altered parts of intestine with creation of a stoma is essential, especially in cases with symptoms of peritonitis.

- A "second look" operation should be performed after a 24-h interval to check for possible ischemic signs in the intestinal wall.
- Bowel resection with an anastomosis is associated with a high risk of anastomotic leak and stricture, and thus the procedure should be limited only to patients in a stable condition with minimal peritoneal contamination.
- Before elective stoma closure, a radiological contrast study has to be performed because of the relatively high risk of stricture.

Procedure II

- Bedside placement of peritoneal drains under local anaesthesia is a more recent approach to surgical treatment. The procedure helps stop the progression of sepsis.

18.1.8 Differential Diagnosis

Many conditions should be considered in the differential diagnosis of NEC:

- Enteroviral infections
- Candidiasis
- Hirschsprung disease
- Bacteremia
- Gastroesophageal reflux disease
- Hospital-acquired infection
- Neonatal sepsis of another origin

Spontaneous intestinal perforation – with the perforation seen on radiography – also occurs in premature babies but has none of the systemic signs usually present in NEC. The prognostic rate of NEC is higher than that of spontaneous intestinal perforation.

18.1.9 Prognosis

The survival rate of all treated babies reaches about 75 %, but the overall mortality of surgically treated patients ranges from 0 to 50 %.

18.2 Pseudomembranous Colitis

18.2.1 Synonyms

Pseudomembranous colitis (PMC) is also referred to as enterocolitis pseudomembranacea, antibiotic-associated colitis, necrotizing colitis, *Clostridium difficile* colitis, or *C. difficile* diarrhea.

18.2.2 Definition

PMC is an acute inflammatory disease of the colon. It is a commonly occurring complication after antibiotic exposure that may lead to serious morbidity, but it is usually treated easily.

18.2.3 Epidemiology/Etiology

- *C. difficile* was first implicated as a causative factor in the 1970s.
- *C. difficile*, a gram-positive, spore-forming, anaerobic bacillus, is isolated in almost all cases.
- *C. difficile* is an unusual component of healthy bowel flora and is found in only 3–5 % of healthy adults.
- The antibiotic-induced change in the balance of normal flora allows overgrowth of *C. difficile*. The bacteria release a powerful toxin that causes an inflammatory reaction and symptoms. The most important toxins are:
  - Toxin A: enterotoxin (causes diarrhea)
  - Toxin B: cytotoxin
- The incidence is 1 in 1,000.
- Almost any antibiotic can cause PMC. Clindamycin, lincomycin, ampicillin, and cephalosporins have been implicated in most of the reported cases.
- PMC complicates 10 % of cases of antibiotic-associated diarrhea [6–8].
- The low incidence of colitis in the pediatric population is attributed to the strength of children's immune systems or protective antibodies received from the mother.
- PMC has various risk factors:
  - Advanced age
  - Chemotherapy

- Antibiotic therapy
- Recent surgery
- Treatment in an intensive care unit
- Presence of cancer, uremia, or burns
- History of PMC

18.2.4 Symptoms

- Diarrhea
- Leukocytosis (50–60 % of patients)
- Fever (30–50 % of patients)
- Abdominal pain or cramping (20–33 % of patients)
- Bloody, mucoid, green, foul-smelling stools
- Urge to defecate
- Others: dehydration, electrolyte disturbances, nausea, vomiting, malaise, anorexia, hypoalbuminemia, anasarca

In most cases, symptoms begin 3–9 days after starting antibiotics. However, symptoms may begin a few weeks after antibiotics are discontinued [9, 10].

Rare extraintestinal manifestations occur in PMC:

- Bacteremia
- Splenic abscess
- Osteomyelitis
- Reactive arthritis or tenosynovitis

18.2.5 Complications

- Dehydration with electrolyte imbalance and hypovolemic shock
- Hemorrhage and sepsis
- Perforation of the colon
- Toxic megacolon
- Recurrent colitis and diarrhea

18.2.6 Diagnosis

- Signs of dehydration include dry skin, dry mouth, glassy appearance of the eyes, sunken fontanelles (in infants), rapid pulse, low blood pressure, confusion, excessive tiredness.
- Signs of toxic megacolon include fever, vomiting, and ileus.
- Signs of perforation include a rigid abdomen and rebound tenderness.

Additional/Useful Diagnostic Procedures

Laboratory Studies

- Complete blood count: Leukocytosis, with white blood cell count varying from 10,000 to 50,000 cells/mL.
- Blood chemistry: Hypoalbuminemia is common.
- Fecal leukocytes: Positive tests for fecal leukocytes, three to five leukocytes per high-powered field, excludes benign diarrhea.
- A stool culture positive for *C. difficile* toxin does not differentiate between toxic and nontoxic.
- Stool assay for *C. difficile* toxins (mostly toxin B) has a sensitivity of 95 %. This test requires 2 days.
- Enzyme-linked immunosorbent assay for toxin A has a sensitivity of 75–85 % and is completed in 2.5 h.
- Latex agglutination test has poor sensitivity and specificity.
- Polymerase chain reaction is used to detect the gene sequences of toxins A and B in the stool. It is a fast, sensitive, and specific diagnostic method, but it is also expensive and still is not available commercially.

Imaging Studies

Endoscopy

- It is the most rapid and definitive diagnostic method.
- The mucosa of the colon is often covered with loosely adherent nodular or diffuse exudates. These raised exudative plaques are 2–5 mm in size. Coalescence of these plaques generates an endoscopic appearance of yellowish pseudomembranes lining the colonic mucosa. When the pseudomembranes are manipulated, ulcerated mucosa is uncovered.

- Rigid proctosigmoidoscopy is diagnostic in 77 % of patients.
- Flexible sigmoidoscopy is diagnostic in 91 % of patients.
- Colonoscopy may be required in 10 % of cases where the disease is localized in the cecum or transverse colon, sparing the rectum.
- It is a hazardous procedure in patients with toxic megacolon.

Plain Abdominal Radiography

- It is useful for ruling out toxic megacolon or colonic perforation.
- An ileus pattern was described in 28 % of patients.
- Small-bowel dilation or air–fluid levels may be present.
- Dilated colon (>7 cm at the largest diameter) can be visualized.

Computed Tomography

- Computed tomography may show distension and diffuse, focal thickening of the wall of the colon, along with pericolonic inflammation.

Histological Findings

- On microscopic examination of the biopsy sample, the earliest sign is focal necrosis of the surface epithelial cells in the glandular areas, plugging of capillaries in the lamina propria, and mucus hypersecretion in adjacent crypts.
- As the disease progresses, necrosis and denudation of the mucosa occurs with thrombosis. Inflammation tends to remain superficial.

18.2.7 Therapy

Conservative Treatment

General Measures

- The antibiotic causing the condition should be stopped.
- Rehydration with electrolyte solutions or intravenous therapy should be started to replace fluids lost through diarrhea.
- Most patients – 75 % symptomatic and 25 % with colitis – will experience complete recovery within 10 days.
- In fulminant or intractable cases, hospitalization is necessary.
- Oral treatment with an antimicrobial agent effective against *C. difficile* is the preferred treatment:
  - Metronidazole is the first-line therapy for PMC, with a response rate of 86–92 %. An oral dosage of 250 mg once daily for 7–10 days is recommended. It is not recommended for children or for pregnant women.
  - Vancomycin is the most reliable treatment for the disease, with a response rate of 90–100 %. The recommended dosage is 125 mg every 6 h for 7–14 days for adults, and 500 mg/1.73 m^2 every 6 h for infants.
  - Second-line agents include oral bacitracin (500–1,000 mg once daily for 7–19 days) and teicoplanin (100 mg twice daily).
  - Newer therapies with fidaxomicin show promising results, with lower recurrence rates.

When parenteral therapy is the only possible treatment, the use of both vancomycin and metronidazole intravenously, supplemented by vancomycin 500 mg once daily via a nasogastric tube or enema, is recommended. Recurrences should be treated with vancomycin. Multiple recurrences should be treated with a long course of oral antibiotics (4–6 weeks).

Other Methods of Treatment

Fecal transplantation is gaining attention as a new method for the treatment of severe *C. difficile* infection with sepsis [11, 12]. Fecal microbiota transplantation from healthy donors is also considered an effective treatment against recurrent *C. difficile* infection and was found to be more effective than vancomycin [13].

Additional/Useful Therapeutic Measures

- Avoid narcotics; postoperative narcotics may play an antiperistaltic role.

- Antidiarrheal agents such as diphenoxylate hydrochloride and loperamide, may protract the disease by prolonging the mucosal exposure to bacterial toxins.
- Anion-exchange resin agents (e.g., cholestyramine, colestipol) eliminate toxins from the colonic lumen. The recommended oral dosage is 4 g once daily. It should not be used with vancomycin.
- In patients with multiple relapses, probiotics such as oral lactobacillus GG and *Saccharomyces boulardii* have been used to restore normal flora.
- A clear liquid diet should be administered until diarrhea resolves.

Surgical Treatment

- Surgery is required in rare cases to treat infections that worsen or do not respond to conservative treatment, or when there are any complications.
- Surgical therapy should be considered only as a lifesaving measure, such as in cases of perforation or toxic megacolon. Two-thirds of patients with megacolon require surgical intervention.
- The overall mortality rate for patients requiring surgery is reported to be as high as 30–35 %.
- Various approaches can be used:
  - Early subtotal colectomy
  - Colectomy
  - Colostomy or ileostomy
  - Resection of diseased bowel
- Surgery is required for fulminant toxic cases that do not respond after a week of intensive medical therapy because the risk of perforation increases after 7 days of ineffective conventional treatment [8].

18.2.8 Differential Diagnosis

- Staphylococcal enterocolitis and typhlitis
- Other bacterial colitis: salmonellosis, shigellosis, *Campylobacter*, *Escherichia coli*, *Yersinia* infection
- Amoebiasis
- Acute exacerbation of Crohn's disease and ulcerative colitis
- Ischemic colitis
- Chemical colitis
- Human immunodeficiency virus colitis

18.2.9 Prognosis

- The overall mortality rate is 2 %.
- The mortality rate in untreated elderly or debilitated patients is 10–20 %.
- The mortality rate in patients with toxic megacolon is 35 %.
- If there are no complications, the prognosis is generally good.
- Pseudomembranous colitis recurs in up to 20 % of cases.

18.2.10 Special Remarks

- Many patients remain asymptomatic carriers of *C. difficile*, and most of them never relapse.
- Some patients may develop PMC without a clearly identified causative agent.
- For prevention, use antibiotics prudently, wash hands, use examination gloves routinely, and clean potentially contaminated surfaces.
- In some cases (5–19 %) the disease is localized to the cecum and the proximal colon.

18.3 Ischemic Colitis

18.3.1 Definition

- Ischemic colitis is the most common ischemic injury of the gastrointestinal tract.
- It is one of the most common disorders of the large bowel in the elderly.
- This condition is occurring with increasing frequency.

18.3.2 Etiology/Epidemiology

- Atherosclerosis
- Shock
- Congestive heart failure

Ischemic colitis is also associated with aortoiliac surgery, with incidence ranging from 3 to 6 %. Various risk factors are connected with such operations:

- Patency of the inferior mesenteric artery
- Preoperative shock
- Intraoperative blood loss
- Previous pelvic radiation therapy

Most patients are elderly. In younger patients, the condition is associated with oral contraceptive use, vasculitis, and hypercoagulable states.

Some cases of ischemic colitis have been described in connection with mild allergy, hypertension, rectal prolapse, acute pancreatitis, sickle cell crisis, colon cancer, systemic lupus erythematosus, amyloidosis, anticardiolipin antibody syndrome, Buerger disease, Degos disease, and Kawasaki syndrome. Other case reports associate the development of ischemic colitis with the use of certain agents (progesterone, ergotamine derivatives, methamphetamine hydrochloride, nonsteroidal anti-inflammatory drugs, and danazol), intravenous vasopressin therapy, renal transplantation, chronic intermittent peritoneal dialysis, cocaine abuse, snake bite, and marathon running [14–16].

18.3.3 Symptoms

Clinical presentation is usually acute:

- Cramping abdominal pain
- Abdominal distension
- Bloody diarrhea
- Local signs of peritoneal irritation over the affected segment

Manifestations vary widely, from severe pain with transmural infarction and early perforation to mild abdominal pain and only slight tenderness. Colonic injury may consist of:

- Reversible colonopathy (35 %)
- Chronic ulcerating colitis (20 %)
- Transient colitis (15 %)
- Gangrene (15 %)
- Colonic stricture (10 %)
- Fulminant extensive colitis (<5 %)

More than two-thirds of patients with ischemic colitis respond quickly and favorably to simple conservative treatment. The most common outcome is spontaneous recovery within 24–48 h. The remaining patients require exploratory laparotomy without the benefit of an established preoperative diagnosis.

18.3.4 Complications

- Chronic ischemic colitis
- Gangrene resulting in perforation and peritonitis
- Stricture, which usually develops 3–4 weeks after the acute insult
- Inflammatory polyposis
- Pyocolon (pus collection within the colon)
- Toxic megacolon

Location and incidence vary:

Descending colon	37 %
Splenic flexure	33 %
Sigmoid colon	24 %
Transverse colon	9 %
Ascending colon	7 %
Rectum	3 %

18.3.5 Diagnostic Procedures

Laboratory Studies
Nonspecific laboratory testing includes a complete blood count, which shows a large number of leukocytes and an absence of other symptoms.

Radiography
Plain radiographic studies show:

- Mild, diffuse bowel dilatation
- Gasless abdomen
- Bowel wall thickening (a radiographic finding of "thumbprinting")
- "Sawtoothing" caused by multiple superficial ulcerations
- Tubular narrowing

Advanced ischemia or colonic infarction is associated with:

- Free air in the abdominal cavity
- Air within the bowel wall
- Air in the portal venous system

In contrast studies, barium must be used with caution because of the risk of perforation and subsequent severe barium peritonitis. The following are seen on contrast imaging:

- Thickening of the bowel wall
- Narrowing and spasm
- Ulcerations
- Eccentric deformity
- Sacculation
- Transverse ridging

Colonoscopy
Three endoscopic stages are recognized:

- Acute: petechiae, pale mucosa, hyperemia, and necrosis
- Subacute: ulceration and exudation
- Chronic: stricture, decreased haustration, and mucosal granularity

Some surgeons suggest that laparoscopy, rather than colonoscopy, should be used for the diagnosis and treatment of fulminant ischemic colitis.

Computed Tomography and Ultrasonography
These procedures may show irregular thickening of the submucosa or narrowing of the lumen. Color Doppler ultrasound has been used to differentiate the bowel wall thickening seen in ischemic colitis from that seen in inflammatory bowel disease. MRI, however, is used more often to confirm the diagnosis.

Angiography
- Angiography is not routinely used in ischemic colitis.
- It rarely shows significant vascular occlusions.
- It is limited to clinical situations in which ischemic colitis involves the ascending colon, such as acute thrombosis or embolism of the superior mesenteric artery.

18.3.6 Differential Diagnosis

- Crohn's disease
- Ulcerative colitis
- Colonic injury induced by nonsteroidal anti-inflammatory drug use
- Pseudomembranous colitis
- Infectious colitides
- Diverticular disease
- Carcinoma of the colon

18.3.7 Therapy

Ischemic colitis accounts for only a small percentage of colonic disease seen in medical and surgical offices. Most patients with ischemic colitis do not have peritoneal signs, which results in frequent misdiagnosis and a large underestimation of its incidence.

Conservative Treatment
Outpatient therapy is possible in patients with mild symptoms. Patients with abdominal pain and no evidence of peritonitis or systemic toxicity should be treated expectantly.

General Measures
- Conservative treatment includes intensive care and monitoring of vital signs.
- Patients must have frequent abdominal examinations.
- Intravenous hydration, bowel rest measures, and administration of wide-spectrum antibiotics that cover enteric flora are usually required.

Pharmaceutical Measures

- The use of pharmaceutical agents other than antibiotics should be avoided, particularly vasoconstricting drugs.
- The use of vasodilators such as glucagon and papaverine is controversial.
- The use of anticoagulants has not gained wide acceptance.
- The use of corticosteroids is contraindicated in patients with ischemic colitis because it can lead to silent colonic perforation.
- Patients usually respond to conservative measures within a few days to 2 weeks.
- Follow-up colonoscopy may be necessary to identify progression of the colonic injury or stricture formation.

Surgical Treatment

- Surgery is indicated in patients with peritonitis, transmural infarction or perforation of the colon, or bleeding from ulcerations.
- Surgical intervention may also be necessary in patients with chronic, segmental colitis or formation of stricture after ischemic injury.
- Before referring patients with stricture to surgery, forceful endoscopic balloon dilation can be attempted in those who are asymptomatic.
- Surgical intervention usually involves resection of the ischemic segment of the colon and exteriorization of the remaining ends of the bowel.
- Primary anastomosis and revascularization are contraindicated.

18.4 Infectious Colitis

18.4.1 Definition

Infectious colitis is one of the most common forms of colitis and is usually caused by bacterial, viral, and parasitic agents. It often occurs during childhood.

18.4.2 Etiology

- Bacterial: The most common bacterial agents responsible for infectious colitis are *E. coli* and species of *Shigella*, *Salmonella*, *Campylobacter*, and *Yersinia*.
- Parasitic: *Entamoeba histolytica* is the most common cause of parasitic colitis worldwide.
- Viral: Cytomegalovirus infection–induced colitis rarely occurs and is mainly found in immunocompromised patients [17, 18].

18.4.3 Symptoms

- *E. coli*–mediated colitis is characterized by diarrhea, abdominal cramps, and fever. It mostly affects children. A risk of hemolytic uremic syndrome and hemorrhagic colitis after infection with enterohemorrhagic *E. coli* strains is estimated to be present in 10–15% of children.
- *Shigella* infections range from asymptomatic ones to mild gastroenteritis to severe dysentery. Dysentery has a sudden onset and presents with high fever (39–40 °C), abdominal pains, and diarrhea. Stools are frequent (more than ten daily) and contain blood and mucus. Symptoms of central nervous system irritation can also be observed.
- *Salmonella* infections usually occur during summer and autumn, most commonly in children. They are characterized by a sudden onset within 8–48 h after ingestion of contaminated food. Patients present with abdominal cramps, nausea, and fever. Stools are watery and sometimes contain blood.
- Enteritis caused by *Campylobacter* is characterized by a sudden onset, fever (sometimes >40 °C), and abdominal pain, followed by diarrhea. Stools are watery and frequent (2–20 times daily), and usually contain blood.
- *Yersinia enterocolitica* infection presents with an abrupt onset of watery diarrhea containing blood. Patients complain of severe abdominal pain, joint pain, and skin eruption. A febrile response occurs in older children.
- Amoebiasis commonly manifests with bloody diarrhea, abdominal pain, and fever.

18.4.4 Complications

In cases of severe diarrhea and vomiting, one must take care of physical signs suggesting dehydration (e.g., dry mucous membranes, decreased skin turgor, orthostasis) and leading to dysregulation of the acid–base balance.

18.4.5 Diagnostic Procedures

Most infectious factors can be cultured from the stool using appropriate media. Gram and methylene blue staining of the stool is recommended. White blood cell counts can be elevated or normal. In many cases, no pathogen is identified, and diagnosis is established based on medical history and clinical symptoms. In typical infectious colitis, the lamina propria of the large intestine is infiltrated by polymorphonuclear leukocytes.

18.4.6 Therapy

Conservative Treatment

- Management of bacterial colitis depends on the clinical symptoms and the patient's general condition. It is always necessary to control the acid–base balance, and supplementation of fluids is required.
- In shigellosis, trimethoprim-sulfamethoxazole is the drug of choice; fluoroquinolones and ceftriaxone are alternatives.
- If *Salmonella* bacteremia is suspected, intravenous cefotaxime (200 mg/kg/day in four divided doses) or ceftriaxone (100 mg/kg/day in two divided doses) should be initiated. Alternative treatments include chloramphenicol (100 mg/kg/day in four divided doses) or, in adolescents, fluoroquinolones. Trimethoprim-sulfamethoxazole is the drug of choice when oral treatment is indicated.
- In *Y. enterocolitica* infection, antibiotic therapy with intravenous gentamicin (5–7.5 mg/kg/day in three divided doses) is indicated in patients with persistent diarrhea or suspected sepsis. Alternative antibiotics may include chloramphenicol, colistin, and kanamycin.
- *Campylobacter* enteritis is usually self-limited. Erythromycin or ciprofloxacin may be used.
- Treatment of amoebic colitis includes metronidazole and iodoquinol or paromomycin [19].

Surgical Treatment

Surgical intervention is indicated for patients who develop toxic megacolon with a subsequent risk of perforation or an existing perforation. The frequency of surgical intervention is low (0.39–3.6 % of cases).

18.5 Collagenous Colitis

18.5.1 Synonyms

Collagenous colitis (CC) is also called microscopic colitis.

18.5.2 Definition

CC, which was first described by Lindstrom in 1976, is a rare inflammatory disorder of the colon. Both CC and another disease, lymphocytic colitis, are also described as microscopic colitis. The disease causes prolonged watery diarrhea. It causes no changes in the endoscopic appearance of the colonic mucosa, but prominent, unique changes in the microscopic assessment of biopsies occur.

18.5.3 Epidemiology/Etiology

CC is recognized as a rare disease, although it has been increasingly diagnosed in the past 20 years. However, the true incidence is still not known. Surprisingly, a few epidemiological studies performed in Scandinavian countries showed a much higher incidence than was expected. In one the rate was similar to that of Crohn's disease. CC usually affects people older than 40 years and it is much more frequent in women than men.

Different aspects of causative agents have recently been discussed, although no definite etiology has been determined. It is supposedly an autoimmune disease. Infection and drugs (nonsteroidal anti-inflammatory drugs, ranitidine, and antidepressants) seem to be possible triggers of inflammation. The coincidence of CC with infections, celiac sprue, and the presence of increased number of mast cells suggests that a luminal agent plays a role in etiology [20, 21].

18.5.4 Symptoms

As mentioned earlier, CC typically presents with watery, nonbloody, high-volume diarrhea. It usually begins suddenly, with no prodromal symptoms. Usually the only symptom is diarrhea. Patients may pass up to 30 stools/day and lose more than 1,500 mL of fluid each day. Some complain of abdominal discomfort and a feeling of distension. Symptoms persist from a few weeks to years.

18.5.5 Complications

The most frequent complications of CC are caused by diarrhea. Malabsorption, dehydration, weight loss, and deficiencies (e.g. electrolytes) are among them.

18.5.6 Diagnostic Procedures

CC is diagnosed in cases of watery, nonbloody diarrhea lasting at least 3 weeks. There should be no changes in endoscopic appearance of the colon. Typical microscopic changes can be seen; these consist of:

- Thickening of the subepithelial collagen wall (>10 mm)
- Infiltration of intraepithelium with lymphocytes
- Mononuclear inflammatory cell infiltration into the lamina propria

One must remember that lymphocytic colitis is an entity with exactly the same symptoms as CC. The diagnosis is based on differences in pathological assessment [22–24].

Additional/Useful Diagnostic Procedures

Some procedures are helpful in diagnosing CC, including stool examination to identify parasites, ova, and other pathogens, and radiological assessment.

18.5.7 Therapy

Conservative Treatment

Because CC is a fairly rare disease, treatment is based on anecdotal evidence. So far, no standard or guidelines have been established for this condition. Antidiarrheal agents (loperamide, diphenoxylate, hydrochloride/atropine sulphate, bismuth subsalicylate) should be administered. These drugs are especially useful in mild cases of the disease. Cholestyramine (when symptoms of bile salt malabsorption appear) and hyoscyamine (when one of the main symptoms is cramping pain) may be helpful.

When the disease does not respond to antidiarrheal drugs, the next therapeutic step is drugs traditionally used to treat inflammatory bowel diseases: topical anti-inflammatory drugs (sulfasalazine, mesalazine) and corticosteroids (prednisone, budesonide). Finally, immunosuppressants (azathioprine, methotrexate) could be used.

Surgical Treatment

Surgery is usually unnecessary. In cases with no positive response to conventional therapy or intolerance to drugs, colectomy or ileostomy is the only choice.

18.5.8 Differential Diagnosis

Inflammatory bowel diseases must be considered (Crohn's disease and ulcerative colitis). One should consider irritable bowel syndrome, celiac sprue, giardiasis, and non-colon-specific diseases such as hyperthyroidism or laxative abuse.

18.5.9 Prognosis

According to anecdotal articles, only 15 % of patients continue to have major symptoms after 6 months of treatment, whereas half of them are totally free of symptoms after the same interval. Unfortunately, in some patients symptoms might come and go over many years.

References

1. Fagenholz PJ, de Moya MA. Acute inflammatory surgical disease. Surg Clin North Am. 2014;94(1):1–30. doi:10.1016/j.suc.2013.10.008.
2. Moldovan R, Vlad N, Curca G, Borcea M, Ferariu D, Dimofte G, Tarcoveanu E. Total necrotizing colitis proximal to obstructive left colon cancer: case report and literature review. Chirurgia (Bucur). 2013;108(3):396–9.
3. Bode L, Jantscher-Krenn E. Structure-function relationships of human milk oligosaccharides. Adv Nutr. 2012;3(3):383–91.
4. Sherid M, Ehrenpreis ED. Types of colitis based on histology. Dis Mon. 2011;57(9):457–89.
5. Andres LA, Ford RD, Wilcox RM. Necrotizing colitis caused by systemic aspergillosis in a burn patient. J Burn Care Res. 2007;28(6):918–21.
6. McDonald EG, Lee TC. Treatment for Clostridium difficile infection in adults. JAMA. 2015;313(19):1974–5.
7. Aldrete Sdel M, Magee MJ, Friedman-Moraco RJ, Chan AW, Banks GG, Burd EM, Kraft CS. Characteristics and antibiotic use associated with short-term risk of clostridium difficile infection among hospitalized patients. Am J Clin Pathol. 2015;143(6):895–900.
8. Bagdasarian N, Rao K, Malani PN. Diagnosis and treatment of Clostridium difficile in adults: a systematic review. JAMA. 2015;313(4):398–408.
9. Leffler DA, Lamont JT. Clostridium difficile infection. N Engl J Med. 2015;372(16):1539–48.
10. Farooq PD, Urrunaga NH, Tang DM, von Rosenvinge EC. Pseudomembranous colitis. Dis Mon. 2015;61(5):181–206.
11. Costello SP, Chung A, Andrews JM, Fraser RJ. Fecal microbiota transplant for Clostridium difficile colitis-induced toxic megacolon. Am J Gastroenterol. 2015; 110(5):775–7.
12. Marcos LA, Gersh A, Blanchard K, Foil S, Mallini B, Farrell SE, Kahler RJ. Fecal transplantation to treat initial severe Clostridium difficile infection with sepsis. Miss State Med Assoc. 2015;56(2):38–40.
13. Cammarota G, Masucci L, Ianiro G, Bibbò S, Dinoi G, Costamagna G, Sanguinetti M, Gasbarrini A. Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent Clostridium difficile infection. Aliment Pharmacol Ther. 2015;41(9):835–438.
14. FitzGerald JF, Hernandez Iii LO. Ischemic colitis. Clin Colon Rectal Surg. 2015;28(2):93–8.
15. Mosińska P, Fichna J. Ischemic colitis: current diagnosis and treatment. Curr Drug Targets. 2015;16(3):209–18.
16. Hines DM, McGuiness CB, Schlienger RG, Makin C. Incidence of ischemic colitis in treated, commercially insured hypertensive adults: a cohort study of US health claims data. Am J Cardiovasc Drugs. 2015;15(2):135–49.
17. Zollner-Schwetz I, Herzog KA, Feierl G, Leitner E, Schneditz G, Sprenger H, Prattes J, Petritsch W, Wenzl H, Kump P, Gorkiewicz G, Zechner E, Högenauer C. The toxin-producing Pathobiont Klebsiella oxytoca is not associated with flares of inflammatory bowel diseases. Dig Dis Sci. 2015;60:3393–8.
18. Horiki N, Furukawa K, Kitade T, Sakuno T, Katsurahara M, Harada T, Tano S, Yamada R, Hamada Y, Inoue H, Tanaka K, Gabazza EC, Ishii N, Fukuda K, Omata F, Fujita Y, Tachibana H, Takei Y. Endoscopic findings and lesion distribution in amebic colitis. J Infect Chemother. 2015;21(6):444–8.
19. Korman T. Diagnosis and management of Clostridium difficile infection. Semin Respir Crit Care Med. 2015;36(1):31–43.
20. Macaigne G. Microscopic colitis. Rev Prat. 2015; 65(3):307–11.
21. Bouma G, Münch A. Microscopic colitis. Dig Dis. 2015;33(2):208–14.
22. Plastaras L, Vuitton L, Badet N, Koch S, Di Martino V, Delabrousse E. Acute colitis: differential diagnosis using multidetector CT. Clin Radiol. 2015;70(3):262–9.
23. Assa A, Vong L, Pinnell LJ, Avitzur N, Johnson-Henry KC, Sherman PM. Vitamin D deficiency promotes epithelial barrier dysfunction and intestinal inflammation. J Infect Dis. 2014;210(8):1296–305.
24. Langner C, Aust D, Ensari A, Villanacci V, Becheanu G, Miehlke S, Geboes K, Münch A, Working Group of Digestive Diseases of the European Society of Pathology (ESP), European Microscopic Colitis Group (EMCG). Histology of microscopic colitis-review with a practical approach for pathologists. Histopathology. 2015;66(5):613–26.
25. Ohlsson B. New insights and challenges in microscopic colitis. Ther Adv Gastroenterol. 2015;8(1):37–47.
26. Farrukh A, Mayberry JF. Microscopic colitis: a review. Colorectal Dis. 2014;16(12):957–64.

Medical Treatment of Inflammatory Bowel Disease

19

Florian Poullenot and David Laharie

19.1 Introduction

With the biologic era that started in the early 2000s with anti–tumor necrosis factor (TNF) agents, the management of inflammatory bowel diseases (IBDs) has been dramatically modified. Recent new concepts and strategic studies have modified clinical practice with changes in the initial care, therapeutic adaptation, and follow-up of patients. Crohn's disease and ulcerative colitis are presented separately in this chapter.

19.2 Crohn's Disease

Aminosalicylates and corticosteroids have long been considered first-line medical therapies for Crohn's disease. Following a historical step-up approach, conventional immunosuppressants (thiopurines or methotrexate) and biologics were restricted for refractory diseases. The main characteristics of treatments used in IBD are summarized in Table 19.1.

F. Poullenot (✉) • D. Laharie, MD, PhD
Service d'Hépato Gastroentérologie, Hôpital Haut-Lévêque.CHU de Bordeaux,
1 av. de Magellan, 33604 Pessac, France
e-mail: florian.poullenot@chu-bordeaux.fr

19.2.1 New Concepts

19.2.1.1 Is There Still Room for First-Line Conventional Therapies (Aminosalicylates and Corticosteroids)?

The clinical benefit of 5-aminosalicylates in Crohn's disease is still under debate. A recent meta-analysis of mild to moderate Crohn's disease showed that its benefit was close to that of placebo [1]. In addition, indications for the use of 5-aminosalicylates' have been decreasing over time, even among patients with mild Crohn's disease [2] with few symptoms and an absence of risk factors for a complicated evolution. In the postoperative setting, 5-aminosalicylates could be given to prevent recurrence since they demonstrated mildly but significantly better efficacy than placebo at a dosage of 4 g/day [3]. Concerning safety, these agents have a good tolerance profile, requiring kidney function surveillance twice a year.

In 2016 corticosteroids maintain a central role in the management of the first flare of Crohn's disease, particularly in the early course, whatever the severity or extent of lesions. For decades, corticosteroids' efficacy has been demonstrated in randomized controlled trials [4] and study population cohorts [5, 6]. Nonetheless, the two main limitations of steroid use in Crohn's disease are its side effects and its lack of efficacy as a maintenance therapy. Importantly, steroids have no

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_19

Table 19.1 Characteristics of treatments used in inflammatory bowel disease

Drug class	Method of administration, dosage	Side effects	Surveillance
Corticosteroids	Oral: prednisone or prednisolone 40 mg/day to 0.8–1 mg/kg/day (single dose) Intravenous: methylprednisolone 0.8–1 mg/kg/day Oral with ileocecal delivery: budesonide 9 mg/day (single dose) Topical betamethasone 5 mg/100 mL (enema once a day)	Cushingoid syndrome Neuropsychological signs Cosmetics Diabetes, high blood pressure Osteoporosis Ocular Risk of infection	Vitamin D and calcium supplementation Initial measurement of bone mineral density Optional potassium supplementation
5-Aminosalicylates	Oral: mesalazine 2–4 g/day (in one or two daily doses) Topical (suppositories and enemas): mesalazine or sodium p-aminosalicylate (1 g/day)	Hypersensitivity (fever, headache) Tubulointerstitial nephritis Acute pancreatitis Interstitial lung disease Pericarditis, myocarditis	Creatinine concentration, 2 times a year
Methotrexate	Parenteral (subcutaneous or intramuscular) or oral (varaible inter- and intra-individual absorption) Methotrexate: 25 mg/week (single dose) as induction, could be reduced to 15 mg/week as maintenance	Digestive intolerance Stomatitis Headache, asthenia Interstitial lung disease Elevated transaminases	Contraception (teratogenicity) Folate by mouth 24 h after injection Noninvasive markers of liver fibrosis Pulmonary radio if cough
Thiopurines	Oral: azathioprine 2.5 mg/kg/day (single dose) Oral form; 6-mercaptopurine 1–1.5 mg/kg/day (single dose)	Myelotoxicity: neutropenia, lymphopenia Digestive intolerance Immunoallergic reaction (acute pancreatitis) Elevated transaminases Opportunistic infections (Epstein-Barr virus, cytomegalovirus) Increased risk of lymphoma and nonmelanoma skin cancer	Regular monitoring of blood count and transaminases TPMT (thiopurine-methyltransferase) genotype Dermatologic surveillance (once a year)
Anti–tumor necrosis factor agents	Intravenous: infliximab induction regimen (5 mg/kg at weeks 0, 2, and 6); maintenance regimen 5 mg/kg every 8 weeks Subcutaneous: adalimumab induction regimen (160 mg at week 0 and 80 mg at week 2), maintenance regimen (40 mg/1–2 week) Subcutaneous: golimumab induction regimen (200 mg at week 0 and 100 mg at week 2), maintenance regimen (50–100 mg for4 weeks according to body weight)	Allergic reactions to infusions and local reactions at injection site Opportunistic infections (bacterial, fungal, viral) Dermatological and rheumatologic paradoxical effects Possible increased risk of melanoma	Screening for sepsis, quantiferon, pulmonary radio, serology (HIV, hepatitis B and C viruses) Contraindication if malignancy within the past 5 years Vaccination status
Vedolizumab	Intravenous: vedolizumab induction regimen (300 mg at weeks 0, 2, and 6); maintenance regimen (300 mg for 4–8 weeks)	Rhinopharyngitis Headache Digestive infections?	Screening: sepsis, quantiferon, pulmonary radio, serology (HIV, hepatitis B and C viruses) Contraindication if malignancy within the past 5 years Vaccination status

impact on mucosal healing of inflammatory endoscopic lesions. Budesonide represents an alternative to "conventional" corticosteroids, with a better safety profile due to its 90 % extraction by the liver. Because budesonide is delivered in the terminal ileum and right colon, it could be considered at a dosage of 9 mg/day in patients with Crohn's disease with mild to moderate flares in these locations, providing clinical remission in nearly 50 % [7].

Thus, a short steroid course remains a pivotal treatment in patients with active disease. It should be followed by quick tapering (within 3 months) to limit exposure and avoid side effects. In the case of steroid-refractory Crohn's disease, including dependence, failure, and intolerance, immunosuppressants and/or biologics should be considered.

19.2.1.2 Early Use of Immunosuppressants (Thiopurines and Methotrexate)

For more than 30 years, thiopurines (azathioprine and 6-mercaptopurine) have been considered as the referential maintenance therapy in refractory Crohn's disease, providing sustained, steroid-free remission [8–11]. However, because most patients who previously responded to thiopurines relapse with time after drug withdrawal, these agents are considered as having only a suspensive action [12, 13]. To modify the course of Crohn's disease and limit thiopurine exposure, it was expected that an early treatment with thiopurines could be beneficial. This strategy was explored in two recent randomized control trials. Unfortunately, no clinical benefit of early treatment with thiopurines was observed in the first 3 years compared with controls who received a placebo in a Spanish trial [15] or a conventional step-up approach in a French one [14]. Moreover, one-third of the patients randomized in the control arm in the French study did not require any immunosuppressants during the study period. This suggests that giving thiopurine to patients with early Crohn's disease with several poor prognostic factors – age at diagnosis <40 years, active luminal disease requiring steroids, perianal lesions at diagnosis – may lead to overtreatment in many patients. Indeed, beyond the risk of opportunistic infection [16] or hematologic and liver toxicities, a neoplastic risk related to thiopurines is now well established; an increased risk of lymphoma [17] and nonmelanoma skin cancer were observed in the large, prospective CESAME cohort [18]. Thus, the trend of early azathioprine administration is declining because biologics have better efficacy than thiopurines [19] and an equivalent safety profile. At the moment, azathioprine is started after a first flare in the case of noncomplicated steroid-refractory disease [2] and, more often, in combination with an anti-TNF agent (cf. Sect. 19.2.1.3).

Methotrexate is the other conventional immunosuppressant that can be used in Crohn's disease. Its efficacy is established by two randomized controlled trials and confirmed by further meta-analysis and seems comparable to that of thiopurines [20–23]. The parenteral route is preferred, with weekly 25-mg methotrexate injections followed by maintenance at a lower dose. Despite more rapid action than thiopurines and no increased risk of induced malignancy, methotrexate is usually limited to patients with previous azathioprine failure or intolerance and is associated with anti-TNF agents, as in inflammatory rheumatisms [24].

19.2.1.3 When Starting an Anti-TNF Early, Should We Also Administer an Immunosuppressant?

Available since 1998, anti-TNF agents have dramatically changed the management of Crohn's disease. Two drugs that have shown efficacy as induction and maintenance treatments are available: infliximab [25, 26] and adalimumab [27, 28]. Usual indications for anti-TNF agents are refractory and severe luminal Crohn's disease after failure or intolerance of systemic steroids, including budesonide, and conventional immunosuppressants. In addition, the efficacy of infliximab has been demonstrated in fistulizing disease, particularly for anoperineal lesions [29]. Beyond their well-known clinical benefit, anti-TNF agents also allow patients to be weaned from steroids, provide mucosal healing, and may

prevent bowel damage that leads to strictures and/or fistulas and surgical resections.

Benefit of anti-TNF agents is inversely correlated with the duration of Crohn's disease; that is, it is better for early lesions, before bowel destruction [30]. This explains the current trend toward earlier and longer treatment with anti-TNF agents. In practice, these drugs could be considered early in the case of an extended and severe first attack of Crohn's disease, mainly when associated with complicated anoperineal lesions. In the case of a steroid-refractory course, anti-TNF agents are more effective than conventional immunosuppressants; this point has been demonstrated only with infliximab over azathioprine. In addition, the combination therapy associating an anti-TNF agent with an immunosuppressant – so-called combotherapy – is the most effective strategy, as shown in the SONIC trial [19]. At the moment, the long-term safety and duration of such combotherapy and how to manage therapeutic deescalation in patients in remission are pending issues.

Concerning anti-TNF tolerance, most side effects are shared by both infliximab and adalimumab. Neoplastic risk related to anti-TNF agents has been scrutinized and was suggested only for melanoma (odds ratio, 1.88) [31]. Infection risk, mainly concerning opportunistic infections, is increased by anti-TNF agents per se, but also by age and associated steroids and immunosuppressants [32]. Importantly, cases of tuberculosis developed while taking anti-TNF agents have become the exception since the implementation of systematic screening before starting treatment. Other common anti-TNF agent side effects are the occurrence of immunologic paradoxical manifestations involving the skin (psoriasis-like and/or eczema-like) or the joints.

19.2.1.4 Is There Still Room for Surgery in the Anti-TNF Era?

Nearly 20% of patients with Crohn's disease are diagnosed with a form complicated by obstruction, intra-abdominal abscess, or fistula [33], leading to early surgery, especially when the complications occur in within the short terminal ilium. Despite advances in medical treatment, the vast majority of patients with Crohn's disease will require surgery during their lifetime because of complications or treatment failure. Nowadays, laparoscopy has become the standard surgical approach in Crohn's disease, even for complicated forms [34]. Last, the combination of intestinal resections and medical therapies, such as biologics that have a low impact on surgical outcomes, is more frequent.

19.2.1.5 Initial Therapeutic Strategy: Graduated Approach or Early Combotherapy?

In the absence of a demonstrated benefit to start conventional immunosuppressants early, two major approaches could be discussed with regard to Crohn's disease.

- The first is a step-up strategy, from steroids to immunosuppressants and then to anti-TNF agents following gradual therapeutic escalation in the case of failure. This careful approach is usually well accepted by patients and could be cost-effective. However, the late introduction of powerful therapies may undertreat the most severe forms, favoring bowel damage and intestinal surgery.
- The second is a maximal strategy that immediately proposes the most effective approach – namely, the combotherapy between an immunosuppressant and an anti-TNF agent, followed if possible by deescalation once a deep remission of Crohn's disease is obtained, including the absence of symptoms and normal biologic and endoscopic findings. Such an approach is supposed to modify the natural history of Crohn's disease. Conversely, it leads to the overtreatment of patients exposed to long-term and multiple periods of immunosuppression, increasing the risk of infections and malignancies as well as direct costs.

19.2.2 What to Do in Clinical Practice?

19.2.2.1 Therapeutic Algorithm

In 2016, the initial therapeutic strategy for Crohn's disease is usually a quick step-up approach taking into account disease severity and

the patient's prognostic factors. The best established factors associated with a poor disease course are young age at diagnosis, stenosing and penetrating phenotyp, anoperineal and/or rectal location, upper and extensive gastrointestinal tract involvement, and severe endoscopic lesions.

To summarize, a therapeutic algorithm [35] has been proposed for managing Crohn's disease at diagnosis (Fig. 19.1): steroids alone in mild disease or associated with immunosuppressants in moderate disease without a poor prognosis and without complications; early anti-TNF agents with or without immunosuppressants in severe disease and in moderate forms with poor prognostic factors and/or extensive intestinal involvement and/or perianal lesions.

In the case of a loss of response to an anti-TNF agent, two primary therapeutic options should be considered before surgery or new therapeutic agents are administered: optimizing the drug (reducing the dosing interval or increasing the dose) or switching to another anti-TNF agent – both ideally according to pharmacokinetics.

Vedolizumab has now become an alternative to anti-TNF agents in Crohn's disease. This intravenously administered humanized monoclonal antibody specifically targets the α4β7 integrin and selectively blocks gut lymphocyte trafficking. It can be use as induction and maintenance therapy after anti-TNF failure [36].

19.2.2.2 Monitoring Patients and Adjusting Therapy

Following the development of the therapeutic armamentarium for Crohn's disease, new therapeutic goals emerged during the past decade. Mucosal healing and the prevention of bowel damage are desirable and achievable. Because there is a poor correlation between clinical symptoms and objective inflammation in Crohn's disease [37], closely monitoring a patient using biomarkers (fecal calprotectin– and protein C–reactive dosages, anti-TNF pharmacokinetics), endoscopy [38], and magnetic resonance imaging [39] identify early therapeutic changes if inflammation is not controlled.

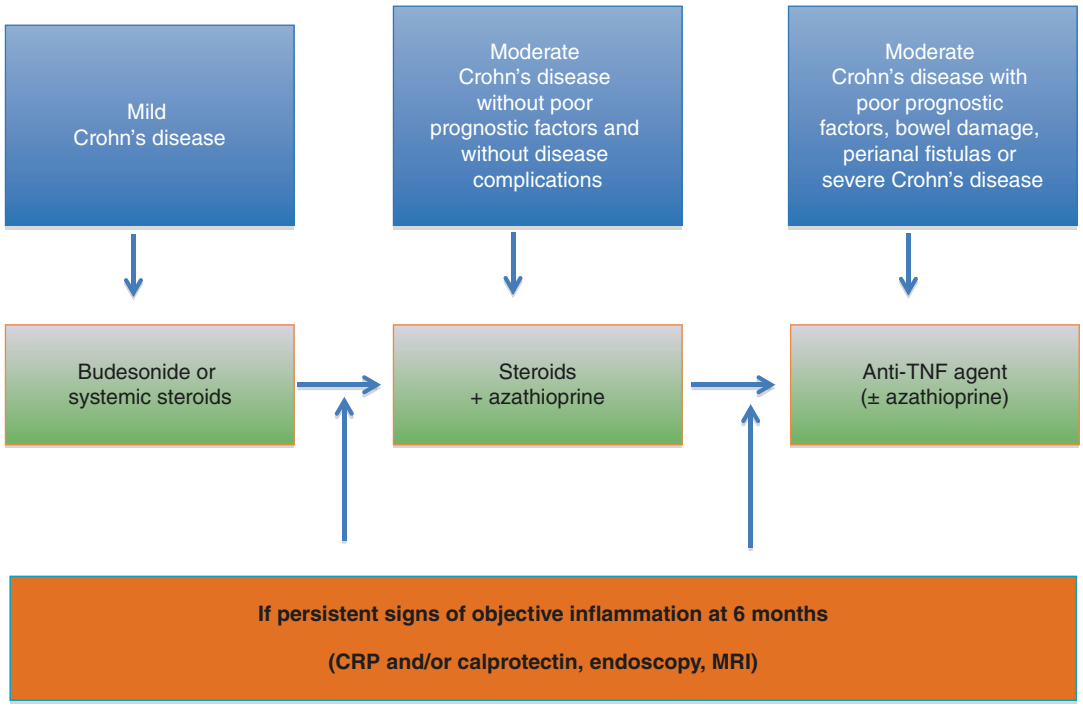


Fig. 19.1 Proposed algorithm for treating Crohn's disease (From Peyrin-Biroulet et al. [35]). *TNF* tumor necrosis factor, *MRI* magnetic resonance imaging

19.2.3 Preventing Postoperative Recurrence: A Special Setting

Crohn's disease most commonly affects the terminal ileum and right colon. Despite therapeutic progress, almost 75 % of patients have surgery during their lifetime as a result of structuring or penetrating complications [40]. After bowel resection, 70–90 % of patients develop significant endoscopic postoperative recurrence on the neoterminal ileum and the anastomosis within 1 year [41], 60 % have a clinical recurrence at 10 years [42], and 70 % will undergo a new surgery at 20 years [43]. Because endoscopic recurrence predicts clinical recurrence, an endoscopic evaluation 6 months after surgery is recommended in order to start treatment early. This strategy has recently been validated by a randomized controlled trial [44]. A therapeutic algorithm for the prevention of postoperative recurrence is proposed in Fig. 19.2 [45].

19.3 Ulcerative Colitis

19.3.1 Mild to Moderate Forms

19.3.1.1 Are Salicylates and Corticosteroids Still Cornerstones of Ulcerative Colitis Treatment?

The efficacy of 5-aminosalicylates has been demonstrated in ulcerative colitis. They remain the standard initial treatment in mild to moderate disease and the first-line maintenance therapy [46, 47]. In population studies, nearly half of patients with ulcerative colitis are controlled with 5-aminosalicylates alone. In active proctitis, topical 5-aminosalicylates administered via suppositories or enemas have also shown good efficacy – better than topical steroids – and should be given first [48, 49]. European Crohn's Colitis Organisation (ECCO) guidelines on 5-aminosalicylate use in mild to moderate ulcerative colitis are summarized in Table 19.2 [50].

Systemic steroids have still an important place in the treatment of active ulcerative colitis refractory to salicylates and severe forms as recommended by ECCO (cf. below). They could be also administered locally in proctitis refractory to 5-aminosalicylates [50].

19.3.1.2 Do Immunosuppressants and Anti-TNF Agents Have a Place in the Early Treatment of Ulcerative Colitis?

Conventional immunosuppressants are considered as a maintenance treatment for ulcerative colitis when 5-aminosalicylates fail or are not tolerated. They have a more limited role in treating ulcerative colitis than in treating Crohn's disease. If the efficacy of thiopurines, mainly azathioprine, has been demonstrated in ulcerative colitis [51, 52], the benefit of methotrexate is more controversial [53]. Conversely, with Crohn's disease, the duration of ulcerative colitis is not correlated with drug efficacy. Anti-TNF agents have no early indication as a first-line treatment in mild to moderate forms of disease.

19.3.2 Refractory Forms

Steroid-refractory ulcerative colitis combines steroid dependence, resistance, and intolerance. In these cases, starting immunosuppressants with or without an anti-TNF agent should be discussed. The efficacy of three anti-TNF blockers – infliximab, adalimumab [54, 55], and golimumab [56, 57] – has been demonstrated in refractory ulcerative colitis, and they are approved for use in the case of steroid and immunosuppressant failure. As observed in Crohn's disease, the combotherapy of immunosuppressants and anti-TNF agents is probably the most effective strategy [58]. In the case of anti-TNF agent failure, vedolizumab should be considered as induction and maintenance treatment in refractory ulcerative colitis before surgery [59]. Management of refractory ulcerative colitis is summarized in Fig. 19.3 [60].

19.3.3 Acute Severe Colitis

Acute severe ulcerative colitis occurs in one of every four patients and could manifest during the

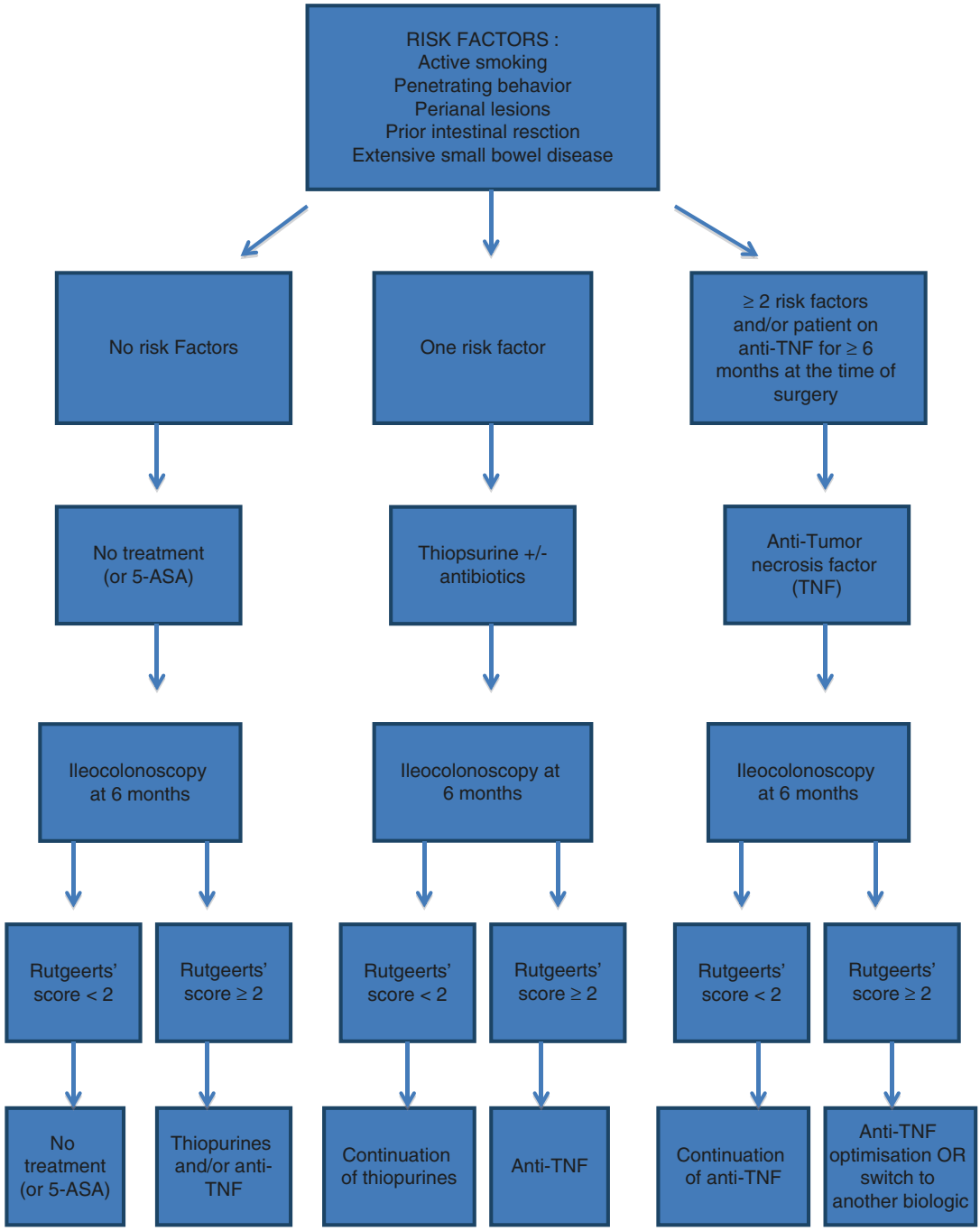


Fig. 19.2 Strategy for the prevention and treatment of postoperative recurrence of Crohn's disease (From Buisson et al. [45])

first attack. This specific situation is a life-threatening emergency that must be managed by experienced medico-surgical teams. Diagnosis of acute severe ulcerative colitis is still based on the traditional Truelove and Witts criteria [61], as recommended by ECCO. In summary, a ulcerative colitis flare with at least six stool emissions in 24 h and associated with general signs (fever, tachycardia,

Table 19.2 Treatment of mild to moderate ulcerative colitis

Disease extent	Induction treatment	Maintenance treatment (for in all situations)
Proctitis	5-ASA (1 g suppository once a day) Switch to topical steroids in the case of failure Add oral salicylates and/or steroid enemas if failure Immunomodulators in refractory proctitis failure[a] (immunosuppressants or anti-TNF)	5-ASA suppository (1 g 3 times/week) Combine with oral salicylate only as second-line treatment (minimum effective dose of at least 1.2 g/day)
Left colitis	5-ASA enema, 1 g per day (single dose) Combine with oral aminosalicylate 2–4 g/day (single dose) If failure[a]: oral steroids	Oral salicylate treatment once daily (>1.2 g/day) Association with topicals (3 times/week)
Pancolitis	Oral aminosalicylates 2–4 g/day (single dose) Combined with topical 5-ASA (suppository or enema) If failure[a]: oral steroids	Oral salicylate treatment once daily (>1.2 g/day) Association with topicals (3 times/week)

Adapted from ECCO recommendations [50]
5-ASA 5-aminosalicylate, *TNF* tumor necrosis factor
[a]In the case of failure of salicylate treatment or before therapeutic change, infectious colitis and problems with compliance should be eliminated

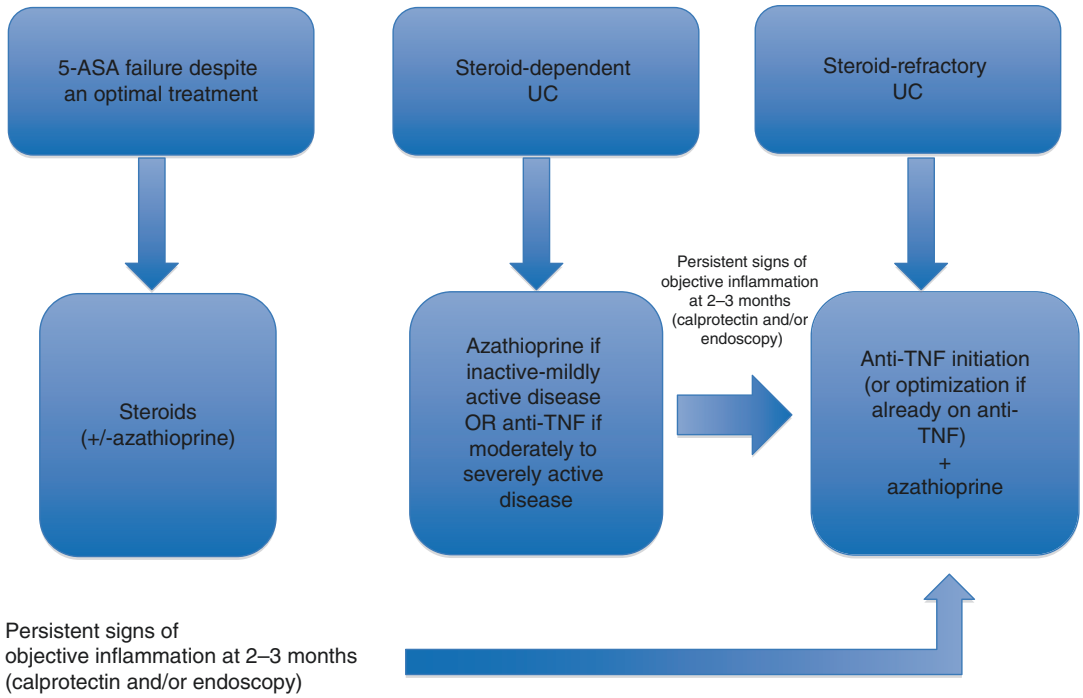


Fig. 19.3 Proposed algorithm for treating ulcerative colitis (From Danese et al. [60]). *UC* ulcerative colitis, *5-ASA* 5-aminosalicylate acid, *AZA* azathioprine, *TNF* tumor necrosis factor

loss of weight) and/or laboratory abnormalities (anemia, increased neutrophils, elevated C-reactive protein, hypoalbuminemia) should be considered as acute severe ulcerative colitis and the patient be admitted to a specific unit.

After ruling out an active colonic infection, including *Clostridium difficile*, intravenous steroids are the mainstay of medical treatment of acute severe ulcerative colitis, with the aim of achieving a quick clinical remission (in less than

a week). In the absence of sufficient improvement that can be predicted after 3 days according to the number of stools and C-reactive protein concentration, two options should be considered: emergent colectomy or second-line medical therapy with intravenous cyclosporine or infliximab. When combined with azathioprine, both drugs have an outstanding efficiency, providing clinical remission within 1 week in more than 80% of patients [62]. A recent strategic therapeutic trial failed to identify a difference in efficacy in the short and medium term between cyclosporine and infliximab [63]. In the case of failure of the second-line medical therapy, emergent colectomy should be performed.

Conclusion

Medical management of IBD upset in the past decade has seen the increased use of immunosuppressants and anti-TNF agents earlier and longer than ever. The advent of anti-TNF agents deeply changed therapeutic strategies. Therapeutic goals have become more ambitious, aiming to modify the disease course. They must take into account disease severity, prognostic factors, and surrogate markers of inflammation, as well as patient safety and direct costs. Although the amount of reassuring data is increasing, there remain practical issues related to treatment duration and the long-term safety of these new drugs. As therapeutic decisions in inflammatory bowel disease become increasingly complex, discussion within multidisciplinary teams should become more widespread, especially with the several monoclonal antibodies that will be available in the future, starting with the anti–α4β7 integrin vedolizumab.

References

1. Ford AC, Kane SV, Khan KJ, Achkar J-P, Talley NJ, Marshall JK, et al. Efficacy of 5-aminosalicylates in Crohn's disease: systematic review and meta-analysis. Am J Gastroenterol. 2011;106(4):617–29.
2. Dignass A, Van Assche G, Lindsay JO, Lémann M, Söderholm J, Colombel JF, et al. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: current management. J Crohn's Colitis. 2010;4(1):28–62.
3. Gordon M, Naidoo K, Thomas AG, Akobeng AK. Oral 5-aminosalicylic acid for maintenance of surgically-induced remission in Crohn's disease. Cochrane Database Syst Rev Online. 2011;1, CD008414.
4. Summers RW, Switz DM, Sessions Jr JT, Becktel JM, Best WR, Kern Jr F, et al. National cooperative Crohn's disease study: results of drug treatment. Gastroenterology. 1979;77(4 Pt 2):847–69.
5. Faubion Jr WA, Loftus Jr EV, Harmsen WS, Zinsmeister AR, Sandborn WJ. The natural history of corticosteroid therapy for inflammatory bowel disease: a population-based study. Gastroenterology. 2001;121(2):255–60.
6. Ho G-T, Chiam P, Drummond H, Loane J, Arnott IDR, Satsangi J. The efficacy of corticosteroid therapy in inflammatory bowel disease: analysis of a 5-year UK inception cohort. Aliment Pharmacol Ther. 2006;24(2):319–30.
7. Seow CH, Benchimol EI, Griffiths AM, Otley AR, Steinhart AH. Budesonide for induction of remission in Crohn's disease. Cochrane Database Syst Rev Online. 2008;3, CD000296.
8. O'Donoghue DP, Dawson AM, Powell-Tuck J, Bown RL, Lennard-Jones JE. Double-blind withdrawal trial of azathioprine as maintenance treatment for Crohn's disease. Lancet. 1978;2(8097):955–7.
9. Candy S, Wright J, Gerber M, Adams G, Gerig M, Goodman R. A controlled double blind study of azathioprine in the management of Crohn's disease. Gut. 1995;37(5):674–8.
10. Willoughby JM, Beckett J, Kumar PJ, Dawson AM. Controlled trial of azathioprine in Crohn's disease. Lancet. 1971;2(7731):944–7.
11. Rosenberg JL, Levin B, Wall AJ, Kirsner JB. A controlled trial of azathioprine in Crohn's disease. Am J Dig Dis. 1975;20(8):721–6.
12. Lémann M, Mary J-Y, Colombel J-F, Duclos B, Soule J-C, Lerebours E, et al. A randomized, double-blind, controlled withdrawal trial in Crohn's disease patients in long-term remission on azathioprine. Gastroenterology. 2005;128(7):1812–8.
13. Treton X, Bouhnik Y, Mary J-Y, Colombel J-F, Duclos B, Soule J-C, et al. Azathioprine withdrawal in patients with Crohn's disease maintained on prolonged remission: a high risk of relapse. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2009;7(1):80–5.
14. Cosnes J, Bourrier A, Laharie D, Nahon S, Bouhnik Y, Carbonnel F, et al. Early administration of azathioprine vs conventional management of Crohn's disease: a randomized controlled trial. Gastroenterology. 2013;145(4):758–765.e2. quiz e14–15.
15. Panés J, López-Sanromán A, Bermejo F, García-Sánchez V, Esteve M, Torres Y, et al. Early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's disease. Gastroenterology. 2013;145:766–74.e1.

16. Rahier JF, Ben-Horin S, Chowers Y, Conlon C, De Munter P, D'Haens G, et al. European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohn's Colitis. 2009;3(2):47–91.
17. Beaugerie L, Brousse N, Bouvier AM, Colombel JF, Lémann M, Cosnes J, et al. Lymphoproliferative disorders in patients receiving thiopurines for inflammatory bowel disease: a prospective observational cohort study. Lancet. 2009;374(9701):1617–25.
18. Peyrin-Biroulet L, Khosrotehrani K, Carrat F, Bouvier A-M, Chevaux J-B, Simon T, et al. Increased risk for nonmelanoma skin cancers in patients who receive thiopurines for inflammatory bowel disease. Gastroenterology. 2011;141(5):1621–1628.e1–5.
19. Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, et al. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010;362(15):1383–95.
20. Feagan BG, Rochon J, Fedorak RN, Irvine EJ, Wild G, Sutherland L, et al. Methotrexate for the treatment of Crohn's disease. The North American Crohn's Study Group Investigators. N Engl J Med. 1995;332(5):292–7.
21. Feagan BG, Fedorak RN, Irvine EJ, Wild G, Sutherland L, Steinhart AH, et al. A comparison of methotrexate with placebo for the maintenance of remission in Crohn's disease. North American Crohn's Study Group Investigators. N Engl J Med. 2000;342(22):1627–32.
22. Patel V, Macdonald JK, McDonald JW, Chande N. Methotrexate for maintenance of remission in Crohn's disease. Cochrane Database Syst Rev Online. 2009;4, CD006884.
23. McDonald JWD, Tsoulis DJ, Macdonald JK, Feagan BG. Methotrexate for induction of remission in refractory Crohn's disease. Cochrane Database Syst Rev Online. 2012;12, CD003459.
24. Feagan BG, McDonald JWD, Panaccione R, Enns RA, Bernstein CN, Ponich TP, et al. Methotrexate in combination within fliximabis no more effective than infliximab alone in patients with Crohn's disease. Gastroenterology. 2014;146(3):681–688.e1.
25. Present DH, Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999;340(18):1398–405.
26. Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002;359(9317):1541–9.
27. Colombel J-F, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007;132(1):52–65.
28. Sandborn WJ, Hanauer SB, Rutgeerts P, Fedorak RN, Lukas M, MacIntosh DG, et al. Adalimumab for maintenance treatment of Crohn's disease: results of the CLASSIC II trial. Gut. 2007;56(9): 1232–9.
29. Sands BE, Anderson FH, Bernstein CN, Chey WY, Feagan BG, Fedorak RN, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004;350(9):876–85.
30. Schreiber S, Reinisch W, Colombel JF, Sandborn WJ, Hommes DW, Robinson AM, et al. Subgroup analysis of the placebo-controlled CHARM trial: increased remission rates through 3 years for adalimumab-treated patients with early Crohn's disease. J Crohn's Colitis. 2013;7(3):213–21.
31. Long MD, Martin CF, Pipkin CA, Herfarth HH, Sandler RS, Kappelman MD. Risk of melanoma and nonmelanoma skin cancer among patients with inflammatory bowel disease. Gastroenterology. 2012;143(2):390–399.e1.
32. Toruner M, Loftus Jr EV, Harmsen WS, Zinsmeister AR, Orenstein R, Sandborn WJ, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. Gastroenterology. 2008;134(4): 929–36.
33. Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. Gastroenterology. 2011;140(6): 1785–94.
34. Eshuis EJ, Slors JFM, Stokkers PCF, Sprangers MAG, Ubbink DT, Cuesta MA, et al. Long-term outcomes following laparoscopically assisted versus open ileocolic resection for Crohn's disease. Br J Surg. 2010;97(4):563–8.
35. Peyrin-Biroulet L, Fiorino G, Buisson A, Danese S. First-line therapy in adult Crohn's disease: who should receive anti-TNF agents? Nat Rev Gastroenterol Hepatol. 2013;10(6):345–51.
36. Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel J-F, Sands BE, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711–21.
37. Peyrin-Biroulet L, Reinisch W, Colombel J-F, Mantzaris GJ, Kornbluth A, Diamond R, et al. Clinical disease activity, C-reactive protein normalisation and mucosal healing in Crohn's disease in the SONIC trial. Gut. 2014;63(1):88–95.
38. Neurath MF, Travis SPL. Mucosal healing in inflammatory bowel diseases: a systematic review. Gut. 2012;61(11):1619–35.
39. Horsthuis K, Lavini C, Bipat S, Stokkers PCF, Stoker J. Perianal Crohn disease: evaluation of dynamic contrast-enhanced MR imaging as an indicator of diseaseactivity. Radiology. 2009;251(2):380–7.
40. Cosnes J, Nion-Larmurier I, Beaugerie L, Afchain P, Tiret E, Gendre J-P. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. Gut. 2005;54(2):237–41.
41. Olaison G, Smedh K, Sjödahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualised ileal ulcers preceding symptoms. Gut. 1992;33(3):331–5.
42. Sachar DB. The problem of postoperative recurrence of Crohn's disease. Med Clin N Am. 1990;74(1):183–8.

43. Michelassi F, Balestracci T, Chappell R, Block GE. Primary and recurrent Crohn's disease. Experience with 1379 patients. Ann Surg. 1991;214(3):230–8. discussion 238–240.
44. De Cruz P, Kamm MA, Hamilton AL, Ritchie KJ, Krejany EO, Gorelik A, et al. Crohn's disease management after intestinal resection: a randomised trial. Lancet Lond Engl. 2015;385(9976):1406–17.
45. Buisson A, Chevaux J-B, Bommelaer G, Peyrin-Biroulet L. Diagnosis, prevention and treatment of postoperative Crohn's disease recurrence. Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver. 2012;44(6):453–60.
46. Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database Syst Rev Online. 2012;10, CD000543.
47. Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev Online. 2012;10, CD000544.
48. Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. Rectal 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database Syst Rev Online. 2010;1, CD004115.
49. Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. Rectal 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev Online. 2012;11, CD004118.
50. Dignass A, Eliakim R, Magro F, Maaser C, Chowers Y, Geboes K, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. J Crohn's Colitis. 2012;6(10):965–90.
51. Ardizzone S, Maconi G, Russo A, Imbesi V, Colombo E, Bianchi PG. Randomised controlled trial of azathioprine and 5-aminosalicylic acid for treatment of steroid dependent ulcerative colitis. Gut. 2006;55(1):47–53.
52. Timmer A, McDonald JWD, Tsoulis DJ, Macdonald JK. Azathioprine and 6-mercaptopurine for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev Online. 2012;9, CD000478.
53. Carbonnel F, Colombel JF, Filippi J, Katsanos K, Peyrin-Biroulet L, Allez M, Nachury M, Novacek G, Danese S, Abitbol V, Bossa F, Moreau J, Bommelaer G, Bourreille A, Dupas JL, Roblin X, Bouhnik Y, Reinisch W, Farkkila M, Brixi H, Seksik P, Malamut G, Coulibaly B, Dewit O, Louis E, Deplanque D, Michetti P, Sarter H, Laharie D. Methotrexate for corticosteroid-dependent ulcerative colitis: results of a placebo randomized controlled trial. Oral presentation 23; ECCO congress Barcelona 2015.
54. Reinisch W, Sandborn WJ, Hommes DW, D'Haens G, Hanauer S, Schreiber S, et al. Adalimumab for induction of clinical remission in moderately to severely active ulcerative colitis: results of a randomised controlled trial. Gut. 2011;60(6):780–7.
55. Sandborn WJ, van Assche G, Reinisch W, Colombel J-F, D'Haens G, Wolf DC, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2012;142(2):257–265.e1–3.
56. Sandborn WJ, Feagan BG, Marano C, Zhang H, Strauss R, Johanns J, et al. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014;146(1):85–95. quiz e14–15.
57. Sandborn WJ, Feagan BG, Marano C, Zhang H, Strauss R, Johanns J, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014;146(1):96–109.e1.
58. Panaccione R, Ghosh S, Middleton S, Márquez JR, Scott BB, Flint L, et al. Combination therapy with infliximab and azathioprine is superior to monotherapy with either agent in ulcerative colitis. Gastroenterology. 2014;146(2):392–400.e3.
59. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel J-F, Sandborn WJ, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699–710.
60. Danese S, Colombel J-F, Peyrin-Biroulet L, Rutgeerts P, Reinisch W. Review article: the role of anti-TNF in the management of ulcerative colitis – past, present and future. Aliment Pharmacol Ther. 2013;37(9):855–66.
61. EDWARDS FC, TRUELOVE SC. The course and prognosis of ulcerative colitis. Gut. 1963;4:299–315.
62. Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, et al. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med. 1994;330(26):1841–5.
63. Laharie D, Bourreille A, Branche J, Allez M, Bouhnik Y, Filippi J, et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. Lancet. 2012;380(9857):1909–15.

Endometriosis

20

Gian Andrea Binda, Alberto Serventi,
and Alessandro Fasciani

20.1 Definition and Etiology

Endometriosis is the presence of endometrial-like tissue outside the uterus that induces a chronic inflammatory reaction. It is not possible to define endometriosis as a 'disease', 'illness' and/or a 'physiological phenomenon' with a known cause or known triggers/mechanisms. Consequently, endometriosis remains a considerable diagnostic and therapeutic challenge as the signs and symptoms of disease vary according to the location and severity of the endometriotic implants, as well as the psychosocial impacts on the woman.

There is a considerable literature on the epidemiology of endometriosis [1] that consistently identifies nulliparous women and women who experience short and heavy menstrual cycles as being at increased risk. Other factors have been studied but the data are less consistent. These epidemiological findings support the retrograde reflux hypothesis. Other hypotheses include the induction theory, the celomic metaplasia theory, and the embryonic rests theory all of which have been put forward to explain the pathogenesis of endometriosis. Although not all of these alternative theories have been abandoned, at present, retrograde menstruation is considered the *primum movens* responsible for the development of the disease, at least in its form of peritoneal implants. There is now a general consensus that peritoneal endometriotic lesions can be attributed to the survival, adhesion, proliferation, invasion and vascularization of endometrial tissue regurgitated through the fallopian tubes during menstruation, an idea referred to as implantation theory. However, the pathogenesis of ovarian endometriosis and of specific forms of deep endometriosis is still controversial. Thus, one of the main debates is whether the different forms of the disease have a common etiology or, conversely, represent separate entities with different pathogeneses.

At present, *superficial* endometriosis (lesions on the surface of peritoneum) is considered a normal phenomenon in women in the childbearing years, whereas *ovarian* and *deep infiltrative endometriosis* (DIE), defined as the penetration >5 mm under the peritoneal surface, are the more severe and generally painful manifestations of

G.A. Binda, M.D. (✉)
Department of Surgery, Galliera Hospital,
via Mura delle Capuccine 14, Genoa 16128, Italy
e-mail: gian.andrea.binda@galliera.it

A. Serventi, M.D.
Department of Surgery, Galliera Hospital,
via Mura delle Capuccine 14, Genoa 16128, Italy
e-mail: aserventi@libero.it

A. Fasciani, M.D.
Department of Gynecology, Galliera Hospital,
Mura delle Cappuccine, 14, Genoa 16128, Italy
e-mail: alessandro.fasciani@fastwebnet.it

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_20

the condition. These lesions are considered very active and can be highly symptomatic since DIE implants are found in specific locations, such as uterosacral ligaments and torus uterinus (retrocervical area of the uterus where the uterosacral ligaments join together) in 53 %, the pouch of Douglas, vagina and recto-vaginal septum (16 %), ureter (2 %), bladder (6 %), vesico-uterine pouch and digestive tract (23 %) [2, 3]. *Intestinal* endometriosis is defined as the presence of lesions affecting the gastro-intestinal tract: the implants are usually serosal but can eventually erode through the subserosal layers and cause marked thickening and fibrosis of the muscularis propria. An intact overlying mucosa is almost always present, because the implanted tissue only rarely invades the mucosa (Fig. 20.1).

20.2 Incidence and Epidemiology

Endometriosis affects 6–10 % of all women of childbearing age. Endometriosis has estimated annual costs of approximately US $12,400 per woman (approximately € 11,000), comprising one-third of direct health care costs with two-thirds attributed to loss of productivity. Based on a review of cost estimates, the annual costs of endometriosis attained $22 billion in 2002 in the United States. These costs are considerably higher than those related to Crohn's disease or to migraine. Decreased quality of life is the most important predictor of direct health care and total costs.

Endometriosis is predominantly found in women of reproductive age of all ethnic and social groups and generally associated with pelvic pain and infertility. Infertility problems can impact on the physical, mental and social well being of a woman and can have a profound effect on her life, including the ability to finish an education, maintain a career, or to create a family. For these reasons the European Union Written Declaration has recognized endometriosis as a disease with an important economic impact on the community demonstrating a significant association with health costs related to diagnostic delays and therapeutic expenses including surgery, drugs, and assisted reproductive technologies (ART) [4].

DIE occurs in up to 30–40 % of patients with endometriosis whereas intestinal endometriosis has been estimated to occur in 8–12 % of these women [5]. Deep gastrointestinal involvement in endometriosis is characterised by fibrous, retractile thickening of the intestinal wall. The most common location is the upper rectum, in contiguity with a lesion of the torus uterinus since its prevalence increases with the severity of pelvic involvement reaching 50 % in stage IV of the American Fertility Society (AFS). Chapron et al. [6] reported the anatomical distribution of DIE lesions in the digestive tract in 426 consecutive patients who underwent complete surgical

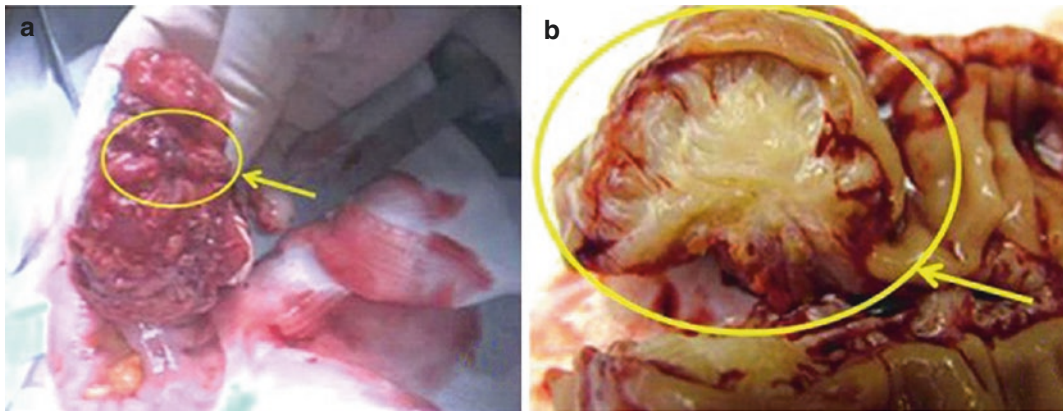


Fig. 20.1 An endometriotic nodule infiltrating the intestinal wall to the submucosal layer. (**a**) lumen reduction, (**b**) fibrotic core

excision of DIE: recto-sigmoid junction and rectum in 65.7 %, sigmoid in 17.4 %, appendix in 6.4 %, small bowel in 4.7 %, cecum and ileocecal junction in 4.1 %, and omentum in 1.7 %. Furthermore rectal lesions are associated with a second intestinal lesion in 54.6 % of cases [7].

20.3 Classification

The revised American Society for Reproductive Medicine (rASRM) score [8] is currently the best-known classification of endometriosis and is the one most widely used throughout the world (Fig. 20.2).

It is relatively easy to use, but it does not take into account the involvement of retroperitoneal structures with deeply infiltrating endometriosis. For this reason, the Enzian classification was developed as a supplement to the rASRM score, in order to provide a morphologically descriptive classification of deeply infiltrating endometriosis (Fig. 20.3) [9].

20.4 Diagnostics

The diagnosis of endometriosis is histological and it follows a surgical procedure in most cases.

Preoperative diagnosis is sometimes very difficult because symptoms are common and mimic others frequent pathology (i.e. irritable bowel syndrome, appendicitis, adhesions, etc.). Opinion leaders continue to support the need of a reliable non-invasive test to distinguish between the pain endometriosis and other causes since there is a significant delay in the diagnosis of this pathology: recent studies report an overall diagnostic delay of 10 years in Germany and Austria, 8 years in the UK and Spain, 7 years in Norway, 7–10 years in Italy and 4–5 years in Ireland and Belgium [10]. Ballard et al. [10] distinguished between delays at the patient level and delays at the medical level. This is generally because both women and family doctors tend to consider this type of pain as normal menstrual discomfort and neglect the need for treatment.

20.4.1 Symptoms

In endometriosis typical symptoms include dysmenorrhoea, deep dyspareunia (pain on deep penetration), dyschezia (pelvic pain with defecation), dysuria (pain with micturition) although the association between endometriosis stage and severity of pelvic symptoms has been demonstrated to be marginal and inconsistent [11]. Symptoms are usually synchronous with menstruation.

Pelvic pain is an important issue in the health care of women contributing to 10 % of all outpatient gynaecological visits, 40 % of laparoscopies and is the indication for 10–15 % of hysterectomies [12]. The existence of a relationship between chronic pelvic pain symptoms and endometriosis is widely accepted, but various other painful pelvic symptoms are also normally present in the general population.

Women presenting with rectal endometriosis are more likely to report an increase in intensity and duration of dysmenorrhoea, while deep dyspareunia appeared to be more severe in women with superficial endometriosis. Women presenting with rectal endometriosis are more likely to present cyclic defecation pain (67.9 %), cyclic constipation (54.7 %) and a significantly longer stool evacuation time, although these complaints are also frequent in women with Stage 1 endometriosis and in women with deep endometriosis without digestive involvement. No independent clinical factor has been found to be related to infiltration of the rectum by deep endometriosis and few women with rectal endometriosis present with rectal stenosis, however these women are significantly more likely to report constipation, defecation pain, appetite disorders, longer evacuation time and increased stool consistency without laxatives. Various digestive symptoms seem to be more related to cyclic inflammation than to rectal infiltration by the nodule, as they occur in women free of rectal involvement [13].

Ileocecal endometriosis may mimic appendicitis while other intestinal locations may cause bloating and discomfort related to narrowing, however intestinal occlusion is exceptional.

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE REVISED CLASSIFICATION OF ENDOMETRIOSIS

Patient's Name _____ Date _____

Stage I (Minimal) - 1-5
Stage II (Mild) - 6-15
Stage III (Moderate) - 16-40
Stage IV (Severe) - > 40
Total _____

Laparoscopy _____ Laparotomy _____ Photography _____
Recommended Treatment _____
_____
Prognosis _____

PERITONEUM	ENDOMETRIOSIS	<1cm	1-3cm	>3cm
	Superficial	1	2	4
	Deep	2	4	6
OVARY	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
OVARY	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
TUBE	R Filmy	1	2	4
	Dense	4*	8*	16
	L Filmy	1	2	4
	Dense	4*	8*	16

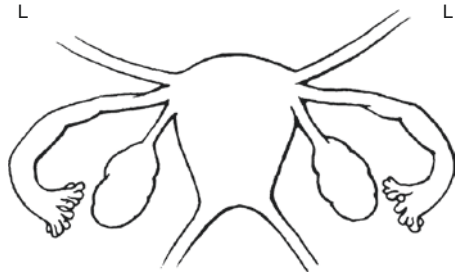
*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Denote appearance of superficial implant types as red [(R), red, red-pink, flamelike, vesicular blobs, clear vesicles], white [(w), opacifications, peritoneal defects, yellow-brown], or black [(B) black, hemosiderin deposits, blue]. Denote percent of total described as R____%, W___% and B___%. Total should equal 100%.

Additional Endometriosis: _____

Associated Pathology: _____

To Be Used with Normal Tubes and Ovaries



To Be Used with Abnormal Tubes and/or Ovaries

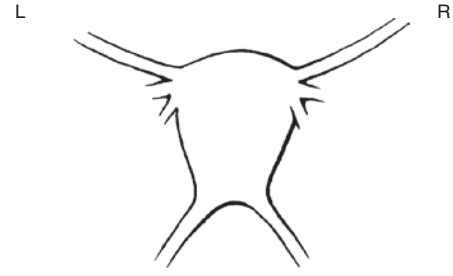


Fig. 20.2 The revised American Society for Reproductive Medicine (rASRM) score for endometriosis

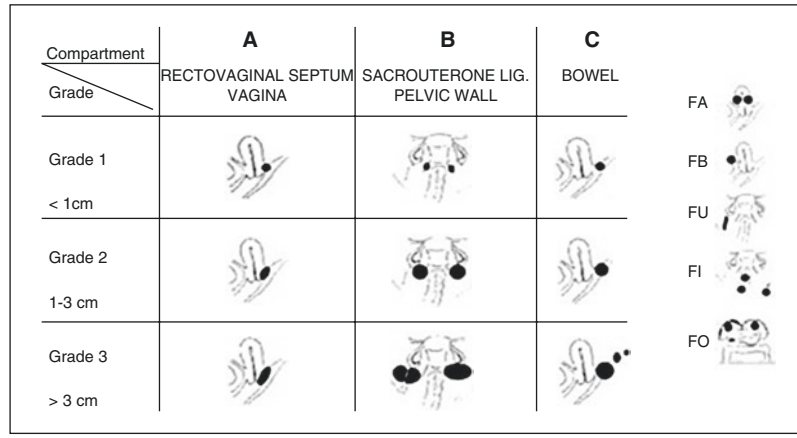


Fig. 20.3 The Enzian classification

20.4.2 Physical Examination

20.4.2.1 The Gynecologist

Patients suspected to have endometriosis should ideally first attend a gynaecologist with a specialist interest. A finding of pelvic tenderness, a fixed retroverted uterus, tender uterosacral ligaments or enlarged ovaries leads to a potential diagnosis of DIE. The diagnosis is more certain if deeply infiltrating nodules are found on the uterosacral ligaments or in the pouch of Douglas, and/or visible lesions are seen in the vagina or on the cervix, however, physical examination is often inconclusive because lesions, most lesions are inaccessible to digital pelvic examination and colposcopy.

20.4.2.2 The Colorectal Surgeon

Since medical management of bowel endometriosis is currently emperic, the expectant management should be carefully balanced with the grade of symptoms by the specialist gynecologist who has the role of referring patients to the colorectal surgeon (CRS) when severe intestinal DIE is suspected.

Pelvic nodules are detected either through direct palpation or by causing pelvic pain on palpation of the anterior rectal wall. Bimanual digital exploration allows evaluation of involvement of the rectovaginal septum. The integrity and function of the anal sphincters is also checked during the examination: this is extremely important should a low rectal resection become necessary.

The clinical exam is completed by a rigid proctoscopy. Visualization of the mucosa allows diagnosis of potential causes of rectal bleeding. Rectal distention by air insufflation may trigger pelvic pain, while palpation of the anterior rectal wall with the proctoscope helps to localize the level of involvement by measuring its distance from the anus.

The surgeon has to confirm the clinical diagnosis of DIE through an appropriate patient history and clinical examination including a proctoscopy; subsequently the CRS has to evaluate a presumable level of intestinal involvement in order to plan the appropriate type of procedure especially when the rectum is affected. Only at this stage the surgeon is able to discuss the case with the patient providing detailed information about the type of surgery and its possible related complications for achieving an appropriated consent.

20.4.3 Imaging

Transvaginal sonography (TVS) performed after bowel preparation should be the first-line imaging examination and is the best imaging modality for identifying intestinal lesions, determining the depth of bowel wall invasion and the circumference of involved bowel. This method allows dynamic evaluation from the anal verge to the sigmoid with high spatial resolution and minimal patient discomfort. The proximity between the

transducer and the targeted structure provides superior contrast resolution, which is important for visualizing small and laterally located lesions. A useful tool for preoperative mapping of endometriosis by TVS (the Endometriosis Surgical-Ultrasonographic System) has recently been developed with the specific aim of creating a common language so that physicians who are dedicated to the diagnosis and treatment of patients with severe endometriosis can accurately share clinical data. It gives clinicians the opportunity to decide on the best surgical approach, to evaluate the potential need to involve other surgical specialists (general surgeon or urologist), to establish a tailored management of the disease, and to properly inform patients of the extent of the disease and therapeutic options [14].

TVS is as accurate as transrectal US for diagnosing intestinal lesions and identifying the bowel layers affected, and it yields better results than magnetic resonance (MR) imaging for the assessment of deeply infiltrating endometrial implants in other pelvic locations, especially small (<1.5-cm-diameter) lesions of the uterosacral ligament and bladder [15]. MR imaging is an excellent method for identifying old hemorrhagic content that characterizes endometriomas and for mapping multiple DIE implants, given its large field of view, multiplanar capabilities, and outstanding contrast resolution. Extensive pelvic adhesions and ureteral involvement are two important indications for MR imaging [16]. In DIE lesions are mostly hypoechoic in comparison with the myometrium: on MR images, they have signal intensity similar to that of smooth muscle, with low signal intensity on T2-weighted images, intermediate signal intensity on T1-weighted images, and minimal enhancement after the intravenous injection of contrast material. Cystic areas may be present, with or without hemorrhagic content.

MR imaging is less sensitive than endorectal ultrasound (ERUS) for DIE in the rectal wall but is more specific, up to 95 % [3]. The MR sensitivity may be improved with by use of endocavity probes [16] or with intra-rectal contrast [17] (Fig. 20.4). Since intestinal involvement is often associated with multifocal disease, MR imaging

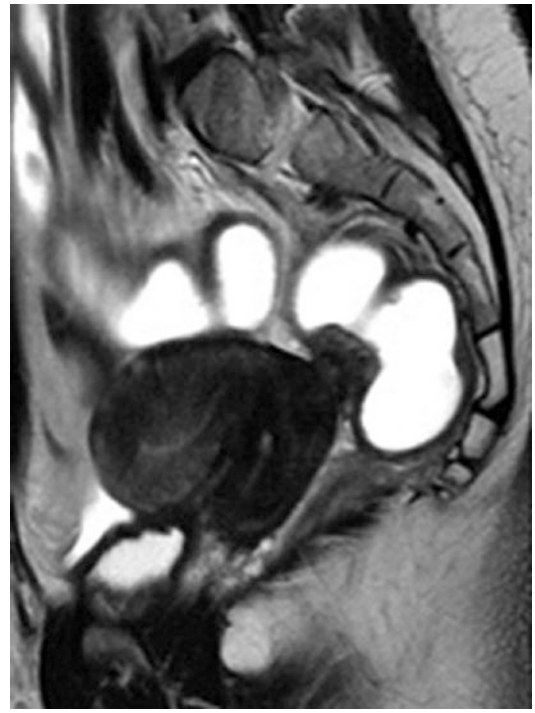


Fig. 20.4 Double contrast pelvic MRI showing the presence and the grade of rectal infiltration by a DIE nodule

is essential for complete staging of disease. ERUS is the standard technique to evaluate DIE of the rectal muscular layer with 97 % sensibility and 85 % specificity [18]. TVS may have similar sensitivity and specificity for rectal endometriosis with less patient discomfort and in expert hands could replace ERUS [7]. CT scan is of less value and is used when MRI is impracticable or for specific sites (e.g. urethral involvement) [17].

20.5 Treatment

Management of patients with endometriosis is multidisciplinary, ideally performed in specialist referral centres [19]. It is very important to identify the objectives and the expectations of the woman at this stage. The planned treatment must take into account any desire for pregnancy, the presence of other infertility associated factors, multifocal lesions and heterogeneity of the disease. Endometriosis is not a malignant condition and radical surgery can have major complications

(intestinal, urinary, vascular), therefore the patient must be involved in the decision on her own 'customised' treatment.

20.5.1 Medical Treatment

Endometriosis is an estrogen-dependent disease that tends to disappear with menopause. Medical treatments, based on the concept that the eutopic and ectopic endometrium respond similarly to sex hormones, are hormonal and based on blocking ovarian function. Several therapeutic classes are available (combined oral oestroprogestative, GnRH analogues etc.) and offer free intervals from pain causing atrophy of endometriotic implants. Their effectiveness is similar, so the choice is based on cost and balance of side effects [20]; in this context, combined oral contraception is often used initially [11]. In infertile patients, in vitro fertilization may be considered either before or following surgery for DIE [21].

20.5.2 Surgery

Bowel surgery should only proceed on the basis of shared decision-making after thorough consideration of risks versus benefits, ideally following multi-disciplinary consultations and full information to the patient who shares the final decision. The role of a purely diagnostic laparoscopy has been questioned and, ideally, there should always be the option of continuing to surgical removal of endometriosis, within the limitations of the surgeon's expertise. It is also important, particularly in cases of more severe endometriosis, that surgeons consider the option of limiting surgical excision at an initial operation in order to refer to a surgeon better equipped to deal with endometriosis, as a single radical surgery has been shown to deliver the greatest benefit [22]. Surgery in the follicular phase of the menstrual cycle avoids the presence of a hemorrhagic corpus luteum and one study suggested an increased recurrence rate for surgery undertaken in the luteal phase, possibly due to re-implantation through retrograde loss of endometrial tissue at subsequent menses while the sites of surgically removed lesions are healing [23].

The experience of the surgeon is critical in a decision for local removal of a nodule infiltrating the intestinal wall as incomplete resection may not relieve symptoms [24], while radical intervention increases the risk of major complications such as ureteric and rectal injuries.

First operations tend to produce a better response than subsequent surgical procedures, with pain improvements at 6 months in the region of 83 % for first excisional procedures versus 53 % for second procedures [22, 25]. Excessive numbers of repeated laparoscopic procedures should therefore be avoided.

The surgical options for treating DIE in the bowel include peeling, disc excision or segmental excision and re-anastomosis. The *peeling technique* has the advantage that it avoids opening the bowel but it carries a risk of incomplete excision [6] and bowel microperforation that may not be recognized potentially leading to post-operative pelvic peritonitis. The hydropneumatic test (visualization of bubbles in the pelvis filled with water after air insufflation of the rectum) may be used to identify microperforation but is not always diagnostic and resection may be considered as safer in some cases.

Nezhat et al. [26] were the first to report a case series of eight patients treated with laparoscopic *disk excision* for endometriosis affecting the anterior colonic wall. Anterior rectal wall excision using a circular stapler was first proposed by Gordon et al. [27] to avoid the risks of a low extraperitoneal anastomosis in cases of nodular endometriosis invading the rectovaginal septum. Others [28, 29] have confirmed the feasibility of laparoscopic full thickness disk excision of endometriosis. The upper limit of the size of the lesion that can be removed is questionable and subjective because it is assessed visually, but it is generally agreed that lesions excised in this way should not exceed 2–3 cm in diameter and should not involve more than one-half of the circumference of the rectum. Disk excision may result in incomplete excision as endometriosis may infiltrate the large bowel wall preferentially along the myenteric plexus up to 3 cm from the palpated lesion [30].

The decision to carry out *segmental bowel resection* should be individualized. A decision to resect is supported by the depth of nodular infiltration, size and multicentricity of nodules, and the risk of incomplete excision [31]. Currently, only a complete surgical resection based on removal of all endometriosis lesions is considered adequate to controls the symptoms [32, 33] and prevent recurrence [34, 35]. The issue of how to treat lymph node involvement is unresolved as the clinical importance of lymph node involvement is not yet clarified [36].

The variety and depth of infiltration into other organs is testified by the number of previous surgical interventions, up to 82% in the series reported by Dousset et al. [37] and by the number of synchronous procedures on the reproductive and urinary organs. Ileocolic locations should be searched carefully intraoperatively because preoperative imaging fails to identify these in over 50% of cases. These may be treated by appendectomy, caecal, ileal or ileocaecal resection depending on the location.

Patients with DIE and rectal involvement may require a sub-total or total proctectomy depending on the level of lesion in relation to the anal sphincter with subsequent low or ultralow coloanal anastomosis. The resection may be extended "en block" to posterior vaginal cul-de-sac, uterosacral ligaments or sigmoid when involved; this is extensive surgery and requires in most cases a protective temporary ileostomy to prevent the sequele of an anastomotic leak or a rectovaginal fistula.

The ureters should always be identified and followed distally to ensure the absence of infiltration by endometriotic nodule. Extrinsic involvement is treated with a "decompression" protected by a double J stent. Intrinsic ureteral involvement is treated by resection followed by ureteral-bladder reimplantation or nephrectomy in case of chronic ureterohydronephrosis. During mobilization, the hypogastric plexus should be identified and preserved to avoid sexual or urinary functional alteration such as peripheral neurogenic bladder. This may be achieved by preserving the superior haemorrhoidal artery. Post operative neurogenic bladder is more common following proctectomy with coloanal anastomosis, total hysterectomy and presence of up to four DIE pelvic locations [37].

In mobilizing the rectum, dissection in the avascular mesorectal 'holy plane' is important to minimise autonomic nerve injury. When the recto-vaginal septum is involved, posterior isolation of the rectum below the nodule is advised and once the nodule is freed from the vaginal wall, the rectum is already mobilized and ready for "en block" resection.

Treatment of adnexal lesions is as conservative as possible combining, ovarian cystectomy, oophorectomy, and/or salpingectomy as required. Non-conservative hysterectomy is performed only in selected patients of more than 40 years old, in case of bilateral adnexal involvement and absence of desire for pregnancy. The presence of DIE involving the bladder is treated by partial cystectomy [38]. All superficial peritoneal lesions should be treated with ablation or excision.

Laparoscopic assisted surgery is ideal in DIE as postoperatively there are fewer peritoneal adhesions (a possible cause of further symptoms), faster recovery, enhanced fertility and better cosmesis. In the only prospective randomized trial to compare open versus laparoscopically-assisted colorectal resection for endometriosis, the patients in the laparoscopic group required less use of parenteral narcotics, had fewer grade 3 complications, and lower median blood loss, in addition to improved fertility [39]. Furthermore, the reduction of adhesion formation following laparoscopy is just as important for patients at risk of further subsequent surgery as is cosmetics in these usually very young patients [40]. Wills [41] reports an 11% conversion rate in 81 rectal resections, 81.4% of which were performed laparoscopically. A review of the literature found the conversion rate to range between 0% and 20%, with an estimated mean of 7.8% [42].

In order to minimize alterations of the abdominal wall, removal of the specimen through the vagina after rectal or colon resection has also been proposed: in one study, conducted on 33 patients, postoperative dyspareunia was not found [43].

20.6 Results

20.6.1 Morbidity

Generally, the surgical complication rates are higher following colorectal resection for DIE than for cancer surgery. Dousset et al. reported **early complications** in 16%, with anastomotic leaks in 2%, rectovaginal fistula in 4%, and reoperations in 7% of 100 cases [37]. A review by Emmanuel and Davis [44], found morbidity rates between 10% and 30%, while Jerby et al. reported lower complications rate after laparoscopic resection surgery [45]. The incidence of anastomotic fistula varies between 0% and 17%, while the incidence of a recto vaginal fistula is greater than 10%. More than 30% of patients experience post operative changes in urinary and intestinal function. It is difficult to discriminate between the effects of resection from the other associated procedures when considering the remission of symptoms in resected patients. Neurologic bladder has been reported in 16–29% of cases [37, 46].

20.6.2 Functional Outcome

There are relatively few studies of **long-term outcome** following colorectal resection for DIE. Complete remission of pelvic pain after intestinal resection has been reported [37, 47–49] with significant improvement in quality of life measured by the QOL SF-36 instrument [50]. Although RCTs have failed to demonstrate the benefit of excision over ablation [51, 52], there is consensus that lesions should be excised where possible, especially DIE [53]. However, even after expert removal of endometriosis, there may be **recurrence** of symptoms and endometriotic lesions that varies from 10% to 55% within 12 months [54], with recurrence affecting 10% of the remaining women each additional year [55]. The risk of needing further surgery is higher in women younger than 30 years at the time of surgery [56, 57], the most frequent indications being a need for hysterectomy or division of intestinal adhesions [37, 49].

20.6.3 Fertility

While some **defecatory symptoms** may improve following surgery, especially irregular bowel habit and pain on defecation, constipation may increase postoperatively [58]. The reasons are unclear but may reflect anterior rectal resection or autonomic denervation. The effect on constipation seems unrelated to the level of resection, however the outcome does not generally have a significant impact on quality of life.

It is difficult to relate **fertility** to DIE surgery since rates range between 23 and 48 [49, 50, 58]. In a randomized trial comparing laparoscopic versus open resection for DIE with rectal involvement, Darai et al. [39] reported a 20% fertility rate in women with infertility, which rose to 60% after laparoscopic surgery. Fewer adhesions and faster recovery could explain the improvement, suggesting that laparoscopy, besides age, duration of infertility and adenomyosis, may be a determinant factor of fertility outcome [59]. It is therefore very difficult to evaluate the impact of intestinal resection on fertility and further studies are needed.

Conclusions

The management of endometriosis requires specialized multidisciplinary treatment. Surgical treatment of bowel endometriosis is associated with a significant rate of complications and any woman undergoing this type of surgery must be fully informed of the possible risks and complications. Surgery for DIE should be undertaken only after a complete preoperative mapping of the disease, a thorough evaluation and should be performed laparoscopically when possible. While successful in treating symptoms with a low risk of recurrence, surgery is always an extensive procedure with a potential morbidity. An experienced team can avoid the pitfalls of inadequate or incomplete surgery and achieve low morbidity rates, especially at the first surgery, since subsequent surgery is more difficult and associated with a higher risk of poor outcome. With this philosophy, different

specialists constitute part of an overall solution in the treatment plan for each patient to manage their individual symptomatic profile.

References

1. Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. Best Pract Res Clin Obstet Gynaecol. 2004;18:177–200.
2. Chamiè LP, Blasbalg R, Mendes Alves Pereira R, Warmbrand G, Serafini PC. Findings of pelvic endometriosis at transvaginal US, MR imaging and laparoscopy. Radiographics. 2011;31:E77–100.
3. Chapron C, Vieira M, Chopin N, Balleyguier C, Barakat H, Dumontier I, et al. Accuracy of rectal endoscopic ultrasonography and magnetic resonance imaging in the diagnosis of rectal involvement for patients presenting with deeply infiltrating endometriosis. Ultrasound Obstet Gynecol. 2004;24:175–9.
4. Bianconi L, Hummelshoj L, Coccia ME, Vigano P, Vittori G, Veit J, Music R, Tomassini A, D'Hooghe T. Recognizing endometriosis as a social disease: the European Union-encouraged Italian Senate approach. Fertil Steril. 2007;88:1285–7.
5. Bergqvist A. Extragenital endometriosis. A review. Eur J Surg. 1992;158:7–12.
6. Chapron C, Chopin N, Borghese B, Foulot H, Dousset B, Vacher-Lavenu MC, Vieira M, Hasan W, Bricou A. Deeply infiltrating endometriosis: pathogenetic implications of the anatomical distribution. Hum Reprod. 2006;21:1839–45.
7. Piketty M, Chopin N, Dousset B, Millischer-Bellaische AE, Roseau G, Leconte M, Borghese B, Chapron C. Preoperative work-up for patients with deeply infiltrating endometriosis: transvaginal ultrasonography must definitely be the first-line imaging examination. Hum Reprod. 2009;24:602–7.
8. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. Fertil Steril. 1997;67(5):817–21.
9. Haas D, Shebl O, Shamiyeh A, Oppelt P. The rASRM score and the Enzian classification for endometriosis: their strengths and weaknesses. Acta Obstet Gynecol Scand. 2013;92:3–7.
10. Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. Fertil Steril. 2006;86:1296–301.
11. Vercellini P, Somigliana E, Vigano P, Abbiati A, Daguati R, Crosignani PG. Endometriosis: current and future medical therapies. Best Pract Res Clin Obstet Gynaecol. 2008;22:275–306.
12. Gelbaya TA, El-Halwagy HE. Focus on primary care: chronic pelvic pain in women. Obstet Gynecol Surv. 2001;56:757–64.
13. Roman H, Ness J, Suciu N, Bridoux V, Gourceroi G, Leroi AM, Tuech JJ, Ducrotté P, Savoye-Collet C, Savoye G. Are digestive symptoms in women presenting with pelvic endometriosis specific to lesion localizations? A preliminary prospective study. Hum Reprod. 2012;27:1–10.
14. Exacoustos C, Malzoni M, Di Giovanni A, Lazzeri L, Tosti C, Petraglia F, Zupi E. Ultrasound mapping system for the surgical management of deep infiltrating endometriosis. Fertil Steril. 2014;102:143–50.
15. Chamiè LP, et al. Transvaginal US after bowel preparation for DIE: protocol, imaging appaerances and laparoscopic correlation. Radiographics. 2010;30:1235–49.
16. Balleyguier C, Chapron C, Dubuisson JB, Kinkel K, Fauconnier A, Vieira M. Comparison of magnetic resonance imaging and transvaginal ultrasonography in diagnosing bladder endometriosis. J Am Assoc Gynecol Laparosc. 2002;9:15–23.
17. Biscaldi E, Ferrero S, Leone Roberti Maggiore U, Remorgida V, Venturini PL, Rollandi GA. Multidetector computerized tomography enema versus magnetic resonance enema in the diagnosis of rectosigmoid endometriosis. Eur J Radiol. 2014;83:261–7.
18. Schroder J, Lohnert M, Doniec JM, Dohrmann P. Endoluminal ultrasound diagnosis and operative management of rectal endometriosis. Dis Colon Rectum. 1997;40:614–7.
19. D'Hooghe T, Hummelshoj L. Multi-disciplinary centres/networks of excellence for endometriosis management and research: a proposal. Hum Reprod. 2006;21:2743–8.
20. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod. 2005;20:2698–704.
21. De Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. Lancet. 2010;376:730–8.
22. Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. Fertil Steril. 2004;82:878–84.
23. Johnson NP, Hummelshoj L, World Endometriosis Society Montpellier Consortium. Consensus on current management of endometriosis. Hum Reprod. 2013;28:1552–68.
24. Vercellini P, Fedele L, Aimi G, De Giorgi O, Consonni D, Crosignani PG. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. Hum Reprod. 2006;21:2679–85.
25. Wills HJ, Reid GD, Cooper MJ, Morgan M. Fertility and pain outcomes following laparoscopic segmental bowel resection for colorectal endometriosis: a review. Aust N Z J Obstet Gynaecol. 2008;48:292–5.
26. Nezhat, Nezhat F, Ambroze W, Pennington E. Laparoscopic repair of small bowel and colon: a report of 26 cases. Surg Endosc. 1993;7:88–9.
27. Gordon SJ, Maher PJ, Woods R. Use of the CEEA stapler to avoid ultra-low segmental resection of a full-thickness rectal endometriotic nodule. J Am Assoc Gynecol Laparosc. 2001;8:312–6.

28. Landi S, Pontrelli G, Surico D, Ruffo G, Benini M, Soriano D, Mereu L, Minelli L. Laparoscopic disk resection for bowel endometriosis using a circular stapler and a new endoscopic method to control postoperative bleeding from the stapler line. J Am Coll Surg. 2008;207:205–9.
29. Woods RJ, Heriot AG, Chen FC. Anterior rectal wall excision for endometriosis using the circular stapler. ANZ J Surg. 2003;73:647–8.
30. Anaf V, El Nakadi I, Simon P, et al. Preferential infiltration of large bowel endometriosis along the nerves of the colon. Hum Reprod. 2004;19:996–1002.
31. Abrao MS, Podgaec S, Dias Jr JA, Gonçalves MO. Diagnosis of rectovaginal endometriosis. Hum Reprod. 2008;23:2386.
32. Abbott J, Hawe J, Clayton R, Garry R. The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with 2–5 year follow-up. Hum Reprod. 2003;9:1922–7.
33. Chopin N, Vieira M, Borghese B, Foulot H, Dousset B, Coste J, et al. Operative management of deeply infiltrating endometriosis: results on pelvic pain symptoms according to a surgical classification. J Minim Invasive Gynecol. 2005;12:106–12.
34. Chapron C, Fauconnier A, Dubuisson JB, Barakat H, Vieira M, Bréart G. Deep infiltrating endometriosis: relation between severity of dysmenorrhoea and extent of disease. Hum Reprod. 2003;18:760–6,73.
35. Garry R, Clayton R, Hawe J. The effect of endometriosis and its radical laparoscopic excision on quality of life indicators. BJOG. 2000;107:44–54.
36. Noel JC, Chapron C, Fayt I, Anaf V. Lymph node involvement and lymphovascular invasion in deep infiltrating rectosigmoid endometriosis. Fertil Steril. 2008;89:1069–72.
37. Dousset B, Leconte M, Borghese B, Millischer AE, Roseau G, Arkwright S, Chapron C. Complete surgery for low rectal endometriosis: long-term results of a 100-case prospective study. Ann Surg. 2010;251:887–95.
38. Chapron C, Bourret A, Chopin N, Dousset B, Leconte M, Amsellem-Ouazana D. Surgery for bladder endometriosis: long-term results and concomitant management of associated posterior deep lesions. Hum Reprod. 2010;25:884–9.
39. Daraï E, Dubernard G, Coutant C, Frey C, Rouzier R, Ballester M. Randomized trial of laparoscopically assisted versus open colorectal resection for endometriosis: morbidity, symptoms, quality of life, and fertility. Ann Surg. 2010;251:1018–23.
40. Dowson HM, Bong JJ, Lovell DP, Worthington TR, Karanjia ND, Rockall TA. Reduced adhesion formation following laparoscopic versus open colorectal surgery. Br J Surg. 2008;95:909–14.
41. Wills HJ, Reid GD, Cooper MJW, Tsaltas J, Morgan M, Woods RJ. Bowel resection for severe endometriosis: an Australian series of 177 cases. Aust N Z J Obstet Gynaecol. 2009;49:415–8.
42. Daraï E, Bazot M, Rouzier R, Houry S, Dubernard G. Outcome of laparoscopic colorectal resection for endometriosis. Curr Opin Obstet Gynecol. 2007;19:308–13.
43. Ghezzi F, Cromi A, Ciravolo G, et al. A new laparoscopic-transvaginal technique for rectosigmoid resection in patients with endometriosis. Fertil Steril. 2008;90:1964–8.
44. Emmanuel KR, Davis C. Outcomes and treatment options in rectovaginal endometriosis. Curr Opin Obstet Gynecol. 2005;17:399–402.
45. Jerby BL, Kessler H, Falcone T, Milsom JW. Laparoscopic management of colorectal endometriosis. Surg Endosc. 1999;13:1125–8.
46. Dubernard G, Rouzier R, David-Montefiore E, Bazot M, Daraï E. Urinary complications after surgery for posterior deep infiltrating endometriosis are related to the extent of dissection and to uterosacral ligaments resection. J Minim Invasive Gynecol. 2008;15:235–40.
47. Fleisch MC, Xafis D, De Bruyne F, Hucke J, Bender HG, Dall P. Radical resection of invasive endometriosis with bowel or bladder involvement-long-term results. Eur J Obstet Gynecol Reprod Biol. 2005;123:224–9.
48. Koh CE, Juszczyk K, Cooper MJ, Solomon MJ. Management of deeply infiltrating endometriosis involving the rectum. Dis Colon Rectum. 2012;55:925–31.
49. Varol N, Maher P, Healey M, Woods R, Wood C, Hill D, Lolatgis N, Tsaltas J. Rectal surgery for endometriosis-should we be aggressive? J Am Assoc Gynecol Laparosc. 2003;10:182–9.
50. Dubernard G, Rouzier R, David-Montefiore E, Bazot M, Darai E. Use of the SF-36 questionnaire to predict quality-of-life improvement after laparoscopic colorectal resection for endometriosis. Hum Reprod. 2008;23:846–51.
51. Wright J, Lotfallah H, Jones K, Lovell D. A randomized trial of excision versus ablation for mild endometriosis. Fertil Steril. 2005;83:1830–6.
52. Healey M, Ang WC, Cheng C. Surgical treatment of endometriosis: a prospective randomized double-blinded trial comparing excision and ablation. Fertil Steril. 2010;94:2536–40.
53. Koninckx PR, Ussia A, Adamyan L, Wattiez A, Donnez J. Deep endometriosis: definition, diagnosis, and treatment. Fertil Steril. 2012;98:564–71.
54. Vercellini P, Barbara G, Abbiati A, Somigliana E, Viganò P, Fedele L. Repetitive surgery for recurrent symptomatic endometriosis: what to do? Eur J Obstet Gynecol Reprod Biol. 2009;146:15–21.
55. Guo SW. Recurrence of endometriosis and its control. Hum Reprod Update. 2009;15:441–61.
56. Shakiba K, Bena JF, McGill KM, Minger J, Falcone T. Surgical treatment of endometriosis: a 7-year follow-up on the requirement for further surgery. Obstet Gynecol. 2008;111:1285–92.
57. Jatan AK, Solomon MJ, Young J, Cooper M, Pathma-Nathan N. Laparoscopic management of rectal endometriosis. Dis Colon Rectum. 2006;49:169–74.
58. Armengol-Debeir L, Savoye G, Leroi AM, Gourcerol G, Savoye-Collet C, Tuech JJ, Vassilieff M, Roman H. Pathophysiological approach to bowel dysfunction after segmental colorectal resection for deep endometriosis infiltrating the rectum: a preliminary study. Hum Reprod. 2011;26:2330–5.
59. Ferrero S, Anserini P, Abbamonte LH, Ragni N, Camerini G, Remorgida V. Fertility after bowel resection for endometriosis. Fertil Steril. 2009;92:41–6.

Appendicitis

21

P. Ronan O'Connell

21.1 Introduction

The appendix has long been considered to be a vestigial organ with little or no physiological function; its importance to surgery is related only to a potential to become inflamed, causing abdominal pain and on occasion progressing to perforation, causing peritonitis. However, there is an increasing body of evidence that indicates roles for the appendix in early maturation of the gut immune system and as a repository for the colonic microbiome [1]. These functions may be of relevance in the apparent protective effects of childhood appendicectomy against later development of ulcerative colitis [2] and deleterious effects on recovery from *Clostridium difficile* infection and other infectious colitides [3]. New genetic and proteomic sequencing techniques, coupled with bioinformatic analysis, will undoubtedly provide greater insights into the physiology of the appendix in health and its role in the pathophysiology of appendicitis and other intestinal diseases.

P.R. O'Connell, MD, FRCSI
School of Medicine and Medical Sciences, University College Dublin, Elm Park, Dublin 4, Ireland

St Vincent's University Hospital,
Elm Park, Dublin 4, Ireland
e-mail: ronan.oconnell@ucd.ie

21.2 Incidence and Etiology

Acute appendicitis is the most common acute abdominal surgical diagnosis, with over 300,000 patients diagnosed annually in the United States. The incidence increased greatly during the first half of the twentieth century; however; there has been an as yet unexplained decrease in the rate of diagnosis in the past 30 years. Acute appendicitis is relatively rare before the age of 2 years and is most common during late teenage and early adult life. Notwithstanding the frequency of right iliac fossa pain in young females, the incidence of appendicitis is marginally greater in males.

Relatively little is known about the pathophysiology of appendicitis, first described by Reginald Fitz in 1886 as a "perforating inflammation of the vermiform appendix." The incidence of appendicitis, like that of diverticulitis, is less in societies that consume a relatively high-fiber diet; however, this may prove to be a coincident observation and reflect differing microbiota, levels of hygiene, gut immune maturity, or achievement of an early diagnosis. Many episodes of appendicitis resolve spontaneously (just as with diverticulitis), and a history of right iliac fossa pain is not uncommon.

The most widely accepted theory relating to the etiology of appendicitis is that a relative obstruction of the appendiceal lumen, due to lymphoid hyperplasia, a bolus obstruction, or a fecolith, results in mucus accumulation, bacterial

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_21

overgrowth, and mucosal ulceration. Progression to necrosis and perforation occurs when intramural pressure increases, obstructing lymphatic and venous return and leading to ischemic necrosis. Seasonal variation in the incidence, coupled with the clustering of cases, especially in children, suggests a possible, as yet unidentified infective agent. Recent research has found significant variations in microbiota and differences in the expression of antimicrobial peptides between healthy and inflamed appendix samples [4]. Whether these changes are secondary to the inflammatory process or underlie the etiology remains to be determined.

21.3 Diagnosis

The diagnosis of appendicitis has traditionally relied on clinical assessment. Typically, symptoms begin with poorly localized, colicky abdominal pain accompanied by anorexia and mild systemic features of inflammation. The initial visceral pain reflects distention of the appendix; however, as appendiceal inflammation develops, the parietal peritoneum becomes inflamed, leading to more localized somatic sensation. The classical location is in the right iliac fossa, but the position of the appendix is not constant, and a pelvic or retroperitoneal location frequently causes difficulty in clinical diagnosis.

Two syndromes of acute appendicitis can be distinguished: nonobstructive and obstructive. The latter has a more acute presentation, with frequent progression to perforation. This form is commonly associated with the presence of a fecolith that may be identified on a supine abdominal radiograph or computed tomography (CT) scan (Fig. 21.1).

A number of clinical signs described in the era before widely available cross-sectional imaging are used to assist in clinical diagnosis (Table 21.1). In the modern era these are of more historical interest; however, localized tenderness with rebound (not to be repeated) remains a cardinal feature.

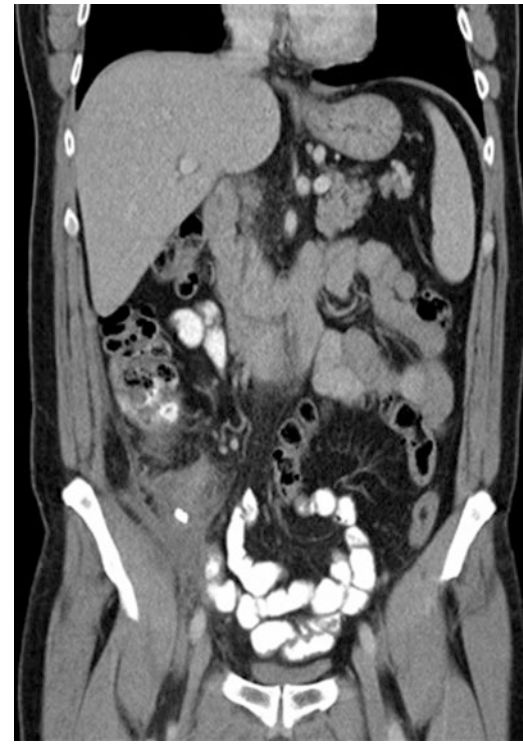


Fig. 21.1 Computed tomography scan of the lower abdomen showing a calcified fecolith at the center of an inflamed appendix mass in the right iliac fossa

Table 21.1 Clinical signs associated with appendicitis

Name	Description
Pointing sign	Patient points to the right iliac fossa when asked to locate the maximum point of tenderness
Dunphy sign	Pain in the right iliac fossa with coughing
Rovsing sign	Pain in the right iliac fossa in response to palpation of the left iliac fossa
Psoas sign	Patient lies with the right hip flexed; pain increases with passive extension of the right hip
Obturator sign	Increased pain with flexion and internal rotation of the right hip

21.3.1 Differential Diagnoses

The clinical diagnosis of appendicitis is challenging because of the extensive differential diagnosis, particularly in young children, the elderly, and women of childbearing age or who are pregnant.

In children, the most common differentials are mesenteric lymphadenitis, acute gastroenteritis, and, in those younger than age 2 years, ileocecal intussusception. Henoch-Schönlein purpura is often associated with right iliac fossa pain; an upper respiratory tract infection and a developing ecchymotic or purpuric rash on the limbs or buttocks usually precede this.

In adults, nonspecific ileitis, *Yersinia enterocolitica* infection, or acute presentation of Crohn's ileitis may be difficult to distinguish clinically; however, imaging is usually a diagnostic indicator of ileitis rather than appendicitis. Perforation of a duodenal ulcer may result in fluid tracking along the right paracolic gutter, whereas sigmoid diverticulitis is an important differential in patients over 40. Inflammation of a Meckel diverticulum may be indistinguishable from appendicitis.

In women of childbearing age, pelvic inflammatory disease, including salpingitis and tubo-ovarian sepsis, should be considered. Typically the pain is low and central within the abdomen. When suspected, a high vaginal swab should be taken and a gynecological opinion obtained. Treatment is usually a combination of ofloxacin and metronidazole orally for 14 days.

Mittelschmertz or midcycle pain is usually the result of a small intraperitoneal bleed following the rupture of a follicular cyst. A pregnancy test is negative and symptoms usually settle within hours. Pelvic ultrasound may demonstrate a small amount of free fluid in the pouch of Douglas. Rupture or torsion of an ovarian cyst or a right-sided tubal pregnancy may be difficult to distinguish, and pelvic ultrasound is helpful. Laparoscopy may be required as an early recourse for both diagnostic and therapeutic purposes.

Appendicitis is the most common abdominal surgical condition in pregnancy, occurring in approximately 1 in 2,000 pregnancies. Ultrasound and magnetic resonance imaging are helpful in establishing the diagnosis and guiding surgical intervention.

21.4 Investigation

While the diagnosis of appendicitis has traditionally been clinical, appendicectomy based on clinical criteria alone leads to a histologically normal appendix being removed in 15–30 % of cases. A number of clinical and laboratory-based scoring systems have been devised to assist in diagnosis [5]. The two most useful are the Alvarado score [6] and the Appendicitis Inflammatory Response (AIR) score [7] (Table 21.2).

Table 21.2 Comparison of parameters used in Alvarado and Appendicitis Inflammatory Response (AIR) scores for diagnosis of appendicitis

	Alvarado score [6]	AIR score [7]
Symptoms		
Nausea/vomiting	1	1
Anorexia	1	–
RIF pain	2	1
Shift to RIF	1	–
Signs		
Rebound tenderness	1	–
Guarding		
Mild	–	1
Moderate	–	2
Strong	–	3
Temperature		
>37.3 °C	1	–
>38.5 °C	–	–
Laboratory		
WBC count		
$>10.0\times10^9$/l	2	1
$\geq15.0\times10^9$/l		2
PMN leukocytes		
>75 %	1	–
70–84 %		1
≥85 %		2
CRP		
10–49 g/l	–	1
≥50 g/l	–	2
Score		
Total	10	12
Low risk	0–4	0–4
Medium risk	5–6	5–8
High risk	7–10	9–12

CRP C-reactive protein, *PMN* plymorphonuclear, *RIF* right iliac fossa, *WBC* white blood cell

While scoring systems in general do not sufficiently discriminate predictive values to be used alone to diagnose appendicitis, Kollar et al. [8] found that the AIR score is accurate in excluding appendicitis in those deemed low risk and more accurate at predicting appendicitis than the Alvarado score in those deemed high risk. They advocate use of the scoring systems for selective CT in those deemed medium risk.

21.5 Imaging

Widespread availability of ultrasound and cross-sectional imaging in modern emergency surgical units has led to the increasing use of and reliance on imaging in supporting a clinical decision to perform appendicectomy. Ultrasound does not expose the patient to ionizing radiation and is highly specific in children and young adults; however, Doria et al. [9] found in a meta-analysis that CT was more sensitive than ultrasound. Kim et al. [10], addressing concerns regarding the dosage of ionizing radiation in children and young adults, showed the noninferiority of low-dose CT to conventional CT in a large series of patients with clinical suspicion of appendicitis.

21.6 Treatment

The accepted treatment for a clinical diagnosis of acute appendicitis has been urgent open appendicectomy performed through an oblique or transverse incision in the right iliac fossa. If a normal appendix is found, other causes such as Crohn's disease, Meckel diverticulitis, or tubal or ovarian pathology should be excluded and the macroscopically normal appendix removed on the basis that removal prevents future diagnostic difficulties. This practice has led to "negative" appendicectomy rates of 15–30 % and has the potential for morbidity, particularly wound infection and long-term risk of adhesive intestinal obstruction. In the particular circumstance that an appendix phlegmon or mass is diagnosed preoperatively, the conventional wisdom is to manage expectantly with antibiotic treatment and subsequent interval appendicectomy.

A number of developments over the past 20 years have led to significant changes to this treatment algorithm. The first, as mentioned above, is the availability of ultrasound and cross-sectional imaging, which has increased diagnostic accuracy and facilitates percutaneous drainage of a periappendiceal or pelvic abscess. The second is the introduction of laparoscopy as both a diagnostic and a therapeutic technique. The third is recognition that medical treatment through the use of antibiotics and observation can be used as a bridge to surgery, thus reducing the volume of out-of-hours operations. Further, conservative treatment is successful in treating a significant proportion of patients with suspected appendicitis, thus avoiding surgery altogether.

21.6.1 Laparoscopic Versus Open Appendicectomy

The open surgical technique for appendicectomy described by McBurney in 1894 has changed little in succeeding years. While Semm described a laparoscopic technique for appendicectomy in 1983, it took many years for general surgeons to accept a laparoscopic approach to treating the appendix, and it was only when laparoscopy became routine for cholecystectomy that laparoscopic appendicectomy began to be widely performed. A large number of randomized trials and systematic reviews have been conducted comparing laparoscopic with open techniques. A recent Cochrane review [11] found small benefits in favor of a laparoscopic approach – shorter hospital stay, fewer wound infections, more rapid return to work, and a reduced risk of negative appendicectomy. However, the surgical procedure takes longer, the operative costs are higher, and there is a higher risk of intra-abdominal abscess formation postoperatively. These observations are in keeping with Andersson [12], who studied the Swedish National Patient Register of almost 170,000 patients over 16 years and found that the differences between open and laparoscopic approaches are small and of limited

clinical importance. Therefore the question of whether to perform an open or laparoscopic appendicectomy in an individual patient must come down to the particular circumstances of the patient, the available equipment, the patient's wishes, and the experience of individual surgeon. The reader is directed to textbooks on operative surgery for details on operative techniques.

21.6.2 "Out-of-Hours" Surgery

The question of the urgency of performing appendicectomy has been the subject of considerable research, as delays in accessing operating room time have been thought to contribute to adverse outcomes. Here it is important to distinguish a patient with peritonitis and clear evidence of perforation from a patient with more usual phlegmonous appendicitis. The former requires urgent intervention to control the origin of sepsis – as would be appropriate for any patient with a visceral perforation. Patients are more often treated with intravenous antibiotics while awaiting access to the operating room. Schnüriger et al. [13] found that restricting access to the operating room between 11:00 pm and 8:00 am did not adversely affect clinical outcomes. A similar study on behalf of the UK National Surgical Research Collaborative [14] found that a delay less than 24 h to appendicectomy did not increase the rate of complications.

21.6.3 Nonoperative Management

There are now several large randomized studies and meta-analyses of the nonoperative management of appendicitis. The largest of these, from Sweden [15], included 369 patients, of whom 202 received antibiotics and 167 went directly for surgery. Of those treated nonoperatively, 96 subsequently had an appendicectomy; overall, however, 48 % of the study cohort were successfully treated conservatively. In a large randomized study from France, Vons et al. [16] found that antibiotic treatment was not inferior to surgical treatment, but 29 % of those treated conservatively went on to have an appendicectomy within 1 year; of these, 87 % were found to have appendicitis. Di Saverio et al. [17], in the Non Operative Treatment for Acute Appendicitis study found that the long-term efficacy of nonoperative management was 83 % among 159 patients treated nonoperatively and followed for 2 years. In a review of the available literature, however, Fitzmaurice et al. [18] concluded that while nonoperative management is successful in a majority of patients, appendicectomy remains the mainstay of treatment.

21.7 Interval Appendicectomy

Convention has been that an elective appendicectomy should be performed 3–4 months following the resolution of an appendix abscess/phlegmon. This practice was based on the premise that the appendix was inherently diseased and that recurrence was likely. Kaminski et al. [19], in a study of nearly 33,000 patients with appendicitis, of whom 864 were managed nonoperatively, only 39 (5 %) had a recurrence requiring appendicectomy. They concluded that routine interval appendicectomy after successful nonoperative treatment is not justified.

A second – and more important – consideration in older patients, is that malignancy, although rare, cannot be excluded. This concern has largely been overcome by the accuracy of cross-sectional imaging and colonoscopy, both of which should be performed once the acute inflammatory episode has resolved.

21.8 Postoperative Complications

The large majority of patients recover quickly following appendicectomy. Mortality is extremely rare and is almost always related to preexisting comorbidities [20]. Approximately 8 % of patients, however, develop a late wound infection or intraperitoneal collection. It is always

wise to advise patients of this possibility and to reattend if there is reason for concern. Superficial wound infections should be treated with antibiotics as appropriate. Use of a wound-protecting shield or endoscopic specimen delivery device to deliver the inflamed appendix at the time of operation is a wise precaution, and perioperative antibiotic treatment should be extended in patients with perforated or gangrenous appendicitis. Early cross-sectional imaging can identify a local, pelvic, or subphrenic collection that can usually be drained percutaneously.

A postoperative ileus is relatively rare, especially if the operation was performed laparoscopically. If the ileus is associated with signs of systemic inflammatory response or sepsis, there must always be a concern regarding visceral injury – usually inadvertent small-bowel perforation – during a difficult dissection. A high index of suspicion and early reintervention guided by imaging is needed. Bleeding from the appendicular artery may lead to a pelvic hematoma or, rarely, hematoperitoneum. Resuscitation and reoperation to arrest further bleeding and evacuate the hematoma are required. Conservative management of an intraperitoneal or pelvic hematoma usually results in a prolonged ileus and a consequent hospital stay.

Portal pyemia is a rare but serious complication of gangrenous appendicitis. It is associated with systemic sepsis and jaundice and may lead to intrahepatic abscess formation. Systemic broad-spectrum antibiotic treatment is required, and anticoagulation should be considered to prevent or treat portal venous thrombosis.

21.9 Special Considerations

21.9.1 Appendicolith

Great care should be taken to ensure that an appendicolith, if present, is removed at the time of operation. This is particularly important if the appendix is perforated because if left in place, the appendicolith may act as a nidus for future intra-abdominal sepsis.

21.10 Crohn's Disease

With the availability of preoperative imaging, it is unusual to make an interoperative diagnosis of terminal ileal Crohn's disease at the time of appendicectomy. Conventional wisdom has been to remove the appendix if the cecum is healthy and an open approach has been used. With a laparoscopic approach, most surgeons would record the findings, leave the appendix in situ, and treat the patient medically.

21.10.1 Mucocele of the Appendix

A mucocele of the appendix should be removed in the usual way, taking care not to rupture it during removal. Use of an endoscopic specimen delivery device is recommended. Occasionally the base may be too wide to allow closure with a ligature, in which case it may be appropriate to transect the base with either an open or endoscopic stapling device.

21.11 Appendiceal Malignancy

The appendix is the most common site of a carcinoid tumor detected once in every 300–400 appendices examined histologically. Approximately 50 % present as appendicitis; the remainder are incidentally found on imaging or during laparotomy/laparoscopy. Unlike carcinoids arising elsewhere in the body, appendiceal carcinoids rarely give rise to metastases. Tumors less than 2 cm in diameter, without mesoappendiceal or cecal involvement, can be treated with simple appendicectomy; otherwise right hemicolectomy is indicated.

Mucinous neoplasms are the second most common type of tumor of the appendix. Their malignant potential ranges from lowgrade appendiceal mucinous neoplasms to disseminated peritoneal malignancy resulting in pseudomyxoma peritonei. These tumors constitute a particularly difficult challenge, and referral to a regional specialist unit should be considered. Chapter 29 sets out the management options in more detail.

Appendiceal adenocarcinoma is rare, found in approximately 0.1 % of appendectomies. Treatment is by right hemicolectomy, as for cecal carcinoma.

References

1. Bollinger RR, Barbas AS, Bush EL, Lin SS, Parker W. Biofilms in the normal human large bowel: fact rather than fiction. Gut. 2007;56(10):1481–2.
2. Frisch M, Pedersen BV, Andersson RE. Appendicitis, mesenteric lymphadenitis, and subsequent risk of ulcerative colitis: cohort studies in Sweden and Denmark. BMJ. 2009;338:b716.
3. Seretis C, Seretis F, Goonetilleke K. Appendicectomy and clostridium difficile infection: is there a link? J Clin Med Res. 2014;6(4):239–41.
4. Arlt A, Bharti R, Ilves I, Hasler R, Miettinen P, Paajanen H, et al. Characteristic changes in microbial community composition and expression of innate immune genes in acute appendicitis. Innate Immun. 2015;21(1):30–41.
5. Wray CJ, Kao LS, Millas SG, Tsao K, Ko TC. Acute appendicitis: controversies in diagnosis and management. Curr Probl Surg. 2013;50(2):54–86.
6. Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med. 1986;15(5):557–64.
7. Andersson M, Andersson RE. The appendicitis inflammatory response score: a tool for the diagnosis of acute appendicitis that outperforms the Alvarado score. World J Surg. 2008;32(8):1843–9.
8. Kollar D, McCartan DP, Bourke M, Cross KS, Dowdall J. Predicting acute appendicitis? A comparison of the Alvarado score, the appendicitis inflammatory response score and clinical assessment. World J Surg. 2015;39(1):104–9.
9. Doria AS, Moineddin R, Kellenberger CJ, Epelman M, Beyene J, Schuh S, et al. US or CT for diagnosis of appendicitis in children and adults? A meta-analysis. Radiology. 2006;241(1):83–94.
10. Kim K, Kim YH, Kim SY, Kim S, Lee YJ, Kim KP, et al. Low-dose abdominal CT for evaluating suspected appendicitis. N Engl J Med. 2012;366(17):1596–605.
11. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev. 2010;(10):CD001546.
12. Andersson RE. Short-term complications and long-term morbidity of laparoscopic and open appendicectomy in a national cohort. Br J Surg. 2014;101(9):1135–42.
13. Schnüriger B, Laue J, Kroll D, Inderbitzin D, Seiler CA, Candinas D. Introduction of a new policy of no nighttime appendectomies: impact on appendiceal perforation rates and postoperative morbidity. World J Surg. 2014;38(1):18–24.
14. Bhangu A. Safety of short, in-hospital delays before surgery for acute appendicitis: multicentre cohort study, systematic review, and meta-analysis. Ann Surg. 2014;259(5):894–903.
15. Hansson J, Korner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendicectomy as primary treatment of acute appendicitis in unselected patients. Br J Surg. 2009;96(5):473–81.
16. Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet. 2011;377(9777):1573–9.
17. Di Saverio S, Sibilio A, Giorgini E, Biscardi A, Villani S, Coccolini F, et al. The NOTA Study (Non Operative Treatment for Acute Appendicitis): prospective study on the efficacy and safety of antibiotics (amoxicillin and clavulanic acid) for treating patients with right lower quadrant abdominal pain and long-term follow-up of conservatively treated suspected appendicitis. Ann Surg. 2014;260(1):109–17.
18. Fitzmaurice GJ, McWilliams B, Hurreiz H, Epanomeritakis E. Antibiotics versus appendectomy in the management of acute appendicitis: a review of the current evidence. Can J Surg J Can Chir. 2011;54(5):307–14.
19. Kaminski A, Liu IL, Applebaum H, Lee SL, Haigh PI. Routine interval appendectomy is not justified after initial nonoperative treatment of acute appendicitis. Arch Surg. 2005;140(9):897–901.
20. Andersson MN, Andersson RE. Causes of short-term mortality after appendectomy: a population-based case-controlled study. Ann Surg. 2011;254(1):103–7.

Benign Tumors

22

Christian Gingert and Franc H. Hetzer

22.1 Introduction

This chapter gives a short and easily understandable overview of benign colon tumors. Benign tumors can roughly be divided into two major groups, namely, epithelial and mesenchymal lesions. These groups may then be separated in subgroups, which are explained in more detail later in the chapter.

Polyp is a well-known term in nonprofessional settings and is most often connected with tumors of the colon. Researchers from the Mayo Clinic define polyps as a small clump of cells that form on the inner lining of the colon [2].

Most polyps are harmless, but with time some may promote colon cancer. Therefore it is reasonable to perform colonoscopies. Colonoscopies are part of cancer prevention programs in many countries and are paid for by medical insurance [3].

C. Gingert, MD (✉)
Surgery and Orthopedics, Kantonsspital Schaffhausen, Schaffhausen, Switzerland

Faculty of Health (Department of Medicine), University of Witten/Herdecke, Witten, Germany
e-mail: christian.gingert@spitaeler-sh.ch

F.H. Hetzer, MD
Viszeralchirurgie FMH, Spital Linth, Gasterstrasse 25, CH-8370 Uznach, Switzerland
e-mail: franc.hetzer@spital-linth.ch

22.1.1 Classification

Polyps show a certain diversity and hence can be classified by aspect, origin (cell type), and malignant potency (Table 22.1). Polyps can be separated into adenomatous and serrated types, based on the different aspects found during colonoscopy or surgery [4–7].

Adenomatous polyps make up the majority (two-thirds) of all polyps. Although only a small percentage of them are cancerous, most of all malignant polyps are adenomatous.

Serrated polyps have a malignant tendency that depends on their size and location. Small serrated polyps or so-called hyperplastic polyps of the lower colon have almost no tendency to develop malignancy. Larger serrated polyps are mostly flat (sessile) and can be found in the upper colon. They are considered precancerous [7, 8]. Polyps can be classified by origin and malignancy based on histology.

Nonspecific inflammation and/or abnormal mucosal maturation can cause non-neoplastic epithelial polyps, which do not transform into malignant lesions. Neoplastic epithelial lesions are a result of proliferative dysplasia and are premalignant.

As the name implies, mesenchymal polyps originate from connective tissue cells and are located in the submucosal or muscle layer. Some authors summarize mesenchymal lesions and other nonepithelial polyps as polypoid tumors [8].

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_22

Table 22.1 Benign lesions in the colon and rectum

Non-neoplastic lesions	Neoplastic lesions	Mesenchymal lesions	Other lesions
Hyperplastic polyp	Adenoma Tubular adenoma Villous adenoma Tubulovillous adenoma	Lipoma	Endometriosis
Hamartoma Juvenile polyp Peutz-Jeghers polyp		Hamartoma	Pneumatosis cystoides intestinalis
Inflammatory polyps		Leiomyoma	
Lymphoid polyps		Neuroma	
		Angioma	

Refer to Schiedeck [36]

Benign tumours of the colon and rectum (Table 22.1) are separated into four categories:

- Non-neoplastic epithelial lesions
- Neoplastic epithelial lesions
- Mesenchymal lesions
- Other lesions

22.2 Non-neoplastic Epithelial Lesions

- Incidence increases with age.
- Formation occurs sporadically.

22.2.1 Hyperplastic Polyps

Epidemiology
Hyperplastic polyps with a diameter less than 5 mm often occur in a pile and are ubiquitous in the entire colorectum (Fig. 22.1). They definitely have no malignant potency [4].

Symptoms
The main symptom of hyperplastic polyps is prolapse.

Diagnosis
A colonoscopy is necessary to confirm a diagnosis of polyps. Multiple hyperplastic polyps should be excised and sent for histological examination to confirm their benign nature.

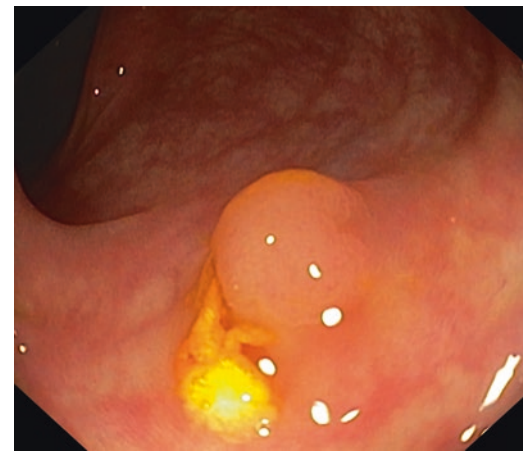


Fig. 22.1

Therapy
Colonoscopic snaring is the therapy of choice; further treatment is not recommended [9].

22.2.2 Hamartomas

Epidemiology
Hamartomas are benign lesions consisting of both epithelial and mesenchymal components. They are classified as a benign mesenchymal lesion; the epithelial components seem to be reactive [10].

Symptoms
Hamartomas are usually asymptomatic. Obstruction and/or bleeding rarely occur.

Diagnosis
A colonoscopy is necessary to confirm the diagnosis of hamartoma. The lesion should be excised and sent for histological examination to confirm its benign nature.

Therapy
Colonoscopic snaring is the therapy of choice; further treatment is not recommended.

22.2.3 Juvenile Polyps

Epidemiology
The term *juvenile polyps* sums up pediatric gastrointestinal polyps that are either of hamartomatous or reactive inflammatory origin. A juvenile polyp is neither a neoplasm nor a premalignant condition.

Their incidence is higher in boys than in girls, and they are usually found in children younger than the age of 10 years. The presence of more than five juvenile polyps defines juvenile polyposis syndrome [11].

Symptoms
Polyps are usually asymptomatic. Obstruction and/or bleeding rarely occur.

Diagnosis
A colonoscopy is necessary to confirm the diagnosis of polyps. Multiple polyps should be excised and sent for histological examination. A histological distinction between a juvenile polyp and an adenomatous polyp is essential. The complete colon has to be examined endoscopically to exclude juvenile polyposis syndrome.

Therapy
Colonoscopic snaring is the therapy of choice; further treatment is not recommended.

22.2.4 Juvenile Polyposis Syndrome

Epidemiology
In contrast to single juvenile polyps, so-called juvenile polyposis syndrome, referring to the presence of more than five juvenile polyps, is associated with malignancy. The risk of patients with juvenile polyposis developing cancer of the colon before 60 years of age ranges from 20 up to 60% [12–14].

These lesions are ubiquitous in the gastrointestinal tract. The disease can be hereditary and is associated with mutations in two genes on chromosomes 10 and 18 [15–17].

Symptoms
Colorectal polyps predominantly cause diffuse symptoms such as bleeding, acute abdominal pain, and diarrhea. Probably as a result of genetic dysfunction, the following concomitant extracolonic manifestations may be found:

- Macrocephaly
- Bony swellings
- Cleft lip/cleft palate
- Double renal pelvis and ureter
- Acute glomerulonephritis
- Undescended testicle
- Bifid uterus and vagina

Therapy
Colonoscopic excisions should be considered if only a few polyps are found. Surgical approaches depend on the site of lesion, especially if the rectum is involved:

- Colectomy and ileorectal anastomosis
- Proctocolectomy and pouch
- Proctocolectomy and ileostomy

Follow-Up
Because of the increased incidence of malignant tumors, even in other organs, careful, risk-adapted follow-up is recommended. In this case the term *risk-adaption* includes a full family history of cancer.

22.2.5 Peutz-Jeghers Syndrome

Epidemiology
Peutz-Jeghers syndrome is a rare, hereditary autosomal-dominant disorder with a mutation on chromosome 19. The typical age at presentation is 10–30 years. There is a signature presentation

with hamartomatous polyposis of the gastrointestinal tract and melanotic pigmented spots. Melanotic pigmented spots appear in early childhood at the age of 2 years and increase in size and colour until puberty; after that they slowly fade. The location of these spots varies Notiz:

- Lips and perioral tissue (94 %) (Fig. 22.2)
- Hands (74 %)
- Oral mucosa (66 %)
- Feet (62 %)

Polyps are located all over the gastrointestinal tract but not the mouth (Fig. 22.3):

- Small intestine (64 %)
- Stomach (49 %)
- Colon (64 %)

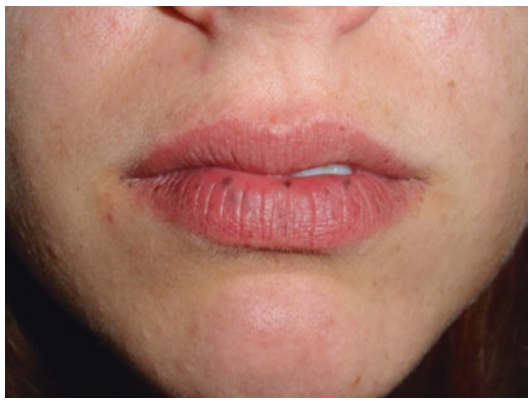


Fig. 22.2 (Reprinted with permission from Prof. Gabriela Möslein)

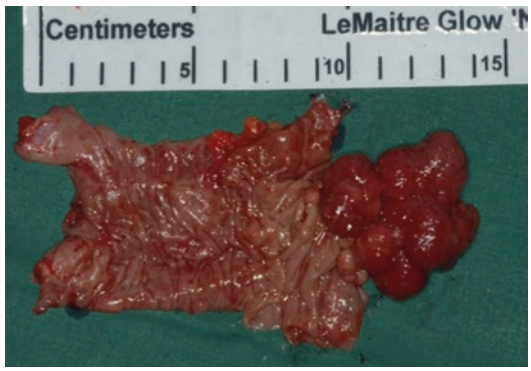


Fig. 22.3 (Reprinted with permission from Prof. Gabriela Möslein)

- Rectum (32 %)
- Esophagus, lungs, bladder, nostrils (occasionally)

Histologically, Peutz-Jeghers polyps consist of connective tissue and well-developed smooth muscle. The risk of polyps undergoing malignant transformation has been regarded as minimal, but recent studies show a lifetime risk of 85 % [4, 17]. Fifty percent of patients with Peutz-Jeghers syndrome die from cancer before the age of 60. Cancer arises in difference locations:

- Stomach (57 %)
- Breast (45 %)
- Other: ovaries, cervix, lungs, pancreas, uterus, testicles

Symptoms
Typical symptoms are intestinal obstruction and bleeding [18].

Diagnosis
Case history (family history, gastrointestinal symptoms) is key. Pigmentation is a signature feature and can be found during a clinical exam. In addition, contrast enema can show multiple polyps, and gastroscopy and colonoscopy allow histological probes.

Therapy
There is no causal therapy. Endoscopic snaring is recommended since the frequency of tumors decreases with age. Surgical approaches are recommended in obstruction or intussusception that cannot be solved colonoscopically, but resections should be done restrictively [19].

22.2.6 Inflammatory Polyps

Epidemiology
Polyps may have an inflammatory origin as a result of long-lasting ulcerative colitis or Crohn's disease of the colon. Histologically they are pseudo-polyps showing inflamed mucosa surrounded by ulcerative tissue, with no tendency for malignant transformation. Malignancy can, however, be a result of chronic ulcerative colitis or Crohn's disease.

Symptoms
Typical symptoms are intestinal obstruction and bleeding.

Diagnosis
Polyps should be excised and send for histological examination to distinguish a diagnosis.

Therapy
Inhibition of the underlying inflammation is a basic treatment. In addition, colonoscopic snaring is recommended.

22.2.7 Lymphoid Polyps

Epidemiology
Lymphoid polyps are benign lesions and are located where piles of lymphoid follicles are present. They must be differentiated from malignant lymphomas. Histologically, lymphoid polyps comprise lymphoid tissue [4, 20].

Symptoms
Polyps are usually asymptomatic. Obstruction and/or bleeding rarely occur.

Diagnosis
Polyps should be excised colonoscopically and send for histological examination to distinguish a diagnosis.

Therapy
Colonoscopic snaring is recommended.

22.3 Neoplastic Epithelial Lesions

22.3.1 Adenomas

Epidemiology
The incidence of adenomatous polyps (adenomas) depends on age, sex, and geography. The incidence in Western countries is 7–12 %. Risk factors may be a diet low in fiber and high in fat, a positive family history of colorectal and/or gynecological cancer, atherosclerosis, nulliparity (in women), and age. Maximum incidence occurs at an age of 60–70 years.

Adenomas originate from the proliferation of glandular epithelium within the colonic or rectal mucosa. Multiple polyps can be found in the colon and rectum (5–100 lesions; familial adenomatous polyposis [FAP] >100).

Though adenomas are histologically proven benign tumors, they are a precursor to colorectal cancer [4].

Polyps are classified by shape into three macroscopic types:

- Pedunculated
- Sessile (flat)
- Semisessile (raised)

In addition, adenomatous polyps can be distinguished by their histological surface:

- Tubular adenomas (65–80 %)
- Tubulovillous adenomas (25 %)
- Villous adenomas (5–10 %)

Each histological type of adenomatous polyp has a different related incidence of early invasive carcinoma (Fig. 22.4 and Table 22.2):

- 30 and 70% in villous adenomas
- 17 % in tubulovillous adenomas
- Rare in tubular adenomas

Symptoms
Bleeding, abdominal cramping, and diarrhea usually occur.

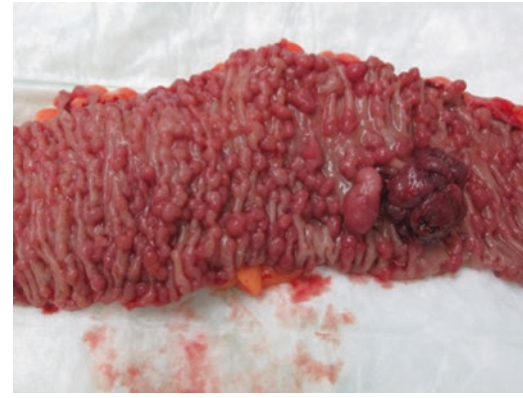


Fig. 22.4 (Reprinted with permission from Prof. Gabriela Möslein)

Table 22.2 Familial adenomatous polyposis (FAP)

FAP is an autosomal-dominant syndrome
Definition of FAP:
1. >100 Polyps in the colon and rectum
2. A member of a family with FAP can have any number of colorectal adenomas
The genetic defect is described on chromosome 5 (q21) in the so-called adenomatous polyposis coli (APC) gene
Patients with a defected APC gene develop cancer around the age of 40 years
FAP is associated with:
Epidermoid cysts
Desmoid tumours
Osteomas
Gliomas
Medulloblastomas

Diagnosis
Occult blood testing can provide (but not necessarily) a first hint. Complete colonoscopy and proctorectoscopy are exams of choice.

Screening
Screening should be performed in patients with symptoms, patients older than 50 years of age, and/or patients with a premalignant condition, such as:

- Ulcerative colitis longer than 10 years
- Crohn's disease with stricture
- FAP
- Hereditary nonpolyposis colorectal cancer syndrome
- History of colon polyps
- Family history of colorectal cancer or polyps

There are no general international screening guidelines, but the first colonoscopy is recommended 10 years earlier than the age at which the cancer was diagnosed in the relative diagnosed with colorectal cancer. In addition, asymptomatic patients older than 50 years and younger patients with a positive family history should be tested annually for occult bleeding.

In the case of a positive result, colonoscopy and proctoscopy with digital examination are a must. Studies show that colonoscopy and digital examination together have the highest sensitivity in diagnosing adenomas and colorectal cancer.

In the case of a negative result, colonoscopy and digital examination should be repeated every 10 years. After a positive result another colonoscopy is indicated after 1 year.

Since there is an increased incidence of adenomas of the duodenum in patients with FAP and an associated risk of developing cancer in that area, gastroduodenoscopy is recommended every 3 years [6, 21–24].

Therapy
The therapy of choice is colonoscopic resection, not biopsy [1]. In cases of colonoscopic failure, surgical resection is indicated.

According to guidelines, a proctocolectomy with an ileal pouch is recommended in patients with FAP before the age of 20 years. Without involvement of the rectum, a subtotal colectomy may be considered. The risk of developing cancer in the rectal remnant is 13–40 % within 25 years. Therefore, these patients should undergo proctorectoscopy every 2 years.

22.4 Mesenchymal Lesions

22.4.1 Lipomas

Epidemiology
Lipomas are benign tumors evolving from adipose connective tissue (Fig. 22.5) and are mostly localized in the right hemicolon (70 %) [25]. They are the most common mesenchymal tumors found in the colon, with an overall prevalence of 2.2–4.4 % (based on findings at autopsy). Lipomas are more common in women (56 %) than men (44 %). The maximum prevalence is found among patients older than 60 years.

Symptoms
Lipomas are usually too small to be symptomatic. Symptoms that can occur are unspecific abdominal pain (23 %) caused by obstruction or intussusception, rectal bleeding (20 %), and, rarely, anaemia, weight loss, nausea, vomiting, and meteorism [26, 27].

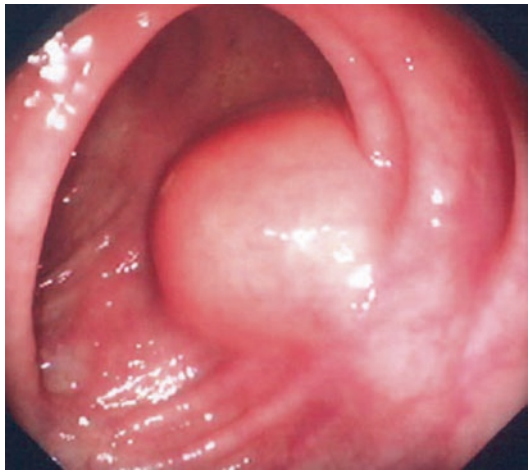


Fig. 22.5

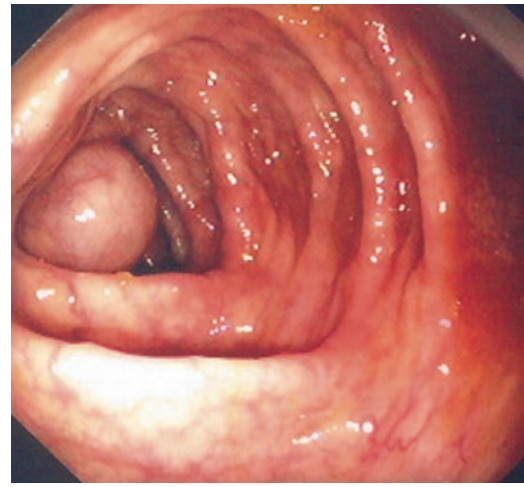


Fig. 22.6

Diagnostic
Key exams are rectal palpation and colonoscopy. Computed tomography and contrast enema can be useful to detect intermittent intussusceptions.

Therapy
Asymptomatic lipomas do not have to be resected. If they are symptomatic, colonoscopic resection, not biopsy, is recommended. In cases of colonoscopic failure, surgical resection is indicated. Rectal lipomas may be excised transanally [27, 28].

22.4.2 Leiomyomas

Epidemiology
Leiomyomas (Fig. 22.6) belong to a subgroup of tumors called gastrointestinal stromal tumors (GISTs). GISTs are heterogeneous, ranging from indolent benign tumors to severe sarcomas. Their shape may be pedunculated or sessile. Intracolonic leiomyomas are rare.

Histologically, leiomyomas are spindle-cell neoplasms. They seem to have a better prognosis than other GISTs with similar mitotic rates.

In cases of high mitotic rate, rapid growth, ulceration, and a lesion larger than 2.5 cm, malignant degeneration must be suspected [29, 30].

Symptoms
Typical symptoms are obstruction and meteorism. Bleeding is also found in rare cases.

Diagnosis
Endorectal ultrasonography is a key exam because it can visualize typical findings of colonic leiomyoma. It may also be used to assess the location of a submucosal tumor. Immunohistopathology is mandatory to exclude differential diagnoses.

Therapy
Colonoscopically snare polypectomy and transanal excision are therapies of choice. Complete removal must be ensured. Follow-up is necessary if any atypia or mitotic activity is found.

22.5 Other Lesions

22.5.1 Neuromas

Epidemiology
Neuromas and neurofibromas are rare lesions in the colon or rectum. These are seldom associated with neurofibromatosis.

Symptoms
Typical symptoms are intestinal obstruction and bleeding.

Diagnostic
A colonoscopy is necessary to confirm the diagnosis of neuroma. The lesion should be excised and sent for histological examination to confirm its benign nature.

Therapy
Colonoscopic snaring and transanal excision are therapies of choice; further treatment is not recommended.

22.5.2 Angiomas

Epidemiology
Angiomas are rare tumors in the colon and rectum. They are typically congenital lesions that can be separated into capillary hemangiomas and cavernous hemangiomas [31]. Capillary hemangiomas evolve from the submucosal layer and have closely packed vessels and capsules. Cavernous hemangiomas are large; huge parts of the colon are involved. Calcification and thrombosis frequently occur.

Symptoms
The key symptom of hemangiomas is bleeding:

- Capillary hemangiomas: bleeding is episodic and slow.
- Cavernous hemangiomas: massive bleeds occur.

Diagnostic
A colonoscopy is necessary to confirm the diagnosis of angioma (typically shows a deep red or blue aspect). Selective angiography can be used to diagnose a vascular malformation.

Therapy
The signature treatment is colonoscopic excision. Angiographically placed endocoils can also be used to control hemorrhage.

22.5.3 Lymphangioma

Epidemiology
(Cystic) lymphangiomas of the colon are extremely rare lesions. The exact cause remains unknown. Macroscopically, they appear as submucosal masses in the large intestine. Histologically, dilated lymphatic channels lined by endothelial cells are found. Lymphangiomas have no malignant potential [32, 33].

Diagnosis
Lymphangiomas are usually found incidentally in asymptomatic patients during routine colonoscopy. They appear as solitary submucosal masses with smooth mucosa [34].

Symptoms
In general, symptoms such as abdominal pain and/or bleeding are rare.

Therapy
Since there is no malignant potential, no therapy is required for asymptomatic patients. Only in symptomatic patients are colonoscopic or surgical excision indicated. Aspiration of the fluid-filled cysts leads to high recurrence rates.

22.5.4 Pneumatosis Cystoides Intestinalis

Epidemiology
Pneumatosis cystoides intestinalis (PCI), also known as pneumatosis coli, refers to the presence of air in the bowel wall (Fig. 22.7). There are several theories regarding the etiology of PCI:

- Trauma theory: Traumatized mucosa allows luminal air to flow into the bowel wall.
- Bacterial theory: Gas-producing bacteria translocate to the submucosa.
- Pulmonary theory: Increased intrathoracic pressure caused by chronic obstructive pulmonary disease, asthma, or mechanical ventilation leads to alveolar rupture. The resulting air tracks along vessels, eventually reaching the bowel wall.

None of these theories explains all cases of PCI. Most likely, several mechanisms occurring simultaneously lead to PCI [35].

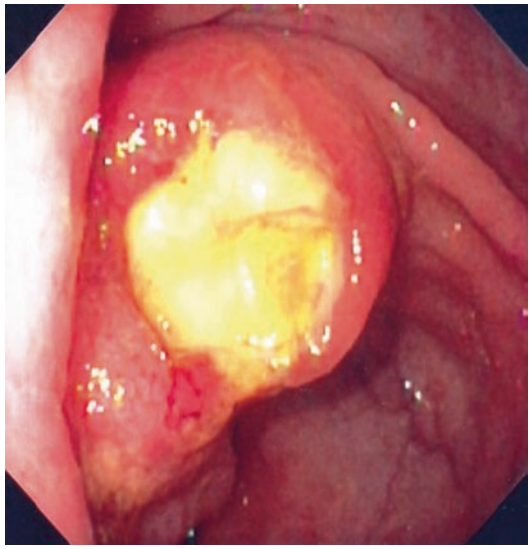


Fig. 22.7

Symptoms

Most patients are asymptomatic. Symptoms that can occur are abdominal cramping, meteorism, diarrhoea, constipation, mucus discharge, rectal bleeding, obstruction, and, in severe cases, peritonitis.

Diagnosis

PCI is usually an incidental finding in asymptomatic patients during routine colonoscopy. Macroscopically, broad-based submucosal masses with a pale appearance or covered with hemorrhagic mucosa can be found.

Endorectal or abdominal ultrasound often leads to diagnosis by showing multiple hyperechoic lesions in the submucosa, which are the result of air-filled cystic spaces.

Therapy

Since there is no malignant potential, no therapy is required for asymptomatic patients. Only in symptomatic patients is colonoscopic or surgical excision recommended. Also, medical therapy has to be considered in cases with a different underlying disease (e.g., bacterial translocation, chronic obstructive pulmonary disease, among others) [35].

References

1. Elmunzer BJ. Endoscopic resection of sessile colon polyps. Gastroenterology. 2013;144:30.
2. www.mayclinic.org/diseases-conditions/colon-polyps/basics/definition/con-20031957
3. Baron TH, et al. Recommended intervals between screening and surveillance colonoscopies. Mayo Clin Proc. 2013;88:854.
4. Rubio CA, Jaramillo E, Lindblom A, Fogt F. Classification of colorectal polyps: guidelines for the endoscopist. Endoscopy. 2002;34:226–36.
5. O'Brien MJ, Winawer SJ, Zauber AG, Gottlieb LS, Sternberg SS, Diaz B, Dickersin GR, Ewing S, Geller S, Kasimian D. The National Polyp Study. Patient and polyp characteristics associated with high- grade dysplasia in colorectal adenomas. Gastroenterology. 1990;98:371–9.
6. Schlemper RJ, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, Dixon MF, Fenoglio-Preiser CM, Flejou JF, Geboes K, Hattori T, Hirota T, Itabashi M, Iwafuchi M, Iwashita A, Kim YI, Kirchner T, Klimpfinger M, Koike M, Lauwers GY, Lewin KJ, Oberhuber G, Offner F, Price AB, Rubio CA, Shimizu M, Shimoda T, Sipponen P, Solcia E, Stolte M, Watanabe H, Yamabe H. The Vienna classification of gastrointestinal epithelial neoplasia. Gut. 2000;47:25–255.
7. Graeme-Cook F. Pathology neoplastic and non-neoplastic. Surg Oncol Clin N Am. 1996;5:487–512.
8. Morson B, Sobin L. Histological typing of intestinal tumors. Geneva: World Health Organization; 1976. p. 13–58.
9. Meyer P. Polyps. In: Marti MC, Givel JC, editors. Surgery of anorectal diseases. Berlin: Springer; 1990. p. 151–61.
10. Schreibman IR, Baker M, Amos C, McGarrity TJ. The hamartomatous polyposis syndromes: a clinical and molecular review. Am J Gastroenterol. 2005;100:476–90.
11. Barnard JA. Gastrointestinal polyps and polyp syndromes in adolescents. Adolesc Med Clin. 2004;15:119–29.
12. Agnifili A, Schietroma M, Mattucci S, et al. Clinical assessment of juvenile polyposis with particular reference to the risk of neoplastic malignancy. Analysis of 412 patients reported in the international literature. Chir Ital. 2000;52:393–404.
13. Desai DC, Neale KF, Talbot IC, et al. Juvenile polyposis. Br J Surg. 1995;82:14–7.
14. Woodford-Richens KL, Rowan AJ, Poulsom R, et al. Comprehensive analysis of SMAD4 mutations and protein expression in juvenile polyposis: evidence for a distinct genetic pathway and polyp morphology in SMAD4 mutation carriers. Am J Pathol. 2001;159:1293–300.
15. Kennedy RD, et al. The natural history of familial adenomatous polyposis syndrome: a 24 year review of a single center experience in screening, diagnosis, and outcomes. J Pediatr Surg. 2014;49:82.

16. Coburn MC, Pricolo VE, DeLuca FG, Bland KI. Malignant potential in intestinal juvenile polyposis syndromes. Ann Surg Oncol. 1995;2:386–91.
17. Giardiello FM, Offerhaus JG. Phenotype and cancer risk of various polyposis syndromes. Eur J Cancer. 1995;31A:1085–7.
18. Cunningham JD, Vine AJ, Karch L, Aisenberg J. The role of laparoscopy in the management of intussusception in the Peutz-Jeghers syndrome: case report and review of the literature. Surg Laparosc Endosc. 1998;8:17–20.
19. Spigelman AD, Arese P, Phillips RK. Polyposis: the Peutz-Jeghers syndrome. Br J Surg. 1995;82:1311–4.
20. Nagaoka S, Bandoh T, Takemura T. Lymphoid hyperplasia of the large intestine: a case report with immunohistochemical and gene analysis. Pathol Int. 2000;50:750–3.
21. Compton CC, Fielding LP, Burgart LJ, Conley B, Cooper HS, Hamilton SR, Hammond ME, Henson DE, Hutter RV, Nagle RB, Nielsen ML, Sargent DJ, Taylor CR, Welton M, Willett C. Prognostic factors in colorectal cancer. College of American Pathologists Consensus Statement 999. Arch Pathol Lab Med. 2000;24:979–94.
22. Arnold CN, Goel A, Blum HE, Boland CR. Molecular pathogenesis of colorectal cancer: implications for molecular diagnosis. Cancer. 2005;04:2035–47.
23. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): S3-Leitlinie Kolorektales Karzinom, Langversion 1.1, 2014, AWMF Registrierungsnummer: 021-007OL. http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html. [Stand: 27.07.2015].
24. Muto T, Bussey HJ, Morson BC. The evolution of cancer of the colon and rectum. Cancer. 1975;36:225–2270.
25. Montgomery D, Reidy J. Giant submucosal colonic lipomata: report of a case and review of the literature. Scott Med J. 2004;49:71.
26. Rogers Jr SO, Lee MC, Ashley SW. Giant colonic lipoma as lead point for intermittent colo-colonic intussusception. Surgery. 2002;131:687–8.
27. Tzilinis A, Fessenden JM, Ressler KM, Clarke LE. Transanal resection of a colonic lipoma, mimicking rectal prolapse. Curr Surg. 2003;60:313–4.
28. Ladurner R, Mussack T, Hohenbleicher F, et al. Laparoscopic-assisted resection of giant sigmoid lipoma under colonoscopic guidance. Surg Endosc. 2003;17:160.
29. Miettinen M, Sarlomo-Rikala M, Sobin LH. Mesenchymal tumors of muscularis mucosae of colon and rectum are benign leiomyomas that should be separated from gastrointestinal stromal tumors: a clinicopathologic and immunohistochemical study of eighty-eight cases. Mod Pathol. 2001;14:950–6.
30. Kuhlgatz J, Sander B, Golas MM, et al. Differential diagnosis of gastrointestinal leiomyoma versus gastrointestinal stromal tumor. Int J Colorectal Dis. 2006;21:84–8.
31. Jensen DM, Machicado GA. Bleeding colonic angioma: endoscopic coagulation and follow-up. Gastroenterology. 1985;88:1433.
32. Yatabe Y, Nakamura S, Nakamura T, et al. Multiple polypoid lesions of primary mucosa-associated lymphoidtissue lymphoma of colon. Histopathology. 1998;32:116–25.
33. Watanabe T, Kato K, Sugitani M, et al. A case of multiple lymphangiomas of the colon suggesting colonic lymphangiomatosis. Gastrointest Endosc. 2000;52:781–4.
34. Irisawa A, Bhutani MS. Cystic lymphangioma of the colon: endosonographic diagnosis with through-the-scope catheter miniprobe and determination of further management. Report of a case. Dis Colon Rectum. 2001;44:1040–2.
35. Hoer J, Truong S, Virnich N, et al. Pneumatosis cystoides intestinalis: confirmation of diagnosis by endoscopic puncture a review of pathogenesis, associated disease and therapy and a new theory of cyst formation. Endoscopy. 1998;30:793–9.
36. Schiedeck T. Coloproctology. Heidelberg: Springer; 2008.

Principles of Tumor Classification

23

Kieran Sheahan

23.1 World Health Organization, Union for International Cancer Control, and American Joint Committee on Cancer Classification of Tumors

A uniform classification is essential for the analysis of treatment results. All tumors should be classified according to the established international recommendations of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) [1, 2] and World Health Organization (WHO) [3]. These have been identical since 1987. Tables 23.1, 23.2, 23.3, 23.4, and 23.5 list all premalignant and malignant tumors of the colon, rectum, anus, and perianal skin. It is important to consider tumors of the anal canal (Table 23.4) and perianal skin separately (Table 23.5). It is also important to note that lymphomas, melanomas, neuroendocrine tumors, gastrointestinal stromal tumors and sarcomas are staged separately from carcinomas.

23.1.1 UICC/AJCC TNM Classification of Tumors of the Colon, Rectum, Anus and Perianal Skin

Staging is the assessment of the degree of spread of a tumor. The staging can be *clinical* or *pathological*.

Clinical staging is used alone in the following circumstances:

- When there is no surgical treatment
- When adjuvant treatment is administered before surgery
- When there are insufficient data to stage the patient pathologically

Pathological staging of colorectal cancer was historically undertaken by a number of different systems. The two used in Europe were the TNM and the older Dukes classification. Originally the Dukes classification used three stages: A, B, and C [4]. The latter was subsequently modified into stages C1 and C2, with the addition of a fourth stage, stage D [5] (see Table 23.6). The UICC and AJCC recently introduced the TNM staging system, which uses four stages (stages I–IV). The anatomic extent of cancer is described by assessing three components:

T: The extent of spread of the primary tumor
N: The presence or absence and extent of regional lymph node metastasis
M: The presence or absence of distant metastasis

K. Sheahan, MB, FRCPI FRCPATH
Department of Pathology, School of Medicine, St. Vincent's University Hospital, University College Dublin, Elm Park, Dublin 4, Ireland
e-mail: k.sheahan@st-vincents.ie

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_23

Table 23.1 Premalignant lesions of the colon and rectum

Premalignant
Epithelial tumors
Adenomas
Tubular
Tubulovillous
Villous
Low-grade dysplasia
High-grade dysplasia
Serrated lesions
Hyperplastic polyp
Sessile serrated lesion/polyp/adenoma
Traditional serrated adenoma
Sessile serrated adenoma with conventional dysplasia
Hamartomas
Cowden-associated polyp
Juvenile polyp
Peutz-Jeghers polyp

Table 23.2 Malignant tumors of the colon and rectum

Carcinomas
Adenocarcinoma
Cribriform (comedo type)
Medullary carcinoma
Micropapillary
Mucinous carcinoma
Signet ring carcinoma
Serrated adenocarcinoma
Adenosquamous carcinoma
Squamous cell carcinoma
Spindle cell carcinoma
Undifferentiated carcinoma
Neuroendocrine neoplasms
Neuroendocrine tumors (Grade 1 and Grade 2)
Neuroendocrine carcinoma
Large-cell carcinoma
Small-cell carcinoma
Mixed adenoneuroendocrine carcinoma

Table 23.3 Mesenchymal tumors of the colon and rectum

Leiomyoma
Lipoma
Angiosarcoma
Gastrointestinal stromal tumor
Kaposi sarcoma
Leiomyosarcoma
Lymphomas
Secondary tumors/metastatic tumors

Table 23.4 Tumors of the anal canal

Premalignant
Epithelial tumors
Anal intraepithelial neoplasia, low grade
Anal intraepithelial neoplasia, high-grade
Paget disease of the anus
Malignant carcinoma
Squamous cell carcinoma
Verrucous carcinoma
Undifferentiated carcinoma
Adenocarcinoma
Mucinous adenocarcinoma
Neuroendocrine neoplasms
Neuroendocrine tumors (Grade 1 and Grade 2)
Neuroendocrine carcinoma
Large-cell carcinoma
Small-cell carcinoma
Mixed adenoneuroendocrine carcinoma
Mesenchymal tumors
Leiomyoma
Lipoma
Angiosarcoma
Gastrointestinal stromal tumor
Kaposi sarcoma
Leiomyosarcoma
Lymphomas
Secondary tumors/metastatic tumors
Anal melanoma

TNM is superior to Dukes because of the greater information it yields, and it is now the preferred system. However, there is controversy because the system is frequently updated. There have been various versions of the TNM staging; thus the version used should be specified (e.g., version 5, version 6, version 7). The most recent seventh edition of the TNM has introduced classification systems for gastrointestinal stromal tumors and neuroendocrine tumors. Currently the United Kingdom and a number of other countries advise using TNM 5 for colorectal cancer, whereas most countries have adopted TNM 7 (Table 23.7) since its introduction in 2009.

23.1.1.1 Stage Grouping

The final stage is determined by the anatomic extent of tumor, comprising the T, N, and M categories in

Table 23.5 Tumors of the anal margin (perianal tumors)

These tumors are best regarded as variants of skin cancer and are treated and staged similar to their skin counterparts
Squamous cell carcinoma
Basal cell carcinoma
Melanoma

Table 23.6 Dukes staging

Dukes A	Tumor penetrates into, but not through, the muscularis propria (the muscular layer) of the bowel wall
Dukes B	Tumor penetrates through the muscularis propria of the bowel wall but does not involve lymph nodes
Dukes C	Pathological evidence of adenocarcinoma in one or more lymph nodes
Dukes D	Tumor spread to other organs such as the liver, lung, or bones

different combinations. Stage grouping varies according to tumor type. In all TNM stage groupings, the final stage is IV, which indicates advanced disease (Table 23.8).

23.1.1.2 Anal Canal Cancer (Table 23.4)

High-risk human papillomavirus infection is a well-established risk factor for the development of anal intraepithelial neoplasia (AIN) and anal squamous cell carcinoma.

Grading of AIN I, AIN II, and AIN III depends on the extent of proliferation of dysplastic squamous cells, similar to how cervical intraepithelial neoplasia is graded. P16 and Ki-67 can be used to assist in the diagnosis of intermediate-grade AIN.

In the United Kingdom: Low-grade AIN comprises AIN I and AIN II, and high-grade AIN equates to AIN III.

In the United States: Low-grade AIN comprises AIN I and high-grade, AIN II and AIN III.

Table 23.9 summarizes the TNM staging. Note that the T stage requires precise pathological measurement of tumor size.

23.1.1.3 Perianal Cancers

Malignant tumors of perianal skin are similar to skin tumors at other skin sites (Table 23.5). Most (90 %) are squamous cell and basal cell carcinomas. Perianal squamous cell carcinoma has a better prognosis than anal canal squamous cell carcinoma (lymph node metastasis is uncommon).

Verrucous carcinoma (synonym: Buschke Löwenstein tumor) is an uncommon human papillomavirus–related well-differentiated squamous cell cancer that is locally destructive but has minimal metastatic potential.

Table 23.7 TNM staging of colorectal cancer (7th edition)

Tis: carcinoma in-situ: intraepithelial (within basement membrane) or invasion of lamina propria (intramucosal), with no extension through the muscularis mucosae into the submucosa
T1: tumor invades the submucosa
T2: tumor invades the muscularis propria
T3: tumor invades beyond the muscularis propria into the subserosa or nonperitonealized pericolic/perirectal tissues
T4: tumor directly invades other organs or structures and/or perforates visceral peritoneum
T4a perforates visceral peritoneum
T4b directly invades other organ or structures
N0: no regional lymph node metastasis
N1: metastasis in one to three regional lymph nodes
N1a: one node positive
N1b: two or three nodes positive
N1c: satellites (tumor deposits) in subserosa, without regional node metastasis
N2: metastasis in four or more regional lymph nodes
N2a: four to six nodes positive
N2b: seven or more nodes positive
M1: distant metastasis
M1a: one organ
M1b: more than one organ or peritoneum
Resection
R0: tumor completely excised locally
R1: microscopic involvement of the margin by the tumor (within 1 mm)
R2: residual macroscopic tumor or gross involvement of the margin

Changes in TNM 7 compared with TNM 6 are highlighted in bold

Table 23.8 Stage grouping

Stage I – pT1/T2N0M0
Stage II – pT3/T4N0M0
Stage III – any pT, N1–2, M0
Stage IV– any pT, any N, M1

Table 23.9 TNM staging for squamous cell carcinoma of anal canal

Tis: carcinoma in situ (Bowen disease, anal intraepithelial neoplasia 2–3)
T1: ≤2 cm
T2: >2–5 cm
T3: >5 cm
T4: adjacent organ(s)
N1: perirectal
N2: unilatateral internal iliac or inguinal
N3: perirectal or bilateral, internal iliac/inguinal

Table 23.10 Neuroendocrine tumors (NETS) of the colon and rectum

The European Neuroendocrine Tumor Society (ENETS) and Union for International Cancer Control TNM staging of neuroendocrine tumors
Large intestine
T1: lamina propria/submucosa and ≤2 cm (T1a: <1 cm, *T1b*: 1–2 cm)
T2: muscularis propria or >2 cm
T3: subserosa
T4: perforates the serosa or other organs
ENETS introduced grading of NETS based on the *Ki-67 index*
Ki-67 index = % of Ki-67-positive cells/2,000 cells
Grade 1 = <2 % Grade 2 = 2–20 % Grade 3 = >20 %

Extramammary Paget disease is an uncommon lesion of the perianal skin. Fifty percent are associated with synchronous adenocarcinomas of the colorectum, usually a local extension from a rectal cancer. The other 50 % are best regarded as adenocarcinoma in situ of the skin, with a propensity to persist and recur locally. These tumors rarely progress to invasive carcinoma.

23.1.1.4 Neuroendocrine Tumors

Consensus guidelines have now been published by the European Neuroendocrine Tumor Society for classifying, staging, and treating neuroendocrine tumors of the colorectum [6] (Table 23.10). The main factors governing the behavior of this group of tumors are their size, extent of infiltration into the intestinal wall, angioinvasion, and whether they produce a clinical hypersecretion syndrome (i.e., functioning). These tumors are staged and graded per AJCC guidelines [2]. The Ki-67 index and mitotic count separate neuroendocrine tumors into grades 1, 2, and 3.

23.1.2 Rules for Pathological TNM Staging of Colorectal Adenocarcinoma

- Staging following radio-chemotherapy is assigned the prefix "*y*." This can be pathological (yp) or clinical (yc) staging.
- Multiple synchronous tumors of the same type in one organ are staged using the highest tumor stage and by adding (*m*) for multiple, for example, T3 (m) or number of tumors, that is, T3 [4] for four tumors.
- The number of lymph nodes is often lower in resections after neoadjuvant cancer
- Re-treatment staging, following recurrence, is assigned *rTNM*.
- Completeness of resection (*R*): this is required in tumor resection specimens and is considered an important prognostic factor; however, it is not always possible to comment on. This is classified as:
  - *R0*: tumor completely excised locally
  - *R1*: microscopic involvement of the margin by tumor (the majority of pathologists consider tumors within 1 mm of the circumferential radial margin as involved/positive)
  - *R2*: macroscopic tumor left behind or gross involvement of the margin

23.1.3 Quality of Total Mesorectal Excision and Abdominoperineal Resection

Total mesorectal excision grading in rectal cancer and total mesocolic resection in colon cancer may also be assessed. Assessment of the quality of surgery is an important responsibility for a pathologist, and there is a standardized grading method for assessing total mesorectal excision specimens. Description of the three planes of sections have been published [7], and studies have

confirmed the benefit of feedback to the surgical team.

The *mesorectal fascial plane or complete excision* has a smooth surface with no defect larger than 5 mm (Fig. 23.1a). The *intramesorectal plane or near complete excision* has an irregular mesorectal surface (Fig. 23.1b). The muscularis propria is not visible except at the insertions of the levator ani muscles. The *muscularis propria plane or incomplete excision* shows little bulk to the mesorectum, with deep defects extending to a visible muscularis propria (Fig. 23.1c). The macroscopic assessment of the plane of excision is directly linked to prognosis in rectal cancers [8]. Thus feedback to the surgeon regarding the plane of resection is vital to improve the quality of mesorectal excision [9]. Many surgeons have subsequently applied this principle to colonic surgery, adopting a complete mesocolic excision, thereby ensuring complete removal of the colonic mesentery, along with lymphatic and vascular tissues, within an intact peritoneal sheath [10].

23.1.4 Tumor Regression Grading: Tumor Response to Therapy

My practice uses a modified three-point grading system to assess response to chemoradiotherapy in rectal cancer. *Grade 1*, *complete tumor regression*, shows no viable tumor cells and fibrosis extending through the bowel wall or an isolated single cell or small clusters of tumor cells scattered through fibrosis. In g*rade 2*, *partial tumor regression*, fibrosis predominates, outgrowing the residual tumor. *Grade 3*, *no tumor regression*, shows the residual tumor outgrowing the fibrosis and extensive residual tumor without fibrosis. Thus far, only complete tumor regression correlates with improved survival [11, 12].

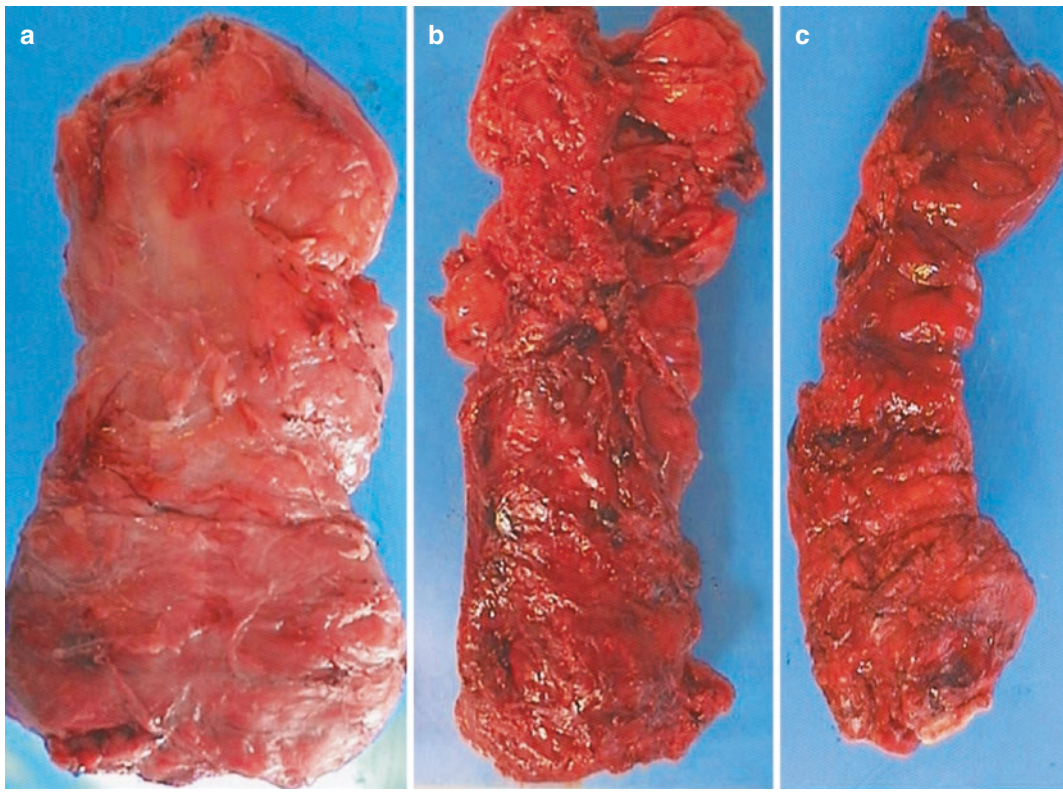


Fig. 23.1 Examples of the surgical excision planes of rectal cancer specimens (total mesorectal excision [*TME*]). (**a**) Mesorectal fascia; (**b**) intramesorectal; (**c**) muscularis propria

23.1.5 Satellite Tumor Deposits

Whether satellite tumor deposits should be considered lymph node metastases or satellite tumor nodules for the purposes of staging has been a topic of debate for many years; the approach to tumor deposit classification has changed in the last three editions of the TNM staging system. In the TNM 5 classification, extramural deposits of tumor with no lymph node structure were regarded as lymph node deposits if they measured >3 mm in diameter and were staged as pN1 [13]. This rule was changed in TNM 6, when the contour of the deposit became the diagnostic feature. Deposits with a round contour were classified as lymph node metastases (pN1), and deposits with an irregular outline were classified as venous invasion [14]. The TNM 6 approach was criticized, and the changes were not considered to be evidence-based or reproducible. In the United Kingdom, the Royal College of Pathologists recommended that the TNM 5 be used for staging colorectal cancer resection specimens instead of TNM 6 [9]. The TNM 7 classification proposed a new pN1c category for tumor deposits in the absence of lymph node metastases [1]. There is growing evidence that both the presence and number of tumor deposits carry an adverse prognosis [15, 16].

References

1. Sobin LH, Gospodarowic MK, Wittekind C, editors. International Union Against Cancer (UICC), TNM classification of malignant tumors. 7th ed. New York: Wiley-Blackwell; 2009.
2. Edge S, Byrd D, Compton C, et al., editors. Colon and rectum. AJCC cancer staging manual. 7th ed. New York: Springer; 2010.
3. Bosman FT, Carneiro F, Hruban RH, Theise ND, editors. WHO classification of tumors of the digestive system. Lyon: IARC; 2010.
4. Dukes CE. The classification of cancer of the rectum. J Pathol Bacteriol. 1932;35:323–32.
5. Turnbull Jr RB, Kyle K, Watson FR, et al. Cancer of the colon: the influence of the no touch isolation technic on survival rated. Ann Surg. 1967;166:420–7.
6. Ramage JK, Goretzki PE, Manfredi R, et al. Consensus guidelines for the management of patients with digestive neuroendocrine tumors: well-differentiated colon and rectum tumor/carcinoma. Neuroendocrinology. 2008;87:31–9.
7. Quirke P, Morris E. Reporting colorectal cancer. Histopathology. 2007;50:103–12.
8. Quirke P, Steele R, Monson J, Grieve R, Khanna S, Couture J, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. Lancet. 2009;373:821–8.
9. Williams G. Dataset for colorectal cancer, 2nd ed. UK: Royal College Of Pathologists; 2007 [updated 2007; cited 2007 September]; second edition. Available from: http://www.rcpath.org/index.asp?PageID=1153.
10. West NP, Hohenberger W, Weber K, Perrakis A, Finan PJ, Quirke P. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. J Clin Oncol. 2009;28:272–8.
11. Ryan R, Gibbons D, Hyland JM, Treanor D, White A, Mulcahy HE, et al. Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. Histopathology. 2005;47:141–6.
12. Beddy D, Hyland JM, Winter DC, Lim C, White A, Moriarty M, Armstrong J, Fennelly D, Gibbons D, Sheahan K. A simplified tumor regression grade correlates with survival in locally advanced rectal carcinoma treated with neoadjuvant chemoradiotherapy. Ann Surg Oncol. 2008;15(12):3471–7.
13. Sobin LH, Wittekind CH, editors. International Union Against Cancer (UICC), TNM classification of malignant tumors. 5th ed. New York: Wiley-Liss Publications; 1997.
14. Sobin LH, Wittekind CH, editors. International Union Against Cancer (UICC), TNM classification of malignant tumors. 6th ed. New York: Wiley-Liss Publications; 2002.
15. Puppa G, Sonzogni A, Colombari R, Pelosi G. TNM staging system of colorectal carcinoma: a critical appraisal of challenging issues. Arch Pathol Lab Med. 2010;134:837–52.
16. Jin M, Roth R, Rock JB, Washington MK, Lehman A, Frankel WL. The impact of tumor deposits on colonic adenocarcinoma AJCC TNM staging and outcome. Am J Surg Pathol. 2015;39:109–15.

Genetics

24

Malika Bennis, Jérémie H. Lefevre,
and Emmanuel Tiret

24.1 Basics

The two main inherited colorectal cancer syndromes, familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC), also known as Lynch syndrome, are characterized by a single mutation leading to a dramatically increased predisposition for colorectal cancer. FAP is an autosomal-dominantly inherited condition that has been shown to be to the result of mutations in the adenomatous polyposis coli (*APC*) gene, a tumor suppressor gene active in the Wnt/Wingless signaling pathway [1]. The much more common HNPCC is caused by a germ-line mutation in one of the DNA mismatch repair genes (*hMLH1*, *hMSH2*, *hMSH6*) [2]. These genes correct errors in DNA replication, and any defect in this repair system leads to the rapid accumulation of mutations. Both syndromes are characterized by early onset of colorectal tumors, synchronous and metachronous tumors, and numerous extracolonic benign and malignant manifestations.

Another inherited syndrome has recently been reported, the *MYH*-associated polyposis (MAP) syndrome, which is caused by a biallelic germline mutation of a DNA base excision repair gene: human *MUTYH* [3]. The hereditary transmission is recessive, but MAP syndrome also predisposes to synchronous and metachronous colorectal neoplasms and, like the two main dominantly inherited colorectal cancer syndromes, requires practice parameters for treatment and surveillance.

24.1.1 Familial Adenomatous Polyposis

Although FAP accounts for less than 1 % of all colorectal cancers, it has provided greater knowledge about carcinogenesis among the general population and about colon cancer in particular. Histologically, FAP is characterized by multiple adenomas, averaging less than 5 mm in diameter. The oft-cited number of 100 polyps varies according to the age of the patient. Because puberty is the general age at onset, an adolescent with less than ten adenomas and a confirmed family history of FAP must be considered as affected.

Two phenotypes have been described: classic FAP and attenuated adenomatous polyposis.

M. Bennis, MD
Department of Digestive Surgery,
Hôpital Saint-Antoine, APHP, Paris, France
e-mail: malika.bennis@aphp.fr

J.H. Lefevre, MD, PhD • E. Tiret, MD (✉)
Department of Digestive Surgery,
Hôpital Saint-Antoine, APHP, Paris, France

Université Pierre et Marie Curie, Paris VI, Paris, France
e-mail: jeremie.lefevre@aphp.fr;
emmanuel.tiret@aphp.fr

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_24

Attenuated adenomatous polyposis regroups a subset of patients whose phenotype does not quite fit with classic FAP, in that the age at onset of both adenomas and cancer is later, usually from the age of 40 years onward; adenomas are fewer in number, often sessile, 1–2 mm in diameter, with apparent rectal sparing. However, in 1992 this variant was linked to the *APC* gene and so declared part of the normal spectrum of FAP. Nevertheless, with the description of the MAP syndrome, genetic testing has allowed to show that some of these attenuated polyposis were in fact genuine *MYH*-related polyposis, not linked to *APC* [4].

The *APC* gene, which controls epithelial growth, was discovered in 1991. The *APC* protein, when functional, inhibits the Wnt signaling pathway by degrading β-catenin. When inactivated, *APC*/β-catenin pairing is impossible and the excess β-catenin enters cell nuclei, activating growth regulator genes such as *c-myc* and vascular endothelial growth factor, which then induce colorectal epithelial proliferation and polyp formation [1].

In sporadic cancer, somatic *APC* mutations are observed in 70 % of cases. The two alleles are mutated, mainly, in the mutation cluster region between codons 1250 and 1550. For patients with FAP, one of the two alleles is already inactivated by a germ-line mutation. A somatic event, such as the loss of the chromosome part containing the wild *APC* gene copy (loss of heterozygosity), leads to *APC* inactivation and thereby to the appearance of adenomas. Other genes like *KRAS* and *p53* may mutate and cancer might then develop in these adenomas.

24.1.2 Hereditary Nonpolyposis Colorectal Cancer

The observation that HNPCC tumors exhibited a distinct molecular abnormality called DNA microsatellite instability (MSI) led to the identification of DNA mismatch repair (MMR) genes as the genetic basis for HNPCC. MMR proteins recognize and then correct base pair mismatches and small insertions or deletions that might occur during normal DNA replication. Multiple genes from the mutS (*hMSH2*, *hMSH3*, *hMSH6*) and mutL (*hMLH1*, *hMLH3*, *hPMS1*, *hPMS2*) families interact to repair these mismatched DNA sequences. Microsatellite DNA sequences, which are defined as short, repetitive mononucleotide or dinucleotide sequences, are particularly susceptible to replication errors. Most microsatellite sequences are located in the noncoding regions of the genome. However, microsatellite sequences can be found within the coding regions of certain growth-regulatory genes, and a loss of MMR proofreading activity results in the accumulation of frameshift somatic mutations in these genes. These target genes include receptors for growth factors (transforming growth factor [TGF]-β receptor II, insulin-like growth factor II receptor), cell cycle regulators (E2F4), regulators of apoptosis (BAX), and some of the MMR genes themselves (*hMSH3* and *hMSH6*).

24.1.3 MAP Syndrome

The high-risk colon cancer syndromes discussed so far display an autosomal-dominant pattern of inheritance. However, the discovery that biallelic mutations in the base excision repair gene *MUTYH* (GeneID 4595) result in an increased risk of colorectal adenomas and cancers led to the first description of an autosomal-recessive colon cancer syndrome [3].

8-Oxo-guanine is a by-product of oxidative DNA damage and it inappropriately pairs with adenines, leading to G:C→T:A mutations. The role of *MUTYH* is to excise the mispaired adenines. Dysfunction of *MYH* results in the accumulation of somatic G:C→T:A mutations in specific growth-regulatory genes, and APC seems to be a preferred target [5]. Genetic testing is now available, and analysis has focused on exons 7 and 13 of the *MYH* gene. Two specific mutations in these exons, Y179C and G396D (previously described as Y165C and G382D), account for 87 % of all *MUTYH* mutations among Northern European populations [6]. For non-Caucasian patients, a founder effect has been described –

E480X is found in Indian patients [7] and c.1227_1228dup (p.Glu396-GlyfsX43) in North African patients – but these mutations are not frequently found [8].

24.1.4 Other Syndromes

24.1.4.1 Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome (PJS) is an autosomal-dominant hamartomatous polyposis syndrome that carries a 39 % lifetime risk of colon cancer [9]. There is, however, a 93 % cumulative risk of developing any type of malignancy. PJS has been linked to germ-line mutations of *LKB1*, a serine-threonine kinase located on chromosome 19p. Among its many functions, *LKB1* regulates p53-mediated apoptosis. Adenosine monophosphate–activated protein kinase was recently identified as a direct phosphorylation target for *LKB1*, implicating *LKB1* in the control of cellular metabolism. However, 50–60 % of patients with classic features of PJS have identifiable germ-line mutations of *LKB1*, suggesting there may be additional disease loci yet to be identified.

24.1.4.2 Juvenile Polyposis Syndrome

Like PJS, juvenile polyposis syndrome (JPS) is inherited in an autosomal-dominant pattern and is characterized by the development of hamartomatous intestinal polyps [10]. Patients with JPS exhibit a 10–38 % lifetime risk of colon cancer, and the average age at diagnosis is 34 years. JPS is clinically diagnosed when there are five or more juvenile polyps in the colorectum, or multiple juvenile polyps throughout the gastrointestinal tract, or any number or juvenile polyps with a family history or juvenile polyposis.

Two genes, *MADH4* and *BMPR1A*, have been linked to JPS. *MADH4*, located on chromosome 18q, encodes the Smad4 protein that regulates intracellular signaling of TGF-β. The *BMPR1A* gene on chromosome 10q encodes a receptor for bone morphogenetic protein, a member of the TGF-β superfamily. However, a pathogenic mutation in one of these two genes is detected in only 40–50 % of patients with JPS.

24.1.4.3 Hyperplastic Polyposis Syndrome

Sporadic hyperplastic polyps are encountered incidentally in the distal sigmoid and rectum and traditionally have been thought not to possess any malignant potential. However, individuals and families rarely exhibit numerous hyperplastic polyps distributed throughout the colon, and approximately 25–35 % of these patients were found to have associated synchronous colorectal cancers [11]. The etiology of this syndrome, called hyperplastic polyposis syndrome, has yet to be elucidated, and its diagnosis remains purely clinical.

24.2 Familial Adenomatous Polyposis

24.2.1 Molecular Screening

Molecular testing for FAP is currently offered by direct mutation analysis and in vitro synthesized protein assay, which looks directly at the truncated protein product of the *APC* gene. The best age for genetic testing is still matter of debate. It should be preceded by counseling about psychological and social issues, and the results should be communicated during a counseling session [12].

Mutation of the *APC* gene, either a point mutation or a genomic deletion, is found in about 85 % of patients with an FAP phenotype. In some patients, however, no mutation can be demonstrated. Moreover, about 20 % of patients with an *APC* mutation explaining their FAP phenotype are de novo mutants without a family history of FAP. The correlation between genotype and phenotype is not relevant enough to guide therapeutic choices [4, 13].

24.2.2 Screening Guidelines

- Early detailed registry pedigrees have provided generational proof that the majority of children and their siblings are diagnosed between the ages of 15 and 25 years.

Consequently, screening guidelines were established for use between ages 10 and 14 years.

- One of the major drawbacks of screening is the lack of compliance from patients subjected to excessive screening. Colonoscopy remains the screening standard, and it is advocated once a diagnosis of FAP has been established either clinically or genetically. However, flexible sigmoidoscopy may be preferred as the first screening tool because it is minimally invasive, allows biopsy, and is generally acceptable to adolescents.
- Follow-up is recommended every 2 years until the age of 35 and every 3–5 years thereafter for at-risk first-degree relatives who have not undergone predictive testing or who analysishave undergone DNA analysis that provides no information about whether they are affected.
- Patients in whom an *APC* mutation cannot be proven but who have several affected and available relatives should be considered as mutants and monitored accordingly.
- Patients who do not have the *APC* mutation found in their family are not at risk and, depending on the quality of the laboratories performing the molecular diagnosis, should not be considered at risk.

24.2.3 Colorectal Polyposis

The known adenoma-carcinoma sequence does not seem to be accelerated in FAP, and therefore the disease is a prototype for cancer prevention through prophylactic surgery. The lifetime risk of colorectal cancer in patients with FAP is approximately 100 % and is related to the severity of colorectal polyposis. The cancer risk for patients with severe polyposis (i.e., >1,000 polyps) is thought to be double the risk for patients with <1,000 polyps.

24.2.3.1 Timing for Colectomy

Although colorectal polyps often start to develop during the teenage years, invasive cancer is exceedingly rare before the end of puberty and even the age of 20 years. In patients with known FAP, screening should commence around the age of 12 years with yearly flexible sigmoidoscopy; if polyps are found, this should be supplemented by colonoscopy. In patients with mild disease, surgery can be deferred until the late teenage years. In severe disease with dense polyposis, surgery should be carried out as soon as possible, but preferably after puberty.

24.2.3.2 Type of Surgery

There are three surgical options in the treatment of FAP:

- Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA)
- Colectomy with ileorectal anastomosis (IRA)
- Proctocolectomy with permanent end ileostomy

Each of these options has advantages and disadvantages:

- IPAA greatly reduces the risk of rectal cancer, especially when performed with mucosectomy and hand-sewn anastomosis. It is, however, a technically more demanding procedure and associated with a higher morbidity than IRA [14]. Nowadays, a diverting stoma is not always mandatory in these young patients [15]. Initial reports of postoperative reduced fertility in women have been contradicted [16, 17]. The reduction of pelvic adhesions with a laparoscopic approach may explain the low impact on fertility observed in recent publications.
- IRA carries low rates of morbidity and mortality, with good functional results, and is commonly performed without a temporary diverting stoma. The major drawback is the persistent risk for cancer in the retained rectum. The overall cumulative risk of rectal cancer has been shown to be up to 30 % by age 60 [18]. It, however, remains an option in individuals with a low rectal cancer risk (mild rectal polyposis, late onset, specific mutations).
- Proctocolectomy with permanent end ileostomy is nowadays rarely performed because a

permanent stoma is usually unacceptable to young patients. However, it still has a role in the treatment of very low rectal cancer, when sphincter preservation is not possible.

The options, including the possibility of a laparoscopically assisted procedure, need to be discussed with each individual patient.

An IPAA should be recommended to patients with rectal polyposis (>20 polyps in the distal 10 cm of the rectum) or when there is concern about compliance with long-term surveillance of the rectum. Young women with FAP need to be counseled about the fertility implications of IPAA. It needs to be emphasized to patients that, regardless of the type of operation performed, long-term follow-up is required for either the rectal stump after IRA or the "neorectum" after IPAA, and for extracolonic manifestations of FAP.

24.2.3.3 Surveillance After Surgery

Regular follow-up is mandatory after any procedure [12]. The standard care includes perianal digital and flexible endoscopic examination at yearly intervals.

The risk of rectal cancer after IRA is closely related to the severity of the polyposis. During surveillance endoscopy, random biopsies to check for dysplasia are mandatory. Adenomas smaller than 5 mm in diameter may be observed and those larger than 5 mm are snared. Over time, repeated endoscopic polypectomy can induce dense scarring, which can make assessment of the rectal mucosa difficult. Reduced rectal compliance due to scarring can eventually result in functional disturbances in stool frequency, urgency, and incontinence, and may eventually lead to proctectomy. Completion proctectomy is indicated for villous adenomas >1 cm and biopsy-proven high-grade dysplasia or invasive cancer.

The nonsteroidal anti-inflammatory drug (NSAID) sulindac has been shown to induce regression of rectal and pouch adenomas [19, 20]. Temporary regression of rectal polyps is observed in approximately two-thirds of patients, but with longer follow-up this effect vanishes. However, new cancers have been observed under sulindac treatment. Celecoxib, a selective cyclooxygenase-2 inhibitor, also induces regression of colonic polyps in FAP but is no longer available because of its adverse cardiovascular effects.

Endoscopic pouch examination allows surveillance of pouch adenomas, which tend to occur more frequently with longer follow-up. Their significance will become clearer in due course, once large cohorts of FAP patients with IPAA achieve 20–25 years of follow-up.

24.2.3.4 Chemoprevention as Primary Therapy for Colorectal Polyposis

The NSAIDs sulindac, celecoxib, and exisulind have been shown to induce regression of colorectal adenomas in FAP. This effect has been demonstrated for up to 4 years in patients with IRA. Of concern are case reports of the occurrence of cancers despite chemoprevention and regular surveillance. It is therefore clear that chemoprevention cannot be recommended as an alternative to surgery. NSAIDs are indicated to control pouch polyposis and rectal polyposis following IRA, especially when surgery is contraindicated or declined. Close surveillance with flexible endoscopy for 6–12 months is mandatory.

24.2.4 Duodenal Adenomas

24.2.4.1 Surveillance

Duodenal adenomas occur in the vast majority of patients with FAP (>90%), but only 10% develop severe disease, and malignant transformation occurs in just under 5%. Nevertheless, immediately after desmoid tumors, duodenal cancer is the most common cancer-related cause of death in patients with FAP after proctocolectomy. Screening of the upper gastrointestinal tract usually begins around the age of 20 years, and subsequent intervals are determined by disease severity [12]. The aim of endoscopy is not to remove all adenomas but to stage and control disease severity.

Treatment for duodenal polyposis is difficult. Endoscopic interventions, which include snaring, electrocoagulation, laser ablation, and photodynamic therapy, should be performed as the first

Table 24.1 Spigelman score to classify the severity of duodenal polyposis

	Points		
	1	2	3
Number of polyps	1–4	5–20	>20
Polyp size (mm)	1–4	5–10	>10
Histology	Tubulous	Tubulovillous	Villous
Degree of dysplasia	Mild	Moderate	Severe

Stage 0: 0 points
Stage I: 1–4 points
Stage II: 5–6 points
Stage III: 7–8 points
Stage IV: 9–12 points

option, but they are often technically demanding, if not impossible, and carry substantial potential for complications. Small adenomas should be biopsied. The Spigelman classification allows staging of the severity of duodenal polyposis according to the number and size of polyps and by the histological type and degree of dysplasia [21] (Table 24.1).

A surgical approach needs to be considered for patients with stage III/IV tumors. Treatment with celecoxib had been shown to be effective in reducing duodenal polyposis, but the drug has been taken off the market.

24.2.4.2 Surgery for Duodenal Adenomas

Both endoscopic and open surgical excision of duodenal adenomas allows down-staging of the polyposis, but it is associated with a high risk of recurrence. The only chance of a permanent cure for patients with advanced duodenal polyposis is a duodenal resection. The operation of choice is a pylorus-preserving pancreaticoduodenectomy or a pancreas-preserving duodenectomy in selected cases when there is no concern about malignancy [22]. In specialist centers the outcome is good, with low recurrence rates and acceptable morbidity. Duodenal polyposis seems to follow the adenoma-carcinoma sequence. Therefore surgery should be discussed with patients with progressive and severe duodenal polyposis because invasive disease carries a poor prognosis, even when treated by radical surgery (Whipple procedure).

24.2.5 Desmoid Tumor

Desmoid tumors are histologically benign but locally invasive monoclonal proliferations of fibroblasts. They are only occasionally seen in the general population but affect 10–15 % of all patients with FAP. Desmoid tumors, together with duodenal polyposis/cancer, are the major cause of morbidity and mortality after proctocolectomy; they lead to death in approximately 10 %. Desmoid tumors arise either within the abdominal cavity, in particular within the small-bowel mesentery or on the abdominal wall, and occasionally on the extremities (Figs. 24.1 and 24.2). Their natural history shows great variation, with episodes of rapid and destructive growth as well as spontaneous regression. Intra-abdominal

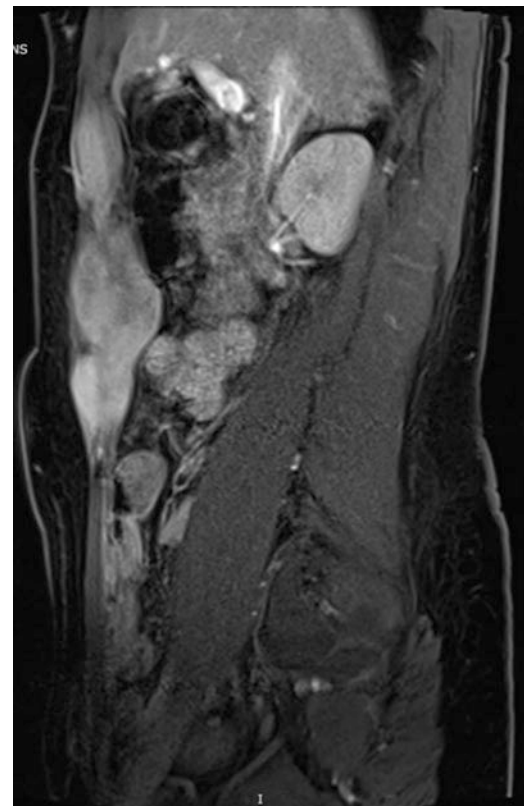


Fig. 24.1 Desmoid tumor of the abdominal wall (MRI)

desmoid tumors can cause small-bowel and ureteric obstruction. Occasionally, a desmoid tumor arising within the small-bowel mesentery, thereby shortening it, makes a restorative procedure with IPAA impossible.

Risk factors for desmoid tumors have been identified among the FAP population: a germline mutation beyond the codon 1444, a family history of desmoid tumor, and a personal history of abdominal surgery [23, 24].

Medical treatment options include NSAIDs, antiestrogens, and chemotherapy and are used in an attempt to stabilize the tumor and induce regression. Several small studies have reported success for treatment with sulindac and/or tamoxifen [25], but evidence from randomized controlled studies is lacking. Cytotoxic therapy with vinblastine and methotrexate has shown some response. A more aggressive regimen combining dacarbazine with doxorubicin seems to be effective in rapidly expanding desmoid tumors. For stable intra-abdominal desmoid tumors, sulindac alone may be used. For slowly growing or symptomatic tumors, tamoxifen can be added. Chemotherapy is reserved for rapidly growing tumors; the rate of growth determines the drug regimen [26].

Surgery is recommended as the first-line treatment for desmoid tumors in the abdominal wall. Morbidity and mortality rates are low, but even with a 1-cm excision, margin recurrence is common. The abdominal wall may require reconstruction with prosthetic material. Surgery for intra-abdominal desmoid tumors is associated with a high risk of major complications (including hemorrhage, recurrence, and long-term parenteral nutrition) and therefore should be avoided whenever possible, unless the rare situation

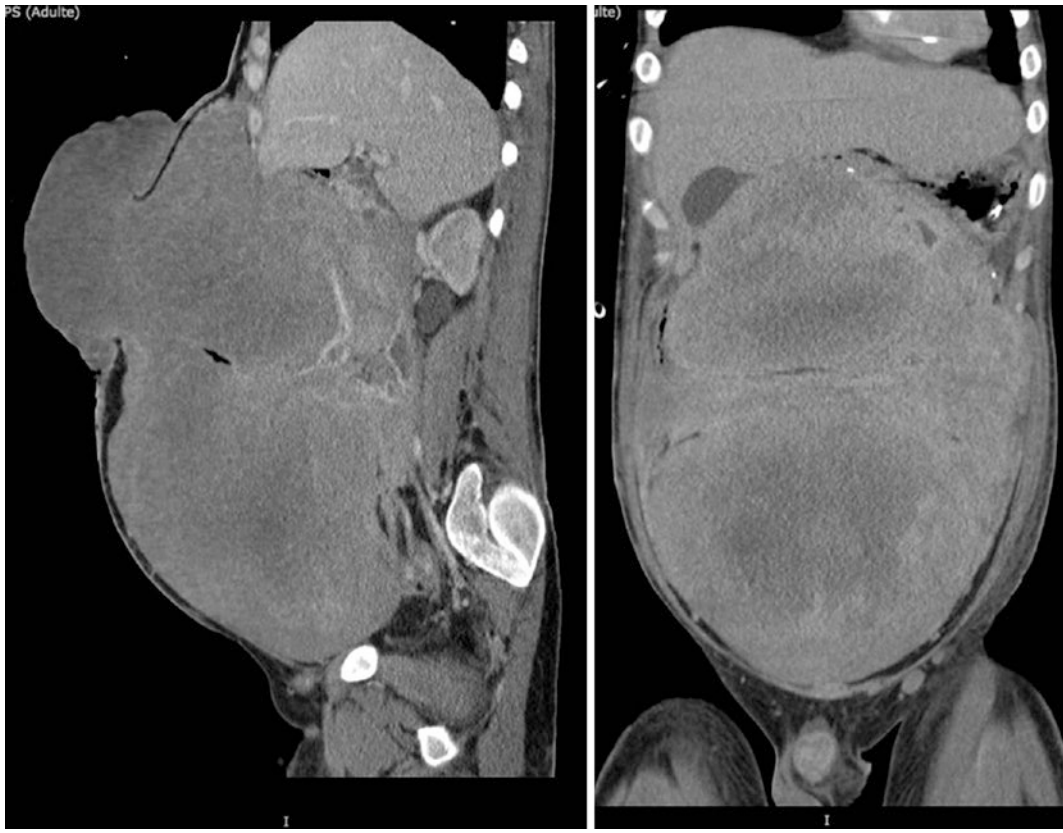


Fig. 24.2 Giant desmoid tumor arising from the mesentery and fistulized through the abdominal wall (CT scan)

occurs where complete resection of the tumor can be performed easily. Intestinal ischemia and perforation resulting in peritonitis may, however, require an emergency laparotomy. In the future, small-bowel transplantation may become a treatment option for intra-abdominal desmoid tumors.

24.3 Hereditary Nonpolyposis Colorectal Cancer Syndrome

24.3.1 Molecular Screening

Following a careful personal and family history of cancer, some patients fulfill the Amsterdam I or II criteria or some of the Bethesda criteria (Table 24.2). However, these criteria are too stringent, and most patients carrying a deleterious germ-line mutation of an MMR gene will not be identified. At present, the recommendation is to try to determine the MSI phenotype after selection with these criteria and to test patients who show an MSI phenotype on polymerase chain reaction products for mutations [27]. An alternative is to test all colorectal cancers with immunohistochemical staining with anti-MLH1 and anti-MSH2 antibodies [28]. The loss of expression of one of these proteins as determined by immunohistochemistry correlates with the MSI phenotype. All patients presenting with a cancer deficient for one of these proteins should therefore be counseled about the search for a mutation on the gene of the deficient protein. Moreover, if several mechanisms can explain the MLH1 deficiency, most patients presenting with an MSH2-deficient cancer will have a germ-line mutation of this gene.

Table 24.2 Clinical guidelines for the diagnosis of hereditary nonpolyposis colorectal cancer (HNPCC)

Amsterdam I criteria	
1.	Three relatives with colorectal cancer, one being a first-degree relative of the other two
2.	Cases that span at least two generations
3.	At least one colorectal cancer case diagnosed before age 50
Amsterdam II criteria	
1.	Three relatives with an HNPCC-associated cancer (colorectal, endometrial, small bowel, ureter, or renal pelvis), one being a first-degree relative of the other two
2.	Cases that span at least two generations
3.	At least one cancer case diagnosed before age 50
Bethesda criteria (*revised in 2004*)	
1.	Colorectal cancer before age 50
2.	Synchronous or metachronous colorectal cancer or other HNPCC-related cancer (endometrial, ovarian, gastric, small bowel, urinary tract, biliary tract, pancreas, brain, or sebaceous gland), regardless of age
3.	Colorectal cancer with MSI-H morphology (characterized by the presence of tumor-infiltrating lymphocytes, mucinous differentiation/signet-ring-cell carcinoma, peritumoral Crohn's-like lymphocytic reaction, medullary growth pattern) before age 60
4.	Colorectal cancer with one or more first-degree relatives with colorectal cancer or another HNPCC-related cancer, with one of the cancers diagnosed before age 50
5.	Colorectal cancer with two or more relatives with colorectal cancer or another HNPCC-related cancer, regardless of age

24.3.2 Screening Guidelines

- HNPCC is more complex than FAP because more genes are involved, penetrance is less complete, and expression is more varied. Furthermore, patients may be diagnosed with HNPCC clinically or biologically. These two subgroups are not identical, especially with regard to the risk of colorectal cancer among their relatives. Therefore, there are no clear recommendations for surveillance.
- However, once a diagnosis of HNPCC has been established by either clinical or molecular criteria, an aggressive cancer screening program should be initiated.
- Colonoscopy should begin between age 20 and 25 and then repeated every 1–2 years.
- Gynecologic examination, annual transvaginal ultrasound, and endometrial aspiration biopsy are recommended because of the high risk of endometrial cancer after age 35.
- Even if some deaths are not linked to colorectal or endometrial cancer, there are no standardized guidelines for screening for other tumors; this is usually based on the specific family history.

- Screening for ovarian cancer should include annual transvaginal ultrasound and pelvic examination.
- Upper gastrointestinal endoscopy should be carried out every 2 years starting from age 30–35 and then every 1–2 years.
- An approach to screening for tumors of the uroepithelial tract should incorporate annual renal ultrasound, urinalysis, and urine cytology.

24.3.3 Colon and Rectum

The theoretical options for HNPCC mutation carriers with a normal colon are surveillance or prophylactic colectomy as a cancer prevention method in highly selected patients. A decision analysis model showed gains in life expectancy for HNPCC patients when offered some intervention [29]. In cohort studies the benefit was greater for prophylactic colectomy when compared to colonoscopic surveillance and decreased the longer surgery was delayed. Randomized controlled data comparing surveillance and prophylactic surgery are, however, not available. During the decision-making process, the patient needs to be told that the optimal management strategy is not yet known and be counseled regarding the risks and benefits of the available options.

For HNPCC mutation carriers with an invasive colorectal cancer, the choice lies between a conventional segmental colectomy and a total colectomy with IRA. Unless the first cancer carries a poor prognosis, prophylactic colectomy seems a reasonable option, as the risk of a metachronous colorectal tumour is around 30 %. However, there is still no clear consensus on the surgical management of colon cancer. The options (partial or total colectomy) should be discussed with the patient, taking into account age, comorbidities, and cancer stage [27]. Regardless of the procedure, lifelong postoperative surveillance is required, with colonoscopy or proctoscopy every year or 2 years in the case of IRA. It seems that the adenoma-carcinoma sequence is accelerated in HNPCC, and there is evidence that cancers can develop within 2 years of a negative colonoscopy [31].

The risk of rectal cancer following a total colectomy with IRA has been shown to be approximately 12 % at 12 years' follow-up, making surveillance mandatory. Patient compliance and the availability of high standard endoscopy will also influence the individual decision.

Rectal cancer is an uncommon index cancer in HNPCC. The principal options are anterior resection of the rectum or proctocolectomy with IPAA. The likely functional outcome, long-term morbidity, and impact on quality of life of each procedure, as well as the need for lifelong colonoscopic surveillance if the proximal colon is preserved, need to be discussed in detail with the patient.

24.3.4 Endometrial Cancer

The cumulative risk of endometrial cancer in women with HNPPC is 42 % and seems to be linked to mutation of *MSH6* in particular and, to a lesser degree, mutation of *MSH2* and *MLH1*. The risk of ovarian cancer is also high, and synchronous ovarian and endometrial cancers have been reported in up to 7 % of patients [32]. The option of prophylactic hysterectomy and bilateral salpingo-oophorectomy needs to be carefully discussed with the patient. At present, the best option seems to be surveillance until the patient has completed childbearing. Hysterectomy and oophorectomy may then be carried out at the time of colectomy or on a separate occasion.

24.4 Other Syndromes

24.4.1 MAP Syndrome

- To date, two guidelines (an international one and a French one) are available [12, 30].
- Screening colonoscopies should start at age 20 for patients with biallelic mutations. The recommended interval depends on the severity of the disease.
- The management of colonic polyps depends on their number:
  - Limited polyps can be removed endoscopically.
  - If polyps are numerous or have a high risk of malignant transformation, the surgical choice lies between a total colectomy and a

restorative proctocolectomy with IPAA, depending on the number of rectal polyps.
- Because of its recessive inheritance, colorectal cancer is often present at the time of diagnosis (around 50 %).
- At least one dermatological evaluation is recommended at the time of diagnosis. Sebaceous lesions are frequent and may lead to carcinoma.
- No desmoid tumors have been found so far in patients with MAP syndrome.
- Siblings of patients with MAP syndrome and patients with a monoallelic *MUTYH* mutation are not in the group at high risk of colorectal cancer. Therefore, colonoscopy should be performed every 5 years starting at age 45.
- Duodenal surveillance of polyps should start at age 25 and subsequently according to the Spigelman score.

24.4.2 Peutz-Jeghers Syndrome

- Because of the risk of colon cancer, colonoscopy is recommended every 3 years starting at age 18.
- In addition, upper gastrointestinal endoscopy should be performed every 3 years starting at age 25.
- Screening for small-bowel cancer should be undertaken with a small-bowel series or videocapsule endoscopy every 2 years.
- Screening for pancreatic cancer should include endoscopic or abdominal ultrasonography starting at age 30 and every 1–2 years thereafter.
- Annual breast examination with mammography every 2–3 years starting at age 25 is recommended.
- Screening for endometrial and ovarian cancers should start at age 20 with an annual pelvic examination, Pap test, and pelvic ultrasound.
- In men, annual testicular examination should commence at age 10, and testicular ultrasonography should be performed if feminine features are observed.

24.4.3 Juvenile Polyposis Syndrome

- Patients with JPS should have their first colonoscopy around age 15–18, and this should be repeated every 1–2 years.
- Upper gastrointestinal endoscopy is recommended from age 25 and then every 1–2 years.

24.4.4 Hyperplastic Polyposis Syndrome

- Cancer screening guidelines have not been established yet. However, a possible strategy is to repeat colonoscopy 1 year after the diagnosis is made and then every 2–3 years.
- Colectomy may be appropriate in cases where the polyp burden is unmanageable endoscopically.

References

1. Fearnhead NS, Britton MP, Bodmer WF. The ABC of APC. Hum Mol Genet. 2001;10(7):721–33.
2. Jasperson KW, Tuohy TM, Neklason DW, et al. Hereditary and familial colon cancer. Gastroenterology. 2010;138(6):2044–58.
3. Al-Tassan N, Chmiel NH, Maynard J, et al. Inherited variants of MYH associated with somatic G:C→T:A mutations in colorectal tumors. Nat Genet. 2002; 30(2):227–32.
4. Lefevre JH, Parc Y, Svrcek M, et al. APC, MYH, and the correlation genotype-phenotype in colorectal polyposis. Ann Surg Oncol. 2009;16(4):871–7.
5. Jones S, Emmerson P, Maynard J, et al. Biallelic germline mutations in MYH predispose to multiple colorectal adenoma and somatic G:C→T:A mutations. Hum Mol Genet. 2002;11(23):2961–7.
6. Nielsen M, Morreau H, Vasen HF, et al. MUTYH-associated polyposis (MAP). Crit Rev Oncol Hematol. 2011;79(1):1–16.
7. Sampson JR, Dolwani S, Jones S, et al. Autosomal recessive colorectal adenomatous polyposis due to inherited mutations of MYH. Lancet. 2003; 362(9377):39–41.
8. Lefevre JH, Colas C, Coulet F, et al. Frequent mutation in North African patients with MUTYH-associated polyposis. Clin Genet. 2011;80(4):389–93.
9. Beggs AD, Latchford AR, Vasen HF, et al. Peutz-Jeghers syndrome: a systematic review and recommendations for management. Gut. 2010;59(7):975–86.

10. Brosens LA, Langeveld D, van Hattem WA, et al. Juvenile polyposis syndrome. World J Gastroenterol. 2011;17(44):4839–44.
11. Hyman NH, Anderson P, Blasyk H. Hyperplastic polyposis and the risk of colorectal cancer. Dis Colon Rectum. 2004;47:2101–4.
12. Vasen HF, Moslein G, Alonso A, et al. Guidelines for the clinical management of familial adenomatous polyposis (FAP). Gut. 2008;57(5):704–13.
13. Giardiello FM, Krush AJ, Petersen GM, et al. Phenotypic variability of familial adenomatous polyposis in 11 unrelated families with identical APC gene mutation. Gastroenterology. 1994;106(6):1542–7.
14. Aziz O, Athanasiou T, Fazio VW, et al. Meta-analysis of observational studies of ileorectal versus ileal pouch-anal anastomosis for familial adenomatous polyposis. Br J Surg. 2006;93(4):407–17.
15. Hor T, Zalinski S, Lefevre JH, et al. Feasibility of laparoscopic restorative proctocolectomy without diverting stoma. Dig Liver Dis. 2012;44(2):118–22.
16. Beyer-Berjot L, Maggiori L, Birnbaum D, et al. A total laparoscopic approach reduces the infertility rate after ileal pouch-anal anastomosis: a 2-center study. Ann Surg. 2013;258(2):275–82.
17. Rajaratnam SG, Eglinton TW, Hider P, et al. Impact of ileal pouch-anal anastomosis on female fertility: meta-analysis and systematic review. Int J Colorectal Dis. 2011;26(11):1365–74.
18. Bulow C, Vasen H, Jarvinen H et al. Ileorectal anastomosis is appopriate for a subset of patients with familial adenomatous polyposis. Gastroenterology. 2000;119:1454–60.
19. Labayle D, Fischer D, Viehl P et al. Sulindac causes regression of rectal polyps in familal adenomatous polyposis. Gastroentrology. 1991;101:635–9.
20. Niv Y, Frazer GM. Adenocarcinoma in the rectal segment in familal polyposis coli is not prevented by sulindac therapy. Gastroenterolgy. 1994;107:854–7.
21. Spigelman AD, Williams CB, Talbot IC, et al. Upper gastrointestinal cancer in patients with familial adenomatous polyposis. Lancet. 1989;2(8666):783–5.
22. Caillie F, Paye F, Desaint B, et al. Severe duodenal involvement in familial adenomatous polyposis treated by pylorus-preserving pancreaticoduodenectomy. Ann Surg Oncol. 2012;19(9):2924–31.
23. Nieuwenhuis MH, Lefevre JH, Bulow S, et al. Family history, surgery, and APC mutation are risk factors for desmoid tumors in familial adenomatous polyposis: an international cohort study. Dis Colon Rectum. 2011;54(10):1229–34.
24. Lefevre JH, Parc Y, Kerneis S, et al. Risk factors for development of desmoid tumours in familial adenomatous polyposis. Br J Surg. 2008;95(9):1136–9.
25. Janinis J, Patriki M, Vini L et al. The pharmacological treatment of agressive fibromatosis: a systematic review. Ann Oncol. 2003;14:181–90.
26. Desurmont T, Lefevre JH, Shields C, et al. Desmoid tumour in familial adenomatous polyposis patients: responses to treatments. Fam Cancer. 2015; 14(1):31–9.
27. Vasen HF, Blanco I, Aktan-Collan K, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. Gut. 2013;62(6):812–23.
28. Canard G, Lefevre JH, Colas C, et al. Screening for Lynch syndrome in colorectal cancer: are we doing enough? Ann Surg Oncol. 2012;19(3):809–16.
29. Syngal S, Weeks JC, Schrag D, et al. Benefits of colonoscopy and prophylactic colectomy in patients with hereditary nonpolyposis colorectal mutations. Ann Int. 1998;129:787–96.
30. Buecher B, Bonaiti C, Buisine MP, et al. French experts report on MUTYH-associated polyposis (MAP). Fam Cancer. 2012;11(3):321–8.
31. Vasen HFA, Abdirahman M, Brohet R et al. One to 2-year surveillance intervals reduce risk of colorectal cancer in families with Lynch syndrome. Gastroenterology. 2010;138:2300–6.
32. Soliman PT, Broaddus RR, Schmeler KM et al. Women with synchronous primary cancer of the endometrium and ovaries: do they have Lynch syndrome? J Clin Oncol. 2005;23:9344–50.

Colon Cancer

25

Thomas H.K. Schiedeck and Klaus E. Matzel

25.1 Introduction

Colon cancer is common and usually presents with a history of altered bowel habit, rectal bleeding, or anemia. The onset and severity of symptoms depends on tumor location. Advanced disease at first presentation is not uncommon because diagnosis of proximal tumors is difficult and often delayed. Outcome is most closely related to the extent of disease at presentation. Surgical resection is the primary treatment for any colon cancer, even in advanced stages; adjuvant chemotherapy improves outcome but the prerequesite of adjuvant treatment is complete removal of the primary tumor. Neoadjuvant chemotherapy should be discussed in selected cases.

25.2 Anatomy

The colon is topographically divided into cecum, ascending colon, transverse colon, descending colon, and sigmoid colon. Colonic tumors occur between the ileocecal junction and the rectosigmoid junction (15 cm from the anal verge, as measured with rigid sigmoidoscopy).

The great majority of colon cancers are adenocarcinomas. Rare tumors, such as neuroendocrine tumors (including carcinoid tumors), leiomyosarcoma, hematopoietic neoplasms, and lymphoid neoplasm, are not described in this chapter.

25.3 Incidence

Bowel cancer is the second most common cancer in Europe, with around 447,000 new cases diagnosed in 2012. In Europe in 2012, the highest age-standardized incidence rates for bowel cancer worldwide were in Slovakia for men and Norway for women. The incidence of colorectal cancer increases significantly starting at age 50 years, with the highest rates in the ≥85-year-old age group. Among adults, incidence rates are significantly higher for males than females (17:10). The risk for colorectal cancer is increased in certain groups (see below).

25.4 Etiology/Epidemiology

The great majority (approximately 90 %) of colon cancers are sporadic, and only 5 % are associated with a recognized familial pattern of inheritance. Several extrinsic factors are connected with an increased risk of developing colon cancer.

T.H.K. Schiedeck, MD (✉)
Department of General and Visceral Surgery, Clinic Ludwigsburg, Ludwigsburg, Germany
e-mail: thomas.schiedeck@kliniken-lb.de

K.E. Matzel, MD, PhD
Department of Surgery, Friedrich-Alexander University, Erlangen, Germany

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_25

25.4.1 Extrinsic Factors/Risk

There is some evidence that a diet rich in vegetables is protective because of the presence of substances with anticarcinogenic properties, such as carotenoids, folate, phenols, and flavonoids. Consumption of nondigestible fructo-oligosaccharides may selectively promote the growth and activity of potentially beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* species. Diets high in starch, nonstarch fiber, and carotenoids possibly decrease risk of developing colon cancer. Daily fiber uptake should achieve 30 g to decrease risk. Usage of dietary supplements (e.g., vitamins, calcium, or β-carotenoid) are not recommended. There is no evidence of risk reduction.

High physical activity is known to decrease risk for colon adenomas and colon cancer.

Obesity is connected with a doubled risk of colon cancer (occurring more often in men than women). Starting at a body mass index >25 kg/m^2, a linear correlation between body mass index and risk of colon cancer was detected. Smoking is associated with a doubled risk of colon cancer. There is a positive correlation between alcohol consumption and colon cancer. The uptake of 100 g alcohol/week is connected with a 15 % increased cancer risk. Red meat and processed meat are also associated with a higher risk of colon cancer.

Cox-II inhibitors are associated with a decreased risk of colorectal cancer, but unfortunately their use is accompanied by increased cardiovascular morbidity. Therefore they are not generally recommended. Chronic use of aspirin decreases the risk of colorectal cancer (proven by cohort studies) but increases the incidence of gastrointestinal bleeding and is therefore also not recommended for the prevention of colorectal cancer.

25.4.2 Genetic Factors

Fifteen percent of patients with sporadic colorectal cancer show hereditary nonpolyposis colorectal cancer (HNPCC)–like genome defects: microsatellite instability (MSI) and loss of the MLH1 protein. In sporadic colorectal cancer, this is caused by a mutation of the *BRAF* gene. First-degree relatives of an index patient have a higher (1.6-fold) risk of developing colorectal cancer. In any tumor with MSI and an MLH1 defect, a *BRAF* analysis should performed to distinguish between sporadic colorectal cancer and HNPCC.

25.4.2.1 Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) is associated with a mutation or loss of the FAP gene (also called the adenomatous polyposis [*APC*] gene). The risk of developing colorectal cancer is nearly 100 % in FAP. The onset of this polyp disease occurs in the second decade of life, and more than 100 polyps are characteristic.

Extracolonic intestinal manifestations (occurring in approximately 75 % of patients) include adenomas of the duodenum and the ampulla of Vater, both considered to be precancerous. Incidence of gastric adenomas is less than 10 % in FAP. Extraintestinal manifestations include desmoid tumors, thyroid carcinoma, medulloblastoma, hepatoblastoma, osteoma, epidermoid cysts, and pigment anomalies of the retina.

25.4.2.2 Attenuated Familial Adenomatous Polyposis

Patients with attenuated FAP (attenuated adenomatous polyposis coli [AAPC]) typically present with <100 polyps and at an older age, often the fourth decade. Extracolonic manifestations can occur. AAPC is caused by a heterogenous group of *APC* and *MYH* mutations. Proof of MSI, *APC*, and *MYH* can be helpful to differentiate AAPC from HNPCC.

25.4.2.3 MUTYH-Associated Polyposis

MUTYH-associated polyposis (MAP) is the most important differential diagnosis of FAP. It is diagnosed in 15–20 % of all *APC* mutation–negative colorectal adenomatoses. The phenotype of MAP is similar to that of AAPC. The lifetime risk of developing colorectal cancer is high among patients with MAP (70–80 %). Because MAP is an biallelic (autosomal-reces-

sive) germ-line mutation, the risk of children of index patients or heterozygotic carriers developing colorectal cancer is low.

25.4.2.4 Hereditary Nonpolyposis Colorectal Cancer

HNPCC is associated with germ-line mutations in six DNA mismatch repair (MMR) genes (*MLH1*, *MLH2*, *MSH2*, *MSH6*, *PMS1*, *PMS2*). Almost 90 % of the detected mutations are located in *MSH2* and *MLH1*.

Unlike for FAP, clinical diagnosis is difficult because HNPCC does not present with a distinct phenotype. Thus clinical criteria (Amsterdam I and Bethesda criteria; Tables 25.1 and 25.2) were defined for use as a screening tool for mutations. HNPCC is clinically diagnosed if the Amsterdam I criteria are met. The Amsterdam II criteria refer to extracolonic manifestations (endometrial, urothelial, and small-bowel carcinomas). Because many families today are small, a negative family history does not preclude HNPCC; the less-specific Bethesda criteria aim to determine a diagnosis in small families using clinical means. MSI is found in tumor tissue harvested from 80 to 90 % of patients who fulfill the Amsterdam I/II criteria and in 30 % of patients who fulfill the Bethesda criteria.

General tumor risk in patients with HNPCC is considered to be 80–90 %, with colorectal cancer being the most common (at a median age of 44 years; uncommon before 25 years). The second most common cancer in patients with HNPCC is endometrial carcinoma; lifetime risk is 40–60 % at a median age between 46 and 48 years. Ovarian cancer occurs in 10–15 %; gastric cancer, mostly the intestinal tumor type, in 2–13 %; and small-bowel cancer in 1–4 % (around one-third occur in the duodenum). The relative risk for urothelial cancer in men with a mutation in the MMR germ line is 4.2; for women it is 2.2-fold higher.

Performing additional molecular (pathologic) diagnostics regarding HNPCC is recommended in every person fulfilling one Bethesda criterion. Diagnostic evaluation should include immunohistochemical staining of MMR protein expression and analysis of MSI.

Table 25.1 Amsterdam I criteria

1.	At least three relatives with histopathologically verified colorectal cancer; one must be a first-degree relative of the other
2.	At least two successive generations affected
3.	At least one of the relatives with colorectal cancer diagnosed at less than 50 years of age
4.	Familial adenomatous polyposis has been excluded

Table 25.2 Revised Bethesda guidelines

Tumors from individuals should be tested for MSI in the following situations	
1.	Colorectal cancer diagnosed in a patient who is less than 50 years of age
2.	Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors, regardless of age
3.	Colorectal cancer with the MSI-H histology diagnosed in a patient who is less than 60 years of age
4.	Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under the age of 50 years
5.	Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age

25.4.2.5 Hamartomous Polyposis Syndrome

Peutz-Jeghers syndrome and juvenile polyposis coli (familial juvenile polyposis) are rare hamartomatous polyposis syndromes. Peutz-Jeghers syndrome is an autosomal-dominant germ-line mutation of the *STK11/LKB1* gene. The cumulative lifetime risk for malignant tumors reaches 90 %; the risk for colorectal cancer is 39 % and is mostly commonly diagnosed at an age of 30–50 years.

25.4.2.6 Chronic Inflammatory Bowel Disease

Colorectal cancer risk is increased in patients with ulcerative colitis and is dependent on the manifestations, extent, and duration of the disease. The cumulative lifetime risk of developing cancer in patients with pancolitis is 2 % after 10 years, 9 % after 20 years, and 18 % after 30 years.

Crohn's disease is also associated with an increased risk for colorectal and small-bowel cancers, although it is less well defined. A 3.5- to 7-fold increase is suggested, specifically when the colon is involved in Crohn's disease.

25.5 Diagnosis

Colorectal cancer is diagnosed either as a result of a screening program or when a patient becomes symptomatic. Early colorectal cancer is often asymptomatic (especially if located in the right hemicolon) or presents with nonspecific symptoms; thus screening programs for early detection are of major importance. Since the late 1950s, a gradual shift toward right-sided or proximal colon cancers has been observed.

25.5.1 Screening in the Healthy Population

Screening for colorectal cancer aims for early detection and the removal of precancerous lesions in sporadic colorectal cancer developing in patients older than 50 years. Complete flexible colonoscopy is the gold standard in early detection of colorectal neoplasias. It shows the highest sensitivity and specificity. Two case-control studies demonstrated a 66–90 % reduction in colorectal cancer incidence by flexible colonoscopy. Negative colonoscopy should be repeated after a period of 10 years.

The protective effect of flexible sigmoidoscopy for distal neoplasms seems to last 6–10 years. However, a study of nearly 10,000 patients showed a 0.8 % detection rate for distal adenomas or carcinomas 3 years after negative sigmoidoscopy. The recommend control interval for sigmoidoscopy without pathological findings is 5 years.

The second recommended screening method is fecal occult blood testing (FOBT). The sensitivity of FOBT for confirmed colorectal cancer is 50 % and for polyps is around 10 %. The predictive value of a positive test averages 10 % for cancer. Any (single) positive test result must be followed by complete flexible colonoscopy. The efficacy of FOBT was demonstrated in four large, randomized trials in which colorectal cancer mortality was reduced by 25 % in individuals participating in an annual screening program. Biennial testing is less effective. FOBT is unnecessary in individuals participating in an regular colonoscopy screening program.

Randomized trials have demonstrated that some immunologic FOBTs are superior regarding the detection rate of advanced neoplasias compared with guaiac FOBT. The studies show some immunologic FOBTs (e.g., OC-Sensor) afford the same specificity (>90 %) but higher sensitivity.

The Advisory Committee on Cancer Prevention in the European Union suggested in 1999 that screening programs for colorectal cancer should use FOBT. Colonoscopy should be used to follow-up on positive findings. Screening should be offered to men and women aged 50 to approximately 74 years, with an interval of 1–2 years.

25.5.2 Screening in Populations at Increased Risk

Persons with increased risk for colorectal cancer due to certain predispositions comprise the following three groups:

- Increased family risk (genetic background unknown)
- Proven or potential risk of hereditary colorectal cancer
- Presence of chronic inflammatory bowel disease

First-degree relatives of patients with colorectal cancer are at increased risk of developing colorectal cancer. If an index patient older than 60 years develops cancer, the risk of developing cancer is only minimally increased for his or her relatives.

In patients with a family history of colorectal cancer or adenomatous polyps, advise screening colonoscopy beginning at age 40 years or 10 years younger than the youngest age at the diagnosis in the family. Screening should be repeated at 5-year intervals. This protocol should followed in two groups of patients:

Persons with a first-degree relative (parent, sibling, or child) with colon cancer or adenomatous polyps diagnosed at an age ≤60 years
Persons with two first-degree relatives diagnosed with colorectal cancer at any age

These screening recommendations must be considered provisional, as mortality-reduction studies are not yet available.

Colorectal cancer mortality is lower in patients with FAP who have been screened than in those who present with symptoms. Genetic testing should be performed at age 10 years; if a genetic mutation can be excluded, no further special screening is required. Annual colonoscopy from age 10–12 years should be advised in:

Persons with a genetic diagnosis of FAP
Persons with a risk of FAP in whom genetic testing has not been performed and/or a mutation cannot be excluded

In patients with attenuated FAP, treatment should be based on age, the number of polyps, and the histopathological findings. Colonoscopy should be performed annually throughout the patient's life if colectomy is not indicated. In persons from a family with attenuated FAP, the first colonoscopy should be at age 15 years; if there are no findings, the next colonoscopy should be performed in 5 years. From age 20 years, colonoscopy is recommend annually.

Colonoscopy can reduce risk and mortality from colorectal cancer in families fulfilling the Amsterdam criteria for HNPCC. Genetic testing for HNPCC should be offered to first-degree relatives of persons with a known inherited MMR gene mutation. Among persons with a genetic or clinical diagnosis of HNPCC, yearly or biennial colonoscopy should start at age 20–25 years or 10 years earlier than the youngest age at diagnosis of colorectal cancer in the family.

In asymptomatic biallelic *MUTYH* mutation carriers, colonoscopy is recommended at age 18–20 years. If there are no polyps these patients should undergo lifetime surveillance. In patients with MAP, colonoscopy should be performed annually.

History of Adenomatous Polyps (see Chap. 8.1)

In patients with a history of colorectal cancer, if synchronous neoplasm is excluded at the time of resection with curative intent, subsequent colonoscopy should be performed 2 and 5 years after surgery and every 5 years thereafter.

Colonoscopy with systematic four-quadrant biopsies at 10-cm intervals should be performed in patients with inflammatory bowel disease/ulcerative colitis presenting as long-standing pancolitis (>8 years) or left-sided inflammatory colitis (>15 years). If intraepithelial neoplasia is detected and confirmed, colectomy is indicated. No general recommendation can be given for patients with Crohn's disease.

No randomized controlled trials have studied surveillance colonoscopy in patients with ulcerative colitis or Crohn's colitis. A meta-analysis of case-control studies showed a reduction in the risk of colorectal cancer mortality in patients with ulcerative colitis following a surveillance program.

25.5.3 Symptoms

The majority of patients present with alteration in bowel habit, frank rectal bleeding, or anemia as a result of occult bleeding. Symptoms such as intermittent abdominal pain, nausea, and vomiting are often secondary to partial obstruction or peritoneal dissemination. Patients may occasionally notice a palpable mass, which is more common in right-sided colon cancer.

Intestinal obstruction is most commonly associated with cancer of the sigmoid colon. This may lead to acute colonic perforation if the ileocecal valve is competent. If the valve is incompetent, presentation is less dramatic, with increasing constipation and abdominal distension noticed over many days, ending in a typical symptomatic ileus.

Perforation of colon cancer may be acute or chronic. It may occur at the site of the tumor or more proximal in the distended part of the colon. Perforation may extend into the retroperitoneum, bladder, or genital tract, with fistula formation.

25.5.4 Diagnostic Strategies

Diagnosis is established by colonoscopy and biopsy. The precise location of the neoplasm must be documented and the base of any suspicious polyp tattooed at the time of snare excision. Careful clinical examination for regional lymphatic and distant metastatic disease should be performed.

To exclude liver metastasis, ultrasonography or multislice computed tomography (CT) are the imaging techniques with highest sensitivity (63–86 % and 75–83 %, respectively) and best specificity (98 % and 98 %, respectively). CT has advantages in assigning metastases to anatomic structures such as liver veins, hilar vessels, and the caval vein, which is necessary to estimate resectability. However, magnetic resonance imaging is the optimal tool to evaluate the extent of liver metastasis. To exclude synchronous malignancies, the entire large bowel should be examined if the lumen is not obstructed. If colonoscopy is not possible or complementary information is required, virtual colonography (based on CT or magnetic resonance tomography) or radiography with water-soluble contrast (if there is a risk of perforation) is mandatory.

25.6 Differential Diagnosis

The most common differential diagnoses are:

Diverticular disease with stenosis or phlegmon
Inflammatory bowel disease
Colonic ischemia
Infection
Other malignancies

25.7 Staging

Clinical staging aims to determine the local and distant extent of the disease according to the clinical TNM system (see Chap. 23). Staging requires local assessment of the tumor and screening for metastatic disease. The clinical classification, cTNM, is the basis for clinical decision making and determines the therapeutic algorithm.

25.7.1 Clinical Staging

History, including family history (Amsterdam and Bethesda criteria)
Physical examination

25.7.2 Investigations

- Colonoscopy
- Chest radiography
- CT of the abdomen and pelvis
- Positron emission tomography, which is indicated in the following scenarios:
  - Candidates for resection of isolated colorectal cancer metastases to prevent unnecessary laparotomy
  - Restaging of possible local recurrence or metastatic disease

25.7.3 Laboratory Testing

Elevated levels of serum carcinoembryonic antigen (CEA) that do not normalize after surgical resection imply persistent disease and the need for further evaluation. A postoperative increase in CEA during follow-up indicates a potential recurrence. A liver chemistry panel should also be performed.

25.8 Treatment

Primary treatment for colon cancer is surgical resection of the primary tumor and lymph nodes. Open and laparoscopic approaches are equally safe in experienced hands. The term *curative resection* (R0) should be used when there is histological confirmation of complete excision without residual tumor.

25.8.1 Curative Intent

25.8.1.1 Operative Intervention

Any operative intervention should start with intraoperative staging by inspection and palpation of the liver. As long as a sufficient preoperative diagnostic test (magnetic resonance imaging, CT) is performed, intraoperatively only subserosal metastases (>2 mm) may additionally be detected (by palpation and inspection). In addition, intraoperative liver sonography provides high sensitivity and has a very high positive predictive value (−100 %).

Operative intervention aims to achieve a curative resection. If adjacent organs are involved, en bloc resection is indicated. In colon cancer (unlike rectal cancer), the need for a radical approach has not been proved in prospective randomized trials. However, based on histopathological results, prospective observational studies, and theoretical concepts, surgeons performing colon cancer resections should adhere to the following principles of radicality:

A 2-cm safety margin is sufficient with regard to microscopic tumor spread but insufficient for lymphatic spread (as regional lymph drainage exceeds this distance).

Lymph node metastases travel along the vascular supply, primarily with the paracolic supply, up to 10 cm from the macroscopic edge of the primary tumor. Thus at least 10 cm of the colon should be removed if vascular division is radicular.

The extent of resection is determined by the vascular supply and the consequently defined area of lymphatic drainage. In principle, if the tumor is located between two major vessels, both should be divided centrally (Figs. 25.1, 25.2, 25.3, 25.4, and 25.5).

Complete mesocolic excision in patients with colon cancer improved overall survival and progression-free survival in some cohort studies. This complex surgical procedure provides more radicality but may be connected with higher morbidity. It should performed only by excellent trained surgeons with expertise in colon surgery.

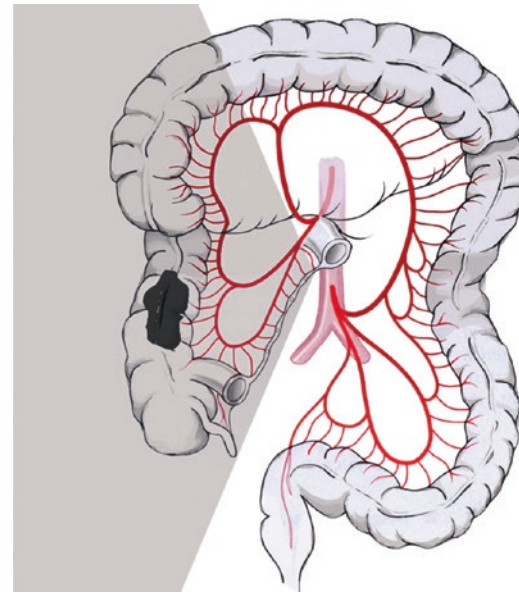


Fig. 25.1 Cancer: ascending colon. Right-sided hemicolectomy with central ligation of the ileocolic artery and the right colonic artery

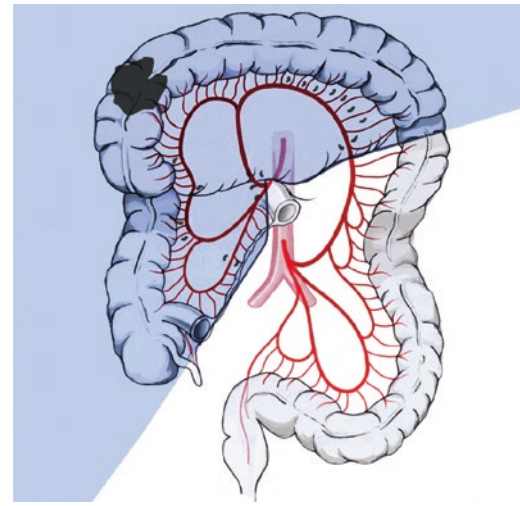


Fig. 25.2 Cancer: hepatic flexure. Extended right hemicolectomy with central ligation of the ileocolic, right colonic, and middle colic arteries

Special Considerations

When patients present with multiple colon cancers, total colectomy is not mandatory, in principle. The extent of the resection should follow the principles of radicality, as described earlier.

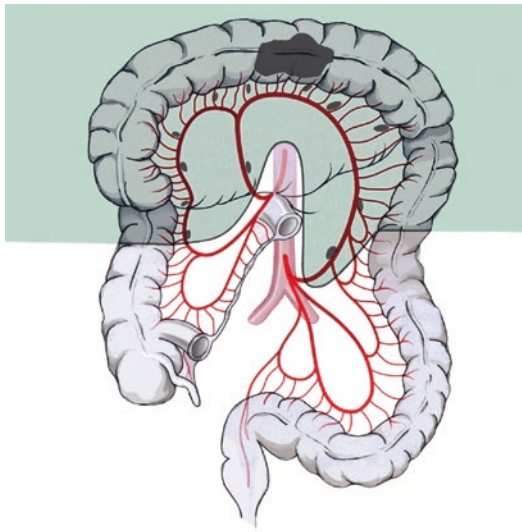


Fig. 25.3 Cancer: transverse colon. Transverse colon resection with central ligation of the middle and left colonic arteries

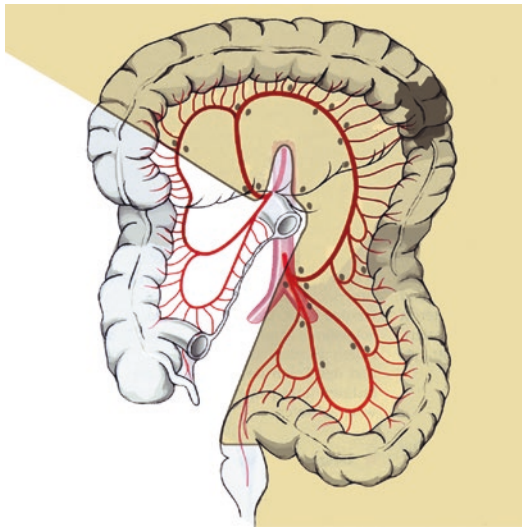


Fig. 25.4 Cancer: splenic flexure. Extended left hemicolectomy with central ligation of middle colic and inferior mesenteric arteries

However, many advocate subtotal colectomy and ileorectal anastomosis.

Synchronous distant metastases can be resected at the same time as the primary tumor or later. Simultaneous liver resection may be connected with high mortality rate in patients aged >70 years. Multiple synchronous liver metastases

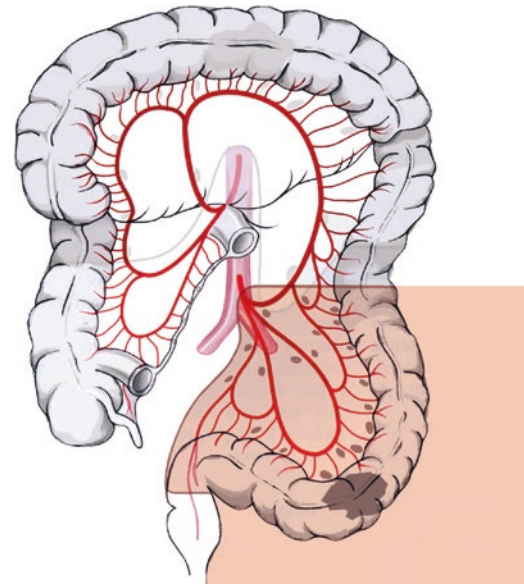


Fig. 25.5 Cancer: sigmoid. Sigmoid resection with central ligation of the inferior mesenteric artery

should be treated using a two-stage concept. In synchronous metastasis with an asymptomatic primary tumor, whether to go for the liver first with or without neoadjuvant chemotherapy should be discussed.

In emergencies, a radical procedure should be performed, if possible. In the case of obstruction, intraluminal stenting can be used for bridging in select cases. If perforation is excluded, obstruction can be considered urgent, not emergent, unless the ileocecal valve is competent and the cecum is at risk of perforation. In the majority of cases with obstruction, the disease is at an advanced stage and neoadjuvant treatment is indicated. For that reason, a diverting stoma may a good option in cases without perforation.

When cancer occurs in patients with FAP, a radical procedure should be attempted via restorative proctocolectomy. If complete resection (R0) is not achievable, limited procedures can be considered. In cases with insufficient anal sphincter, stoma creation can be suggested. Lifelong surveillance is mandatory if a subtotal colectomy with ileorectal anastomosis is feasible. The patient must be counseled accordingly. Subtotal colectomy with ileorectal anastomosis

is acceptable for cancer in patients with attenuated FAP with limited manifestation in the rectum.

For patients with HNPCC with cancer, oncological resection may be performed as in sporadic colonic cancer; however, prophylactic subtotal colectomy may be considered in patients known to have a genetic mutation.

Restorative proctocolectomy is indicated if anal sphincter function is adequate for cancer in patients with ulcerative colitis.

Local/Limited Procedures

A local procedure for colon cancer should be considered oncologically adequate only if, after complete full-thickness resection (R0), tumor stage is confined to pT1, grade is good or moderate (G1–2), no lymphatic (L0) or vascular invasion (V0) has occurred, and the tumor diameter is less than 3 cm.

25.8.1.2 Postoperative Histopathological Evaluation/ Histopathological Reporting

To ensure correct histopathological classification, the following information must be answered in the report:

Location of the primary tumor
Type of tumor
Level of invasion (pT)
Tumor grading (G)
Status of local lymph nodes (pN)
Number of examined lymph nodes (≥12 are recommended)
Number of lymph nodes with tumor involvement
Distance of resection margins
Completeness of tumor removal (R)
Invasion of lymphatic and vascular vessels (L, V)
MSI (in HNPCC)

25.8.2 Adjuvant Treatment

The prerequisite for adjuvant therapy is complete removal of the primary tumor (local R0). The indication is based on histopathological staging, especially nodal status (pN), determined by the examination of at least 12 lymph nodes. Positive immunocytological detection of isolated tumor cells and/or positive cytological findings from peritoneal lavage are not considered indications. Arguments for adjuvant therapy in addition to tumor classification are special intraoperative risk factors such as T4 stadium, tumor perforation, fewer than 12 nodes examined, and/or an emergency situation.

25.8.2.1 Contraindication for Adjuvant Therapy in Colon Cancer

All items are primary contraindications for adjuvant treatment. Incomplete removal is explicitly mentionened because this situation may be improved by additional surgery.

Union for International Cancer Control (UICC) stage I

Poor performance status

Liver cirrhosis (Child-Pugh score of B or C)

Cardiac insufficiency (New York Heart Association heart failure classes III or IV)

Preterminal and terminal renal failure

Reduced bone marrow function

Inability to participate in follow-up

25.8.2.2 UICC stage II (relative contraindication)

In special risk situations (see Sect. 25.8.2.1), adjuvant treatment in UICC stage II disease may be discussed, but based on available data, adjuvant therapy should not be recommended in general for patients with UICC stage II disease. If chemotherapy is given, it should be administered only within controlled studies.

Good general health status provided a patient age older than 70 years is not a contraindication for adjuvant treatment.

25.8.2.3 Neoadjuvant Treatment

Neoadjuvant chemotherapy, radiotherapy, and radiochemotherapy are not generally indicated in colon cancer. In nonobstructing tumors with distant metastases, neoadjuvant treatment may be an option to control the disease before resection. Moreover, it should be discussed whether the first treatment (resection) of (liver) metastases is

advisable; however, this should be performed only when following controlled study protocols.

Adjuvant Treatment Protocols

Adjuvant chemotherapy is advised for patients with stage III colon cancer (R0). Several randomized clinical trials demonstrated a significant reduction in recurrence and improved overall survival after 5-fluorouracil (5-FU)– and folinic acid–based adjuvant therapy. In the meantime, other studies demonstrated that a 5-FU/folinic acid and oxaliplatin regimen significantly improves disease-free survival.

In patients with contraindications to oxaliplatin, fluoropyrimidine monotherapy is advocated. Oral administration is recommended. Because of its high toxicity, bolus administration should not be used.

Adjuvant chemotherapy is not indicated for patients with stage II colon cancer (R0). As mentioned earlier, in a setting implying increased risk of recurrence it may be considered, but then should be used only within controlled studies.

Several chemotherapy regimens are commonly used:

Leucovorin- 5 Flurouracil + oxaliplatin (MOSAIC trial): 200 mg/m^2 folinic acid (2-h infusion on days 1 and 2), plus 5-FU (400 mg/m^2 bolus followed by 600 mg/m^2 [22-h infusion on days 1 and 2), plus 85 mg/m^2 oxaliplatin (2 h on day 1); 1 cycle every 2 weeks, for a total of 12 cycles.

5-FU/folinic acid regimen: 500 mg/m^2 folinic acid (1- to 2-h infusion), plus 2,600 mg/m^2 5-FU (24-h infusion) once a week for 6 weeks (days 1, 8, 15, 22, 29, and 36). A second cycle should start at week 8; a total of two cycles is recommended.

Mayo regimen: 20 mg/m^2 folinic acid (intravenous), plus 425 mg/m^2 5-FU (intravenously for <5 min) on days 1–5 in weeks 1, ,4 and 8; three additional cycles occur at 5-week intervals thereafter.

Oral 5-FU prodrug regimen: capecitabine 1250 mg/m^2 twice daily on days 1–14; repeated every 3 weeks for eight cycles.

Toxicity

Typical side effects of chemotherapy are neuropathy (oxaliplatin) and neutropenia, diarrhea, and alopecia (irinotecan).

25.8.3 Palliative Treatment

Depending on the patient's situation, various modes are used for palliative treatment (e.g., surgery, endoscopic interventions, radiotherapy, chemotherapy, and interventional radiology). Surgery should be attempted even with only palliative intent to minimize the risk of complications from the primary tumor, such as stenosis, bleeding, and tumor infiltration of adjacent organs. In a French randomized, multicenter trial, a risk reduction of 58 % in overall survival was shown for resected compared with nonresected patients.

If resection of the primary tumor is not indicated, bowel passage can be reestablished by local treatment, bypass procedures, or stoma creation. If the tumor is not resectable, therapeutic options depend on the patient's general status and comorbidity. Strategies include:

- Turn unresectability into resectability (especially in liver/lung metastases)
- Prolong progression-free survival
- Provide the best supportive care

Several combinations of chemotherapy with palliative are advocated, depending on the patient's general condition and tumor characteristics (e.g., a *KRAS* mutation). The following regimens are used: 5-FU/folinic acid/irinotecan infusions and 5-FU/folinic acid/irinotecan/oxaliplatin infusion. In patients with comorbidities or contraindications for oxaliplatin or irinotecan, less toxic regimens with capecitabine or uracil/tegafur (5-FU prodrug) are good alternatives.

Various regimens of 5-FU with irinotecan and/or oxaliplatin are used as second- and third-line treatments. Depending on KRAS status, they are usually combined with antibodies against the vascular endothelial growth receptor or epidermal

growth factor receptor (bevacizumab, cetuximab, panitumumab).

25.8.4 Special Considerations: Metastases and Local Recurrence

Patients with resectable metastases of the liver or lung should undergo primary resection. Positron emission tomography/CT is advocated, as disease is subsequently upstaged in 30% of patients. Patients presenting with liver metastases that are not amenable to radical resection should be treated with systemic chemotherapy. Resectability must be evaluated by a surgeon with expertise in liver surgery. Surgical resection is superior to interventional procedures and therefore the method of choice. The role of all interventional procedures has not been proven yet. Radiofrequency ablation is an option in all patients who do not qualify for surgical resection (unresectability, poor general condition, recurrence following liver surgery). Selective internal radiation therapy may be used in disseminated liver metastases without other therapy options. Laser-induced interstitial thermotherapy should be evaluated in studies only.

Isolated bone metastases with pain should be treated with local radiation. A single, high-dose application seems to be equivalent to fractioned radiation.

In local recurrence, the reintervention aims for radicality. If an R0 resection is not achievable, reintervention aims to relieve symptoms and avoid complications such as stenosis, bleeding, obstruction, and ileus.

In patients with limited peritoneal carcinosis, cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy is an option. Treatment should be administered within a study protocol or at least a register. The following criteria should be fulfilled:

- Preoperative Peritoneal Carcinosis Index <20
- No extra-abdominal metastases
- Resection must achieve R0 or R1 status
- Treatment in a specialized center

25.8.5 Current Treatment Recommendations

- The mainstay of therapy is surgery with curative intent, in particular colon resection with lymphadenectomy (guided by vascular supply).
- Histopathological evaluation should include at least 12 lymph nodes.
- Adjuvant chemotherapy is indicated in UICC stage III disease.
- Surgery is the treatment of choice for resectable distant metastases.

25.9 Follow-Up

The follow-up regimen should be adapted to the tumor stage. In UICC stage I disease after R0 resection, the risk of recurrence is low. Colonoscopy in years 2 and 5 can detect secondary tumors early. The regimen should be modified in cases of increased risk of recurrence (e.g., G3/4, L+, V+, tumor perforation) and should include regular follow-up with CEA levels measured every 6 months (up to year 5), ultrasound or CT of the abdomen and pelvis every 6 months for 2 years, and chest radiography every year.

In patients with HNPCC after hemicolectomy, colonoscopy is indicated every year if adenomas were present; after subtotal colectomy, sigmoidoscopy is advised every second year. In patients after colectomy with ileal pouch–anal reconstruction, pouchoscopy is indicated yearly and duodenogastroscopy every 3 years (annually in patients with adenomas).

Suggested Reading

1. Ahmed S, et al. Survival impact of surgical resection of primary tumour in patients with stage IV colorectal cancer. Cancer. 2014;120:683–91.
2. Amado RG, Wolf M, Peeters M, Van Cutsem E, Siena S, Freeman DJ, Juan T, Sikorski R, Suggs S, Radinsky R, Patterson SD, Chang DD. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol. 2008; 26(10):1626–34.

3. Aretz S. The differential diagnosis and surveillance of hereditary gastrointestinal polyposis syndromes. Dtsch Arztebl Int. 2010;107(10):163–73.
4. Bertelsen CA, et al. Can the quality of colonic surgery be improved by standardization of surgical technique with complete mesocolic excision? Colorectal Dis. 2011;13(10):1123–9.
5. Brenner H, et al. Long-term risk of colorectal cancer after negative colonoscopy. J Clin Oncol. 2011; 29(28):3761–7.
6. Bulow S. Clinical features in familial polyposis coli. Results of the Danish Polyposis Register. Dis Colon Rectum. 1986;29(2):102–7.
7. Cao C, et al. A systematic review and meta-analysis of cytoreductive surgery with perioperative intraperitoneal chemotherapy for peritoneal carcinomatosis of colorectal origin. Ann Surg Oncol. 2009;16(8): 2152–65.
8. Chang GJ, et al. Lymph node evaluation and survival after curative resection of colon cancer: systematic review. J Natl Cancer Inst. 2007;99(6):433–41.
9. de Gramont A, C.B., Navarro M, Tabernero J, Hickish T, Topham C, Bonetti A, Clingan P, Lorenzato C, André T. Oxaliplatin/5FU/LV in adjuvant colon cancer: updated efficacy results of the MOSAIC trial, including survival, with a median follow-up of six years. J Clin Oncol 2007 ASCO Annual Meeting Proceedings (Post-Meeting Edition) Vol 25, No 18S (June 20 Supplement), 2007: 4007, (2007).
10. Falcone A, et al. Phase III trial of infusional fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI) compared with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI) as first-line treatment for metastatic colorectal cancer: the Gruppo Oncologico Nord Ovest. J Clin Oncol. 2007; 25(13):1670–6.
11. Feliu J, et al. XELOX (capecitabine plus oxaliplatin) as first-line treatment for elderly patients over 70 years of age with advanced colorectal cancer. Br J Cancer. 2006;94(7):969–75.
12. Ferlay J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer. 2013;49(6):1374–403.
13. Ferrand F, et al. Impact of primary tumour resection on survival of patients with colorectal cancer and synchronous metastases treated by chemotherapy: results from the multicenter, randomised trial Federation Francophone de Cancerologie Digestive 9601. Eur J Cancer. 2013;49:90–7.
14. Floriani I, et al. Performance of imaging modalities in diagnosis of liver metastases from colorectal cancer: a systematic review and meta-analysis. J Magn Reson Imaging. 2010;31(1):19–31.
15. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg. 1999;230(3):309–18.
16. Guillem JG, et al. Colonoscopic screening for neoplasms in asymptomatic first-degree relatives of colon cancer patients. A controlled, prospective study. Dis Colon Rectum. 1992;35(6):523–9.
17. Hohenberger W, et al. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation – technical notes and outcome. Colorectal Dis. 2009;11(4):354–64. discussion 364-5.
18. Imperiale TF, et al. Results of screening colonoscopy among persons 40 to 49 years of age. N Engl J Med. 2002;346(23):1781–5.
19. Jasperson KW, et al. Hereditary and familial colon cancer. Gastroenterology. 2010;138(6):2044–58.
20. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev. 2007; (1):CD002200.
21. Jones N, et al. Increased colorectal cancer incidence in obligate carriers of heterozygous mutations in MUTYH. Gastroenterology. 2009;137(2):489–94. 494 e1.
22. Killeeen S, Mannion M, Devaney A, Winter DC. Complete mesocolic resection and extended lymphadenectomy for colon cancer: a systematic review. Colorectal Dis. 2014;16(8):577–94.
23. Kim KH, et al. Comparative analysis of radiofrequency ablation and surgical resection for colorectal liver metastases. J Korean Surg Soc. 2011;81(1):25–34.
24. Kuhry E, et al. Long-term results of laparoscopic colorectal cancer resection. Cochrane Database Syst Rev. 2008(2): CD003432.
25. Lee WS, et al. Pulmonary resection for metastases from colorectal cancer: prognostic factors and survival. Int J Colorectal Dis. 2007;22(6):699–704.
26. Levin B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology. 2008;134(5):1570–95.
27. Levy M, et al. Tumor markers in staging and prognosis of colorectal carcinoma. Neoplasma. 2008;55(2): 138–42.
28. Liang Y, et al. Laparoscopic versus open colorectal resection for cancer: a meta-analysis of results of randomized controlled trials on recurrence. Eur J Surg Oncol. 2008;34(11):1217–24.
29. Maindrault-Goebel F., G.L., B. Mineur CL, Andre T, Bennamoun M, Mabro M, Artru P, Louvet C, de Gramont A. Final results of OPTIMOX2, a large randomized phase II study of maintenance therapy or chemotherapy-free intervals (CFI) after FOLFOX in patients with metastatic colorectal cancer (MRC): a GERCOR study. J Clin Oncol, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: 4013, 2007.
30. Miller PE, et al. Dietary patterns and colorectal adenoma and cancer risk: a review of the epidemiological evidence. Nutr Cancer. 2010;62(4):413–24.
31. Morreau H, Riddel R, Aretz S. MUTYH-associated polyposis. In: Bosman FT et al., editors. WHO classification of tumours of the digestive system. Lyon: IARC/ WHO Press; 2010. p. 156–9.
32. Niekel MC, Bipat S, Stoker J. Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospec-

tive studies including patients who have not previously undergone treatment. Radiology. 2010;257(3):674–84.
33. Nordlinger B, et al. Surgical resection of colorectal carcinoma metastases to the liver. A prognostic scoring system to improve case selection, based on 1568 patients. Association Francaise de Chirurgie. Cancer. 1996;77(7):1254–62.
34. Nordlinger B, et al. Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. Lancet. 2008;371(9617):1007–16.
35. Portier G, et al. Multicenter randomized trial of adjuvant fluorouracil and folinic acid compared with surgery alone after resection of colorectal liver metastases: FFCD ACHBTH AURC 9002 trial. J Clin Oncol. 2006;24(31):4976–82.
36. Sargent DJ, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med. 2001;345(15):1091–7.
37. Schmiegel WH, A.R.-S., Freier W, Dietrich G, Arnold D, Kanzler S, Geissler M, Graeven U, Hegewisch-Becker S, Schmoll H. Comparable safety and response rate with bevacizumab in combination with capecitabine/oxaliplatin (CapOx/Bev) versus capecitabine/irinotecan (CapIri/Bev) in advanced CRC (mCRC): a randomized phase II study of the AIO GI tumor study group. J Clin Oncol, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: 4034, 2007.
38. Schmoll HJ, et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. J Clin Oncol. 2007;25(1):102–9.
39. Stillwell AP, Buettner PG, Ho YH. Meta-analysis of survival of patients with stage IV colorectal cancer managed with surgical resection versus chemotherapy alone. World J Surg. 2010;34(4):797–807.
40. Terry MB, et al. Risk factors for advanced colorectal adenomas: a pooled analysis. Cancer Epidemiol Biomarkers Prev. 2002;11(7):622–9.
41. Van Cutsem E, R.L., Hossfeld D, Bodoky G, Roth A, Aranda E, Nordlinger B, Assadourian S, Wang K, Cunningham D. PETACC 3, randomized phase III trial comparing infused irinotecan/5-fluorouracil (5-FU)/folinic acid (IF) versus 5-FU/FA (F) in stage III colon cancer patients (pts). (PETACC 3). J Clin Oncol, 2005 ASCO Annual Meeting Proceedings., 2005. 23(16S, Part I of II (June 1 Supplement)).
42. Van Damme J-P. Vascular anatomy in abdominal surgery. Stuttgart: Thieme; 1990.
43. van Rossum LG, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. Gastroenterology. 2008;135(1):82–90.
44. Vasen HF, et al. The International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC). Dis Colon Rectum. 1991;34(5):424–5.
45. Verwaal VJ, et al. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. Ann Surg Oncol. 2008;15(9):2426–32.
46. West NP, et al. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. J Clin Oncol. 2010;28(2):272–8.
47. Winawer SJ, et al. Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology. 1997;112(2):594–642.

Rectal Cancer

26

Christian Buchli and Anna Martling

26.1 Epidemiology/Etiology

Colorectal cancer (CRC) accounts for approximately 10 % of the total cancer burden; it is the second most common cancer in women and the third most common cancer in men. The age-standardized incidence rates of CRC vary tenfold across the world, with the highest estimated rates in Australia/New Zealand and the lowest rates in Western Africa. In Europe, the age-standardized incidence rates were 59 and 36 per 100,000 men and women, respectively, in 2012. One-third of all CRCs are situated in the rectum, the most distal part of the large bowel extending 15 cm from the anal verge. Rectal cancer itself is therefore the seventh most common cancer in the world.

26.1.1 Age, Family, and Personal History

About 20–25 % of patients with CRC have a positive family history; however, specific inherited cancer predisposition syndromes account for approximately 5 % of CRC. The lifetime risk of CRC in patients with Lynch syndrome, an autosomal-dominant condition defined by a germ-line mutation in a DNA mismatch repair gene, is 43 % for women and 66 % for men. Familial adenomatous polyposis (FAP), characterized by an autosomal-dominant germ-line mutation of the adenomatous polyposis coli (*APC*) gene, has almost 100 % penetrance; however, one-third of patients with FAP do not belong to identified families and represent de novo mutations or mosaicism. Affected individuals develop hundreds to thousands of adenomas in the colon and rectum early in life, and the lifetime risk of CRC approaches 100 % by age 40 years. Attenuated FAP is also a dominantly inherited mutation of the *APC* gene but presents with fewer than 100 polyps, and about 70 % of the mutation carriers develop CRC at an average age between 54 and 58 years. Recessively inherited mutations of the *MUTYH* gene, involved in the repair of oxidative DNA damage, can result in *MUTYH*-associated polyposis; CRC occurs in 19 % of these patients by the age of 50 years and in 43 % by age 60.

The risk of CRC in inflammatory bowel disease is debated. Severe, long-standing colitis and primary sclerosing cholangitis seem to be of importance. Young age at diagnosis, male sex and extensive disease are risk factors. The cumulative probability of CRC is considerably lower than previously reported cancer risk of 2 % after 10 years, 8 % after 20 years, and 18 % after

C. Buchli, MD, PhD (✉) • A. Martling, MD, PhD
Department of Molecular Medicine and Surgery, Karolinska Institutet, and Center of Digestive Diseases, Karolinska University Hospital, Stockholm SE-171 76, Sweden
e-mail: christian.buchli@karolinska.se; anna.martling@ki.se

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_26

30 years. The standardized incidence ratio for CRC risk in patients with Crohn's disease seems even smaller.

26.1.2 Behavioral Factors (Diet, Tobacco, Alcohol, and Physical Activity)

Dietary factors and obesity are suspected to be responsible for 20 % of all cancers worldwide. A Mediterranean diet has a protective effect against cancer development, whereas a daily intake of 100 g red meat or 50 g processed meat results in a relative risk of around 1.25. The effect of tobacco use on CRC risk is inconsistent; however, excess alcohol consumption is associated with an increased risk of death from CRC. There may be a protective effect of physical activity on risk for colon cancer, but there seems to be no effect on the risk for rectal cancer. In observational studies, acetylsalicylic acid (ASA), a cyclooxygenase-2 inhibitor, seems to reduce the risk of CRC. The potential effects of ASA in the prevention and therapy of CRC and their underlying mechanisms are currently the subject of clinical trials.

26.2 Milestones to Modern Treatment of Rectal Cancer

26.2.1 Total Mesorectal Excision

Total mesorectal excision (TME), the technique of sharp dissection of the mesorectum under direct vision along embryological planes (Fig. 26.1), was popularized in the 1980s. It resulted in adequate cancer clearance and fewer adverse events caused by autonomic nerve injury. The original publication reported a frequency of local recurrence of 3.7 % without the use of (chemo)radiation at a time when less precise dissection was associated with local recurrence rates of 20–30 %. Involvement of the circumferential margin (CRM), defined as cancer cells identified within 1 mm from the radial margin of the specimen, proved to be an important predictor of local recurrence and survival. The TME concept, characterized by accurate preoperative staging, precise surgery, and systematic pathologic assessment of the resected specimen, has resulted in standardized rectal cancer treatment with a positive impact on patient outcomes regarding local recurrence, cancer-specific mortality, and permanent stoma formation.

26.2.2 Radiotherapy

Around the time the TME technique was introduced, several randomized trials explored the effect of radiotherapy (RT) on local recurrence to define the optimal biologically effective dose, fractionation, and time point (before or after surgery) for RT in rectal cancer. In these trials without TME surgery, RT reduced the frequency of local recurrence by half, from around 25 % to 11–14 %. An equivalent benefit was also observed in trials combining RT and TME. RT reduces the relative risk of local recurrence by 50–70 %, and RT combined with the correct plane of surgery almost abolishes the risk of local recurrence. RT for rectal cancer is best given before surgery. The effects on tumor downsizing, local recurrence rate, and survival are similar for the highly

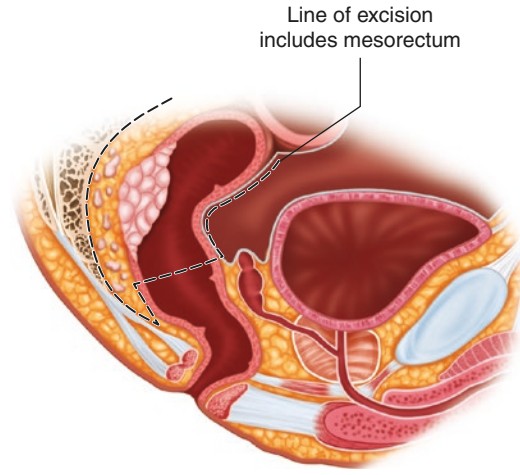


Fig. 26.1 Plane of excision in total mesorectal excision

fractionated schedule with 5 Gy × 5 (short-course RT) and the conventionally fractionated schedule with 1.8–2 Gy × 25–28, often combined with concomitant chemotherapy. The addition of chemotherapy to preoperative RT enhances local control, but a significant survival gain has only been observed in locally advanced cancers.

26.2.3 Revised Abdominoperineal Excision

Observational studies and clinical trials have shown superior oncologic outcomes of anterior resection with TME compared with abdominoperineal excision (APE), which was associated with a higher risk for positive CRM, intraoperative perforation, and an inadequate plane of resection. The concept of extralevator APE was introduced to improve the outcome in low, locally advanced rectal cancer. The abdominal part of the procedure is carried out in the TME plane, but the mesorectum is not dissected off the levator muscles. The patient is then turned into a prone position to complete the perineal excision by resecting the anus, the lower rectum, and the levator muscles en bloc. This technique results in a cylindrical specimen, which avoids the characteristic "waist" at the anorectal junction of specimens after conventional APE (Fig. 26.2).

26.2.4 Extensive Surgery for Locally Advanced or Recurrent Rectal Cancer

Uncontrolled pelvic tumor growth has a disastrous impact on a patient's life, and median survival for locally recurrent rectal cancer treated with supportive care is limited to only a few months. Extensive surgery including multivisceral resection (pelvic exenteration), sacral resection, and hemipelvectomy procedures is used to achieve tumor clearance in advanced or recurrent rectal cancer. Radical resection with negative resection margins (R0) is a strong predictor of outcome in this group, and 5-year survival reached 50 % in selected series. The Beyond TME Collaborative published a consensus statement for staging and treatment of this group of patients with complex presentation of rectal cancer diseases.

26.2.5 Organ Preservation

The first results of a wait-and-see policy in patients with low rectal cancer without detectable cancer growth (complete clinical response) after chemoradiotherapy were published in 2004. Several pilot studies confirmed that standard rectal resection did not enhance survival in these select patients. The evidence regarding patient selection, use of (chemo-)RT in early cancers (T2), response assessment and follow-up is limited and currently restricts the general application of this treatment option. Patients so treated should be entered into a registry such as the International Watch & Wait database (www.iwwd.org)

26.2.6 Chemotherapy

Chemotherapy is the weakest treatment modality for rectal cancer and is based on 5-fluorouracil, described in 1957, or capecitabine, an oral prodrug of 5-fluorouracil. Newer drugs, such as oxaliplatin or irinotecan, and a growing number of biological agents have been shown to improve survival in patients with systemic disease. The value of adjuvant chemotherapy for stage III or perceived-high-risk stage II disease, advised by many oncologists in analogy to colon cancer treatment, is unproven; however, about 20–25 % of these patients develop systemic disease despite local control in the pelvis. Postoperative chemotherapy in patients treated with preoperative (chemo-)RT is not based on strong evidence. Current trials are investigating the effect of preoperative RT and full-dose preoperative chemotherapy.

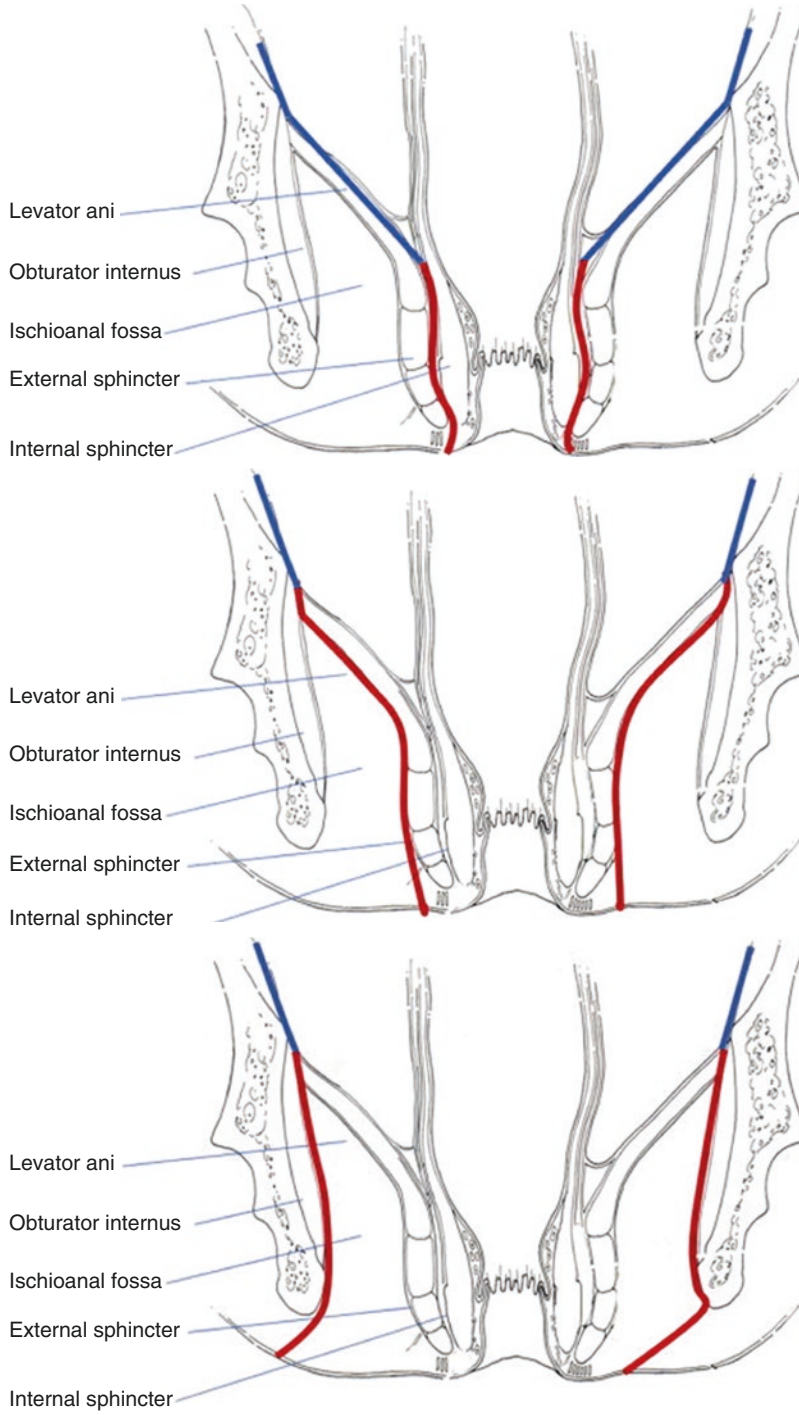


Fig. 26.2 Plane of resection in intersphincteric, extralevator, and ischioanal abdominoperineal excisions. *Blue line* = abdominal part, *Red line* = perineal part

26.3 Modern Rectal Cancer Treatment and Care

26.3.1 Clinical Presentation

The most common clinical signs of rectal cancer are rectal bleeding, altered bowel habit, and tenesmus; however, symptoms are often nonspecific early in the course of disease. Constipation and large-bowel obstruction are uncommon below the rectosigmoid junction because of the larger diameter of the rectum compared with the (left) colon. The clinical symptoms listed here are often reported at the time of diagnosis:

- Hematochezia (rectal bleeding)
- Mucous discharge
- Change in stool caliber, tenesmus, urgency, painful or incomplete defecation
- Abdominal/pelvic pain
- Anemia, fatigue, unexplained weight loss
- Symptoms of overgrowth to urogenital organs or the lumbosacral plexus

Patients with such complaints should undergo proctologic evaluation with digital rectal examination and rectoscopy. Patients with persistent hematochezia and normal proctologic examination, persistent hematochezia after treatment of protologic conditions, two or more of the above symptoms of rectal cancer, or a family history of CRC should have full endoscopic evaluation.

26.3.2 Workup of Rectal Lesions

Workup of rectal lesions includes three steps – "name it, stage it, treat it" – and should provide morphological verification and classification according to the American Joint Committee on Cancer's TNM-based criteria:

- Medical history, physical examination, and venous blood sample (blood count, liver and renal function, carcinoembryonic antigen)
- Proctologic evaluation with digital rectal examination, rectoscopy, and biopsy to assess anal sphincter function, distance between the anal verge and the distal extent of the lesion, mobility against adjacent pelvic structures, and morphological verification
- Complete colonoscopy to exclude synchronous lesions
- Computed tomography of chest and abdomen to assess lymph nodes, liver, and lungs
- Magnetic resonance imaging (MRI) of the pelvis to assess tumor growth in relation to the mesorectal fascia, nodal disease in and outside the mesorectum, extramural vascular invasion, and invasion of other pelvic structures/organs
- Endoanal ultrasound may be useful to assess the depth of invasion in stage 1 tumors

Correct sequencing and timing of multimodal treatment of rectal cancer is essential and is the reason for multidisciplinary team discussion between colorectal surgeons, radiologists, pathologists, oncologists, and specialized nurses. Liver and thoracic surgeons are involved in cases of suspected systemic disease, which may be identified in up to 20 % of patients during primary workup.

26.3.3 Tailored Treatment of Primary Rectal Cancer (Localized or Regional Disease)

26.3.3.1 Preoperative Treatment

Curative treatment for primary rectal cancer should aim for a risk of residual disease in the pelvis less than 5 % and a specimen with >1 mm of CRM in resected patients. The expected gains of additional treatments such as RT, chemotherapy, and more extensive surgery should be balanced against the increased morbidity (Table 26.1).

26.3.3.2 Bowel Preparation

A Cochrane review from 2011 found no advantage for mechanical bowel preparation regarding anastomotic leakage or surgical site infections in

Table 26.1 Tailored treatment for primary rectal cancer stage I–III

Risk group	Height	Clinical tumor and nodal stage	Treatment
Very early	Any	T1 sm1(−2?) N−	Local excision
			Complete with resection (or CRT) if sm ≥2, high grade, or vascular invasion
Early ("good")	Upper	T3a/b N+, mrf−, EMVI−	Standard resection
	Middle	T3a/b N−, mrf−, EMVI−	Complete with Cx or CRT if CRM+ or pN2
	Low	T1-2 N−, mrf−, EMVI−	
Intermediate ("bad")	Upper	T3 N+, mrf−, EMVI+	Preoperative RT/CRT and standard resection
		Limited T4a N−	
	Middle	T3 N+, mrf−, EMVI+	
		Limited T4a N−	
	Low	T2 mrf−	
Advanced ("ugly")	Any	T3 mrf+, T4, lateral nodes+	Preoperative CRT and extended resection; alternatively, preoperative RT and delayed extended resection if Cx not tolerated

According to Glimelius et al. [7]
T tumor stage, *N* nodal stage, *sm* submucosal level of invasion, *mrf* mesorectal fascia, *EMVI* extramural vascular invasion, *CRM* circumferential margin, *preop* preoperative, *RT* radiotherapy, *CRT*, chemoradiotherapy, *Cx* chemotherapy

colorectal surgery. By contrast, the only randomized controlled trial related to rectal cancer surgery found an advantage of mechanical bowel preparation regarding infectious morbidity and a trend toward decreased anastomotic leakage. Three large cohort studies from the United States published in 2015 showed a marked reduction in surgical site infections and anastomotic leaks if mechanical bowel preparation was combined with preoperative oral antibiotics in patients with colonic and rectal resections. These results suggest that a combination of preoperative oral antibiotics and mechanical bowel preparation should be used for patients without an imminent risk for bowel obstruction.

26.3.3.3 Local Excision

Local excision of rectal lesions includes a localized, full-thickness resection of the rectal wall to obtain a specimen that allows differentiation between T1 and T2 cancers. Transanal endoscopic microsurgery and transanal minimally invasive surgery (are preferred over transanal excision because of the decreased risk for incomplete resection. Local excision is applicable in early rectal cancer limited to the mucosa and less than 3 cm in diameter without evidence for nodal disease and extramural venous invasion on MRI. The presence of adverse pathological features such as involved margin, level 3 submucosal invasion, lymphovascular/perineural invasion, or mucinous/signet cell components should prompt salvage rectal resection after wound healing. The risk of nodal involvement is 0–12%, and the proportion with local recurrence at 5 years is 0–24% for T1 cancers, which has implications for the follow-up of these patients.

26.3.3.4 Standardized Procedures for Rectal Resection

The two standardized surgical procedures for the resection of rectal cancers are low anterior resection and abdominoperineal excision. Many colorectal surgeons and patients regard preservation of bowel continuity while saving the anal sphincter as a marker of the quality of surgery for rectal cancer. Patients without a history of fecal incontinence or signs of anal sphincter dysfunction may be evaluated for low anterior resection (Table 26.2).

26.3.3.5 Low Anterior Resection

The usual approach for low anterior resection with TME is a midline incision. The latest review from the Cochrane Database 2014 and the COLOR II trial concluded that laparoscopic and

Table 26.2 Tailored surgical treatment for primary rectal cancer

Tumor height	Procedure
Anal function intact	
High (11–15 cm)	Anterior resection with TME
	PME for tumors at the rectosigmoidal junction
Middle (6–10 cm)	Anterior resection with TME
Low (0–5 cm)	Extralevator APE
	Anterior resection with TME plus intersphincteric dissection in select patients
Anal function impaired	
High (11–15 cm)	Intersphincteric APE
Middle (6–10 cm)	Intersphincteric APE
Low (0–5 cm)	Extralevator APE

APE abdominoperineal excision, *PME* partial mesorectal excision, *TME* total mesorectal excision

Table 26.3 Risk factors for anastomotic leakage

Preoperative	Male sex
	ASA score >2
	Renal disease
	Comorbidity
	Preoperative radiotherapy
Tumor-related	Distal tumor site
	Tumor size >3 cm
	Advanced tumor stage
	Systemic disease
Adjustable	Tobacco use
	Obesity
	Poor nutrition
	Alcohol excess
	Immunosuppressants
	Bevacizumab
Intraoperative	Blood loss/transfusion
	Operating time >4 h

Data according to McDermott et al. [11]

open TME have comparable oncological outcomes and advantages regarding length of hospital stay, wound infections, and bleeding complications after laparoscopic TME. These findings are challenged by two recently published randomized trials (ALaCaRT and ACOSOG Z6051) that did not demonstrate noninferiority of laparoscopic surgery compared with open surgery regarding adequate surgical resection and concluded that the findings do not provide sufficient evidence for the routine use of laparoscopic surgery. Robotic surgery with enhanced visibility and instrument motion could be of value during pelvic dissection, whereas transanal TME is a new, minimally invasive technique with a bottom-up approach to decrease the difficulties encountered in patients with a narrow pelvis and bulky mesorectum.

The colonic *J*-pouch–anal anastomosis results in a better functional outcome compared with a straight coloanal anastomosis but is not better than a side-to-end anastomosis. A defunctioning stoma, usually a loop ileostomy, decreases the risk of symptomatic anastomotic leakage and urgent reoperations.

Anastomotic leakage and pelvic abscesses occur in 11 and 12 % of colorectal anastomoses, respectively. Any deviation from expected postoperative recovery should arouse suspicion of anastomotic leakage, as postoperative morbidity and mortality increase dramatically in these patients if diagnosis is delayed. Even a minor leak increases the risk of further adverse events and prolongs hospital stay (Table 26.3). Immediate evaluation by CT with rectal contrast confirms an anastomotic leak and can detect pelvic abscesses, a consequence of leakage. Size of the leak, the patient's general condition, and the systemic inflammatory response guide the choice of interventions, which can be careful observation, antibiotics, percutaneous/transanal drainage or reoperation.

26.3.3.6 Difficulties in Low Rectal Cancer

Low rectal cancers are at increased risk of infiltrating adjacent organs as the mesorectum is narrow anteriorly and decreases posteriorly towards the anorectal junction, at which point no residual mesentery is left. At this level, cancer that extends through the muscularis propria effectively infiltrates the pelvic floor or vagina/prostate and should be considered stage T4. Discrimination between invasive cancer and fibrosis, particularly after preoperative (chemo-) RT, is difficult because residual islands of viable tumor tissue can be found in about 50 % of patients. Tumor extension into the levator ani

muscle (pelvic floor) or anal sphincter precludes salvage and is an indication for an extralevator APE. In carefully selected patients with strong desire to avoid a permanent stoma, it may be appropriate to perform intersphincteric dissection with hand-sewn coloanal anastomosis and thus extend the TME plane of dissection distally between the internal and external anal sphincters.

26.3.3.7 Extralevator Abdominoperineal Excision

Extralevator APE results in significant tissue defects in the pelvis and perineum, which carry the risk of bowel herniation and small-bowel obstruction. Wound healing may be problematic, and displacement of vagina/ uterus can result in dyspareunia. Primary closure of the levator hiatus and perineal wound, especially following preoperative RT, is not recommended. Omental flaps can be used to fill the pelvic cavity, and a biological mesh or a myocutaneous flap may be used to reconstruct the pelvic floor.

26.3.3.8 Hartmann Procedure

The Hartmann procedure, total or partial mesorectal excision with permanent colostomy, is considered a less invasive surgical option in frail patients who might not tolerate an anastomotic complication or in those with preoperative fecal incontinence. However, the residual rectal stump may itself be the cause of increased postoperative morbidity, and a short rectal stump is associated with an increased risk of pelvic sepsis compared with APE. Surveillance of a long stump can be difficult, and many patients develop incontinence as a result of continued mucous secretion.

26.3.3.9 Pelvic Lymph Nodes Outside the Mesorectum

In Western countries, lateral node metastases along the internal iliac vessels are classified as N2 disease and along the external iliac vessels as systemic diseases (M1). In Japan, these metastases are regarded as regional disease, removed by lateral lymph node dissection, and treated with postoperative chemotherapy. A Japanese trial comparing TME versus TME with lateral node dissection in middle and low rectal cancers without radiological enlargement of lateral nodes reported that 7 % of patients in the lateral dissection group had pelvic lymph node metastasis. Unselected extended lymphadenectomy did not enhance survival but increased sexual and urinary dysfunction, according to a meta-analysis from 2009. Chemoradiotherapy in combination with selected lateral lymphadenectomy might be an option in the absence of studies comparing the benefit of chemoradiotherapy versus lateral dissection.

26.4 Oncologic Outcomes

Time trends of oncologic outcomes based on over 20,000 patients are summarized in Table 26.4.

The 3-year cancer-specific survival is 84.8 % for patients with local or regional disease diagnosed between 2007 and 2014. About 20 % of these patients will develop systemic disease during the 5 years after treatment with curative intent. The median survival for patients with systemic disease is 13.4 months (range, 7–23.2 months) (Fig. 26.3).

The rate of 5-year local recurrence of T1–T3 tumors treated between 2005 and 2009 is 4.2 % in patients treated with preoperative RT and 4.9 % in patients treated with surgery alone. For T4

Table 26.4 Time trends in oncologic outcomes for rectal cancer treatment

	Proportion with outcome, by time period	
	1995–2000	2007–2012
Not resected	15.3 %	25.8 %
Any preoperative radiotherapy	49.5 %	66.5 %
Anterior resection in low tumors (0–6 cm from the anal verge)	19.6 %	10.9 %
Outcome for all resected patients		
90-Day mortality	4.7 %	2.9 %
3-Year local recurrence	7.7 %	4.9 %
5-Year local recurrence	8.7 %	5.0 %
Overall 3-year survival	65.4 %	75.8 %

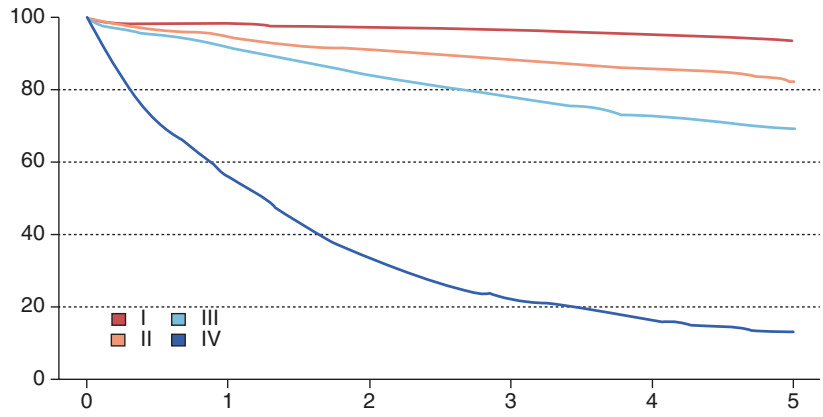


Fig. 26.3 Five-year cancer-specific survival by stage for patients treated between 2007 and 2014

tumors, 5-year local recurrence is 9.3 %. The best results are achieved by standardized use of TME. Extralevator APE reduces local recurrence in locally advanced tumors in the lower third of the rectum. Patients are at increased risk of local recurrence after local excision, which warrants attention in patient selection and follow-up.

26.5 Functional Outcomes

Improved oncologic outcomes have increased the interest in the adverse effects of rectal cancer treatment on functional outcomes in cancer survivors. Bowel, urinary, sexual, and gonadal function may deteriorate, and body image is altered after formation of a permanent stoma. These important issues, which affect quality of life, should be discussed with the patient before the start of any treatment.

26.5.1 Bowel Function

Urgency, frequent bowel movements, and occasional fecal incontinence are common complaints after anterior resection and can be quantified by the low anterior resection syndrome score. The loss of rectal storage function and hyperactive postprandial response of the neorectum, formed of denervated left colon, are reasons for urgency and frequent bowel movements. The morbidity of colostomy is considerable, with skin irritation, parastomal herniation, stenosis, retraction, and prolapse occurring in up to 40 % of patients. Consultation with a stomatherapist to mark the stoma site preoperatively reduces morbidity. Quality of life did not differ between patients undergoing sphincter-saving procedures (anterior resection) and those receiving a permanent stoma after APE/the Hartmann procedure in 14 of 35 studies included in the latest Cochrane review.

26.5.2 Urinary Function

The negative impact on urinary function seems to be less pronounced, and gradual improvement within 6 months might be expected. Injuries to autonomic nerves during pelvic dissection contribute more to negative effects on bladder function than RT.

26.5.3 Sexual Function

The majority of patients with resectable rectal cancer are sexually active at the time of diagnosis, and sexual dysfunction is reported in up to 75 % after treatment. The most common complaints are dyspareunia and vaginal dryness in women and erectile dysfunction and retrograde ejaculation in men. Injuries to the preaortic hypogastric nerves (sympathetic fibers) or the neurovascular bundles (parasympathetic fibers) at the pelvic sidewall during surgery are related to specific functional impairments. RT and the presence of a stoma are associated with increased sexual dysfunction in both sexes.

26.5.4 Gonadal Function

The gonads are exposed to primary and scattered radiation during RT, with adverse effects on fertility and levels of sexual hormones, which must be discussed before starting RT. Cryopreservation of oocytes/semen and hormone replacement in the case of premature menopause or male hypogonadism should be offered to affected women and men.

26.5.5 Other Late Adverse Effects Specific for RT

Specific late adverse events attributed to RT are increased risk of secondary cancers, pelvic or femoral insufficiency fractures, and thromboembolic disorders. Many of these results were observed in studies with out-of-date RT technology and may decrease or even disappear with the use of more refined RT technology. The positive effects of RT on oncologic outcomes and the potential for complete response, enabling organ preservation, are in contrast to the negative effects on postoperative and functional outcomes. Therefore the future use of RT in rectal cancer treatment is an ongoing debate.

26.5.6 Follow-Up

The postoperative multidisciplinary team conference is an opportunity for quality control. The benefit of postoperative chemotherapy and the risk of local or systemic cancer recurrence should be discussed based on quality and histopathological assessment of the specimen. Follow-up after treatment for rectal cancer aims to detect cancer recurrence (local or systemic) and metachronous CRC, to diminish treatment-related adverse effects on functional outcomes/quality of life, and to identify patients from families with increased risk of CRC or specific inherited cancer predisposition syndromes (e.g., Lynch syndrome, FAP).

Patients able to tolerate further interventions and who had complete preoperative colonoscopy, clean resection margins. and no increased familiar risk for CRC can proceed along a standard follow-up schedule:

- Colonoscopy 3–5 years postoperatively
- Proctologic examination after low anterior resection and carcinoembryonic antigen level 1, 3, and 5 years postoperatively
- Computed tomography of the chest and abdomen 1 and 3 years postoperatively
- Regular colonoscopies every 5 years after the end of the 5-year follow-up

The frequency of follow-up should be enhanced and pelvic MRI added in patients with incomplete resections or high risk of systemic recurrence.

Rreferences

1. Appelt AL, Ploen J, Harling H, Jensen FS, Jensen LH, Jorgensen JC, et al. High-dose chemoradiotherapy and watchful waiting for distal rectal cancer: a prospective observational study. Lancet Oncol. 2015;16(8):919–27.
2. Bhangu A, Ali SM, Brown G, Nicholls RJ, Tekkis P. Indications and outcome of pelvic exenteration for locally advanced primary and recurrent rectal cancer. Ann Surg. 2014;259(2):315–22.
3. Bretagnol F, Panis Y, Rullier E, Rouanet P, Berdah S, Dousset B, et al. Rectal cancer surgery with or without bowel preparation: the French GRECCAR III multicenter single-blinded randomized trial. Ann Surg. 2010;252(5):863–8.
4. Breugom AJ, Swets M, Bosset JF, Collette L, Sainato A, Cionini L, et al. Adjuvant chemotherapy after preoperative (chemo)radiotherapy and surgery for patients with rectal cancer: a systematic review and meta-analysis of individual patient data. Lancet Oncol. 2015;16(2):200–7.
5. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Ann Surg. 2012;255(5):922–8.
6. Glimelius B. Neo-adjuvant radiotherapy in rectal cancer. World J Gastroenterol: WJG. 2013;19(46):8489–501.
7. Glimelius B, Tiret E, Cervantes A, Arnold D, Group EGW. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol: Off J Eur Soc Med Oncol ESMO. 2013;24 Suppl 6:vi81–8.
8. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery – the clue to pelvic recurrence? Br J Surg. 1982;69(10):613–6.

9. Lutgens MW, van Oijen MG, van der Heijden GJ, Vleggaar FP, Siersema PD, Oldenburg B. Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. Inflamm Bowel Dis. 2013;19(4):789–99.
10. Martling AL, Holm T, Rutqvist LE, Moran BJ, Heald RJ, Cedemark B. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm Colorectal Cancer Study Group, Basingstoke Bowel Cancer Research Project. Lancet. 2000;356(9224): 93–6.
11. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg. 2015;102(5):462–79.
12. Nagtegaal ID, van de Velde CJ, Marijnen CA, van Krieken JH, Quirke P, Dutch Colorectal Cancer G, et al. Low rectal cancer: a call for a change of approach in abdominoperineal resection. J Clin Oncol. 2005;23(36):9257–64.
13. Pachler J, Wille-Jorgensen P. Quality of life after rectal resection for cancer, with or without permanent colostomy. Cochrane Database Syst Rev. 2012;12:CD004323.
14. Petersen SH, Harling H, Kirkeby LT, Wille-Jorgensen P, Mocellin S. Postoperative adjuvant chemotherapy in rectal cancer operated for cure. Cochrane Database Syst Rev. 2012;3:CD004078.
15. Quirke P, Durdey P, Dixon MF, Williams NS. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. Lancet. 1986;2(8514):996–9.
16. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev: Off J Eur Cancer Prev Organ. 2013;22(6):492–505.
17. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. Lancet. 2009;373(9666):811–20.
18. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. Lancet Oncol. 2011;12(6):575–82.
19. Vennix S, Pelzers L, Bouvy N, Beets G, Pierie J, Wiggers T, et al. Laparoscopic versus open total mesorectal excision for rectal cancer (review). Cochrane Database Syst Rev. 2014;4:1–85.

Anal Intraepithelial Neoplasia and Anal Cancer

27

Daniel Dindo and Friederike Remmen

27.1 Etiology

- The majority of anal carcinomas is caused by infection with human papillomavirus (HPV), the same virus that is a major cause of cervical carcinoma. HPV has a genome of approximately 8,000 base pairs, making it a small DNA virus. The virus is limited to the basal cells of stratified epithelium, as this is the only tissue in which it can replicate. HPV lesions are known to arise from the proliferation of infected basal keratinocytes, and infection typically occurs when the host basal cells are exposed to HPV through a compromised epithelial barrier such as occurs during sexual intercourse or in minor skin abrasions. The virus is released as a result of the degeneration of desquamating cells. HPV is resilient, surviving for months at low temperatures and without a host.
- Of the more than 170 known subtypes of HPV, 15 have been identified as having oncogenic potential (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 68, 59, 68, 73, and 82) and are therefore considered to confer a high risk of cancer. Furthermore, three are potentially high-risk subtypes (26, 53, 66), and 12 (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP 6108) have been classified as low-risk subtypes [1]. In cervical carcinoma, HPV-16 is the most common high-risk subtype and is also present in almost three-quarters of all anal carcinomas. The oncogenic potential increases when additional HPV subtypes are associated with the infection – so-called mixed infections, which are very common among the male homosexual population (men who have sex with men [MSM]) [2].
- In addition to a shared aetiology, there are other parallels between anal and cervical carcinoma. For example, the transformational zone (where two different epithelia meet) of both the cervix and the anal canal is prone to HPV infections. The transformational zone of the cervix is where squamous epithelium of the ectocervix meets the cylindrical epithelium of the endocervix; in the anal canal it is the border between the squamous epithelium of the anus and the cylindrical epithelium of the rectum, anatomically known as the linea dentata.
- Anal carcinoma begins with precancerous stages, as does cervical cancer. In another analogy to cervical intraepithelial neoplasia,

D. Dindo, MD, PhD (✉) • F. Remmen, MD
Hirslanden Medical Center,
Witellikerstr. 40, CH-8032 Zurich, Switzerland
e-mail: dindo@bluewin.ch

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_27

anal dysplasia is divided into three stages (anal intraepithelial neoplasia [AIN] 1–3). In AIN 1, the mutations in the basal cells are confined to the lower third of the epithelium; in AIN 2, cell mutations can be found in the first two-thirds of the epithelium, and the entire epithelium is affected in AIN 3 (Fig. 27.1). Typically seen in viral infections are nuclear polarization, nuclear pleomorphism, and hyperchromatism. Koilocytosis, which presents with a cytoplasmic halo around the cell nucleus, is especially common in actively replicating virus infections. A low-grade dysplasia is classified as AIN 1, whereas severe dysplasia corresponds to AIN 2 or 3. Spontaneous regression can occur in low-grade lesions but rarely occurs in severe lesions [3].

- Little is known about the progression rate from high-grade AIN to anal carcinoma. In a small study, three of six immunosuppressed patients developed anal carcinoma within 5 years [4]. Another study observed 72 patients with high-grade dysplasia, among whom 13 % (8 patients) progressed to anal carcinoma [5]. Interestingly, no development of anal carcinoma was seen in a group of 446 human immunodeficiency virus (HIV)–positive homosexual patients in whom a high-grade dysplasia was treated. However, five patients who refused dysplasia treatment progressed to anal carcinoma [6].
- As mentioned before, HPV infections (especially HPV-16 and -18) are strongly associated with the appearance of squamous cell carcinoma of the anus. In particular, persisting

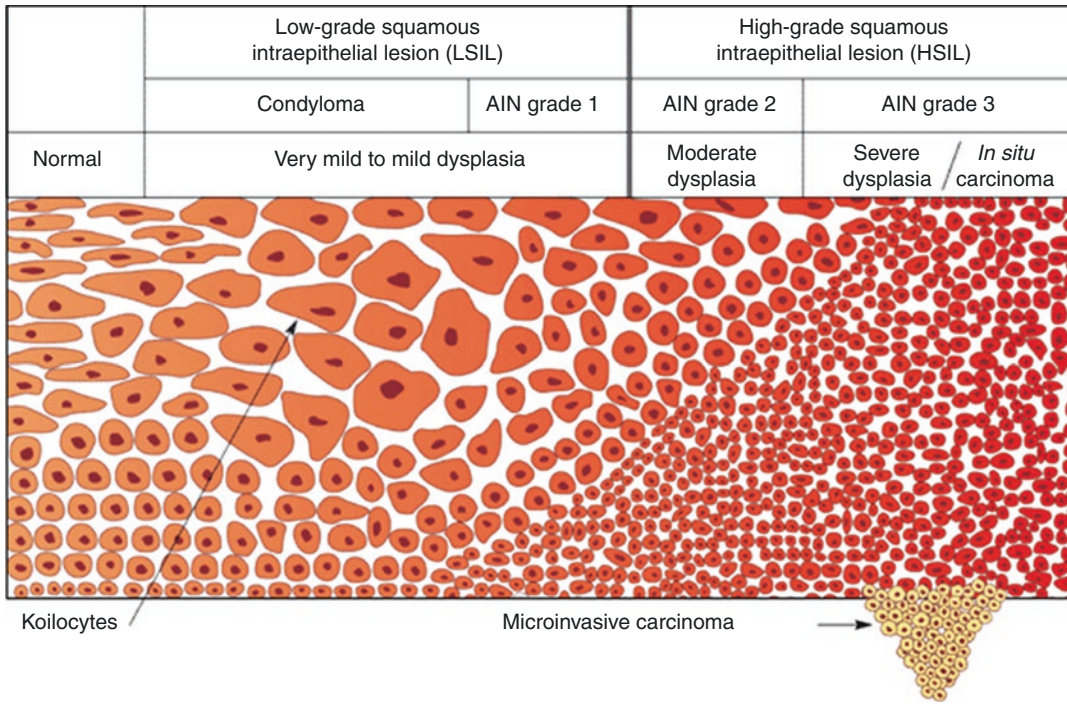


Fig. 27.1 Schematic representation of squamous intraepithelial lesions (From *The PRN Notebook* vol. 10, no. 4, December 2005 (available at www.prn.org; reprinted without permission). Koilocytes are a typical representation of human papillomavirus–infected cells. Koilocytes may show the following cellular changes: nuclear enlaregment, hyperchromasia, irregular contour of the nuclear membrane, and a clear area around the nucleus, known as a perinuclear halo. As illustrated, the proportion of the epithelium that is replaced by dysplastic cells (presenting a large nucleus-to-cytoplasm ratio) increases with increasing severity of the dysplasia. In anal intraepithelial neoplasia (AIN) I, dysplastic cells are found in the basal third of the epithelium, in AIN II in the basal two thirds, and in AIN III throughout the whole epithelium

HPV infections caused by anal intercourse and a high number of sexual partners over a lifetime increase the risk of developing anal carcinoma. In addition to HPV infection, other important risk factors are
  - HIV infection
  - Immune suppression after transplant or long-term use of corticosteroids
  - A history of other HPV-related cancers
  - Autoimmune disorders
  - Social deprivation
  - Cigarette smoking
- Anal cancer is subdivided into two categories:
  - Cancer of the anal canal
  - Cancer of the anal margin

The anal canal extends from the anorectal junction to the anal margin. The pigmented skin immediately surrounding the anal orifice is considered the anal margin, which extends laterally to a radius of ~5 cm (Fig. 27.2). Lymphatic drainage of the proximal anal canal flows to perirectal nodes along the inferior mesenteric artery. Close to the dentate line, lymphatic vessels drain to internal pudendal nodes and to the internal iliac system. The region below the dentate line and the perianal region drain to the femoral, inguinal, and external iliac nodes.

27.2 Incidence

- Approximately 20 % of HIV-negative MSM suffer from anal dysplasia, 5–10 % of whom already exhibit severe epithelial dysplasia (AIN 2–3). In HIV-positive MSM, the prevalence of severe AIN reaches up to 50 % [7]. In a study investigating 448 HIV-positive MSM, anal cancer was already present in 2.5 % of the patients [6].
- There has not been much research on the prevalence of anal dysplasia among women, despite the fact that 6 % of HIV-negative and 21 % of HIV-positive women were found to suffer from anal dysplasia [8].
- Anal cancer has gained particular attention since the late twentieth century as a result of its rapidly increasing incidence. Since the 1970s the incidence of 1 in 100,000 has doubled, and the sex distribution has changed from more women being affected to now having both sexes equally affected [9]. Since the beginning of the AIDS epidemic in 1982, the incidence has especially been increasing among MSM, in whom the incidence of anal carcinoma has increased from 3.7 (1973–1978) to 20.6 in 100,000 people (1996–1999) [10]. Cervical carcinoma had reached the same level of incidence before standardized screening tests were introduced, after which it dropped dramatically [11]. Meanwhile, the incidence of anal carcinoma in HIV-positive MSM has reached 137–225 in 100,000 [12, 13], and the incidence is 10–100 times higher among immunosuppressed patients [14]. The increasing incidence of anal cancer was not influenced by the introduction of highly active antiretroviral treatment.
- The increasing incidence of anal cancer was not influenced by the introduction of HAART (Highly Active Anti Retroviral Treatment).

27.3 Epidemiology

- Approximately 80 % of sexually active adults will contract a genital HPV-infection at some point in their lives.
- Approximately 80 % of sexually active adults will contract a genital HPV infection at some point in their lives. Infection with a specific HPV subtype typically lasts 6 months to 2 years, and it is assumed that 90 % of patients spontaneously eradicate the virus within this time period [15].
- In HIV-negative MSM the prevalence of HPV is 50-–60 % [16] whereas in HIV-positive MSM it is almost 100 % [2].
- In HIV-negative MSM, the prevalence of HPV is 50–60 % [16], whereas among HIV-positive MSM it is almost 100 % [2]. The prevalence of anal HPV infections among heterosexual men was found to be 12 %. In 7 % of the patients examined, an oncogenic HPV subtype was present in the anal canal [17]. In women, the

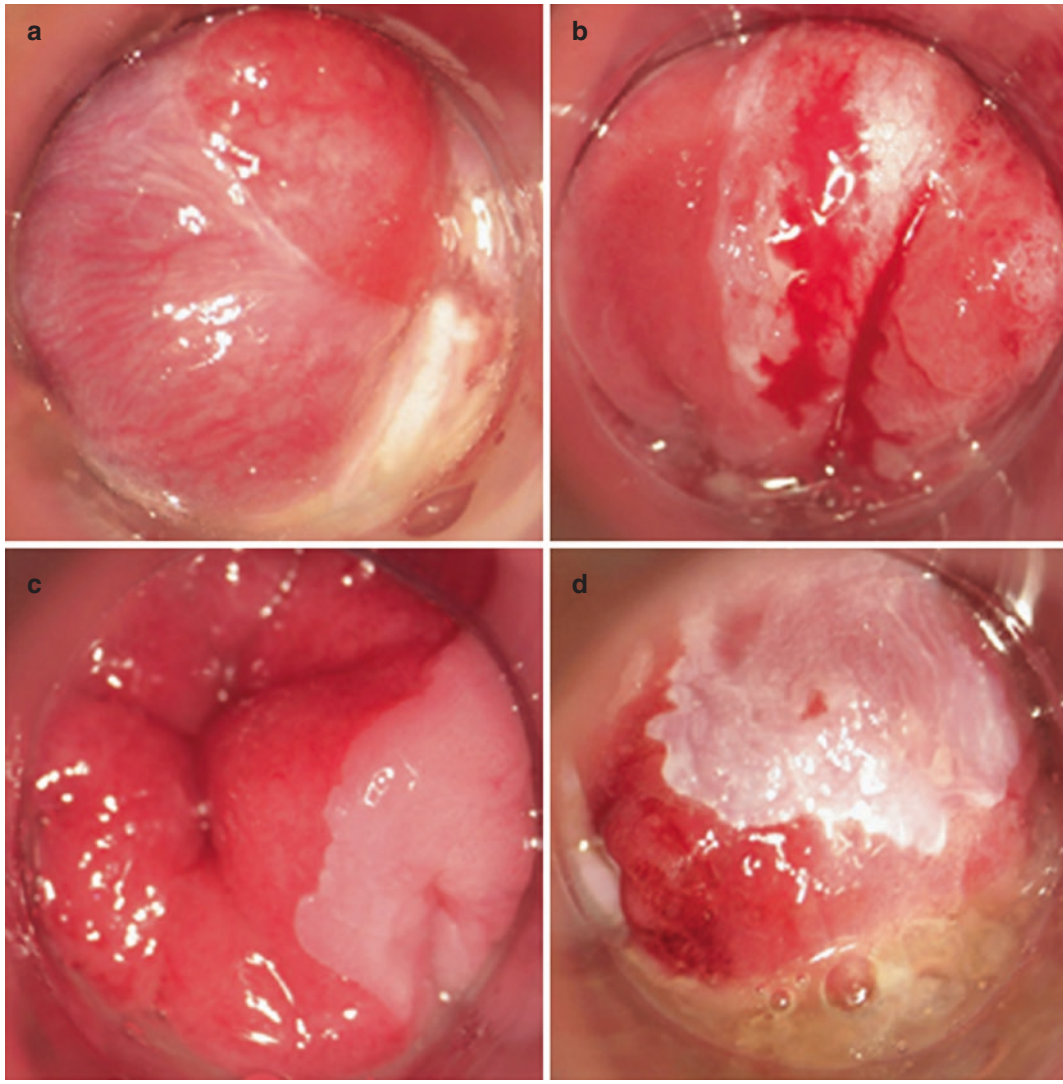


Fig. 27.2 Clinical presentation of endoanal dysplasia using high-resolution anoscopy (HRA) (From Kreuter et al. [31]; reprinted without permission) (**a**) Normal squamocolumnar junction without any signs of human papillomavirus–associated lesions. (**b**) Anal dysplasia (AIN 2). The lesion bleeds easily and is slightly thickened. Opaque areas with characteristic punctuation and mosaic structure are seen. (**c**) Anal dysplasia (AIN 2). Homogenous, well-demarcated, hyperkeratotic area with a granular surface. (**d**) Anal dysplasia (AIN 3). Large hyperkeratotic area with satellite lesions. The surface of the lesion is focally spiked and granular

prevalence of anal HPV infections lies between 13 and 29 % and is comparable to that of cervical infections [18]. The prevalence of anal HPV infections in men seems to remain stable with age [16], contrasting with the age-specific prevalence of cervical HPV infections in women, which decreases after the age of 30.

- The prevalence of anal HPV infections in men seems to remain stable with age [16].
- The risk of dysplasia increases if a high-risk subtype persists for over a year [19]. Viruses are currently regularly typified by only approximately 13 % of surgeons and dermatologists working in the field of coloproctology [20].

27.4 Diagnostics

- As the symptoms of AIN are unspecific and similar to common benign anorectal diseases, it is important that all patients are properly clinically assessed to avoid delays in diagnosis. This is especially true for high-risk patients. It is mandatory to take biopsies of all unclear anal lesions to exclude anal dysplasia and cancer. Occasionally, AIN presents with symptoms such as itching or mild bleeding, but the majority of patients with anal dysplasia are asymptomatic.
- High-resolution anoscopy (HRA) facilitates examination of the anal region and canal with 20× magnification and as such has proven itself superior to conventional proctoscopy. It enables the detection and targeted treatment of subclinical dysplasia, and in most cases it eliminates the need for a standard biopsy (anal mapping). A traditional proctoscopy without HRA misses 50 % of anal dysplasias [5]. However, HRA was only used to diagnose anal dysplasia by 23 % of responders in a survey targeting over 6,000 surgeons and dermatologists in the field of coloproctology in Europe and Australia [20].
- Polymerase chain reaction and in situ hybridization are used to type HPV upon a diagnosis of anal HPV infection, although the importance of this typification is questioned.
- Patients with anal cancer present with perianal lesions that can be wartlike, ulcerative, or both. Although local pain is often missing, approximately one-third of patients with anal cancer experience pain caused by the invasion of the tumor into the anoderm and the sphincter complex. Incontinence or tenesmus may also result from sphincter involvement. A localized inguinal lymphadenopathy can also be a symptom of metastatic disease. Rectal bleeding is usually the first symptom of anal cancer and occurs in over half of patients [21].

27.5 Screening

- Since the implementation of standardized screening tests, the incidence of cervical carcinoma has decreased by 70 % in developed countries. The effectiveness of regular gynecological checkups to prevent cervical cancer is no longer questioned. However, there are currently no general recommendations for screening tests for anal carcinoma in high-risk patients.
- Regular screening tests are now starting to be recommended. For example, the Department of Public Health of the State of New York currently recommends yearly screening tests for all HIV-positive MSM, HIV-negative MSM with a history of genital condyloma, and women with abnormal gynecological cytology [22]. Available data indicate that these recommendations should also include HIV-positive women.
- In hypothetical models, regular anal smears were cost-effective for both HIV-positive and HIV-negative MSM [23, 24]. Prospective studies of cost efficiency are currently still outstanding.
- Screening on a yearly basis in HIV-positive MSM provides clinical benefit and increases quality-adjusted life expectancy. Screening performed every 2–3 years is sufficient for HIV-negative MSM [23, 24]. The screening test should consist of a digital rectal examination (DRE) and anal brush cytology. Anal cytology has a sensitivity of 60–80 % and is similar to that of cervical cytology. If there is abnormal brush cytology, HRA is recommended [23].
- Anal cytology has a sensitivity of 60-–80 % and is similar to that of cervical cytology. If there is abnormal brush cytology, a high resolution anoscopy (HRA) is recommended [23]

27.6 Staging

- The seventh edition of the American Joint Committee on Cancer's Cancer Staging System (2010) is used internationally to

classify anal cancer [25] (Table 27.1). After confirming a diagnosis, further investigation includes computed tomography (CT) of the chest, abdomen, and pelvis to assess the size of the primary tumor and rule out metastatic disease. Magnetic resonance imaging (MRI) of the pelvis allows more accurate local staging of a primary tumor and reveals the extent of tumor invasion into the external sphincter and perirectal tissue. It is therefore advantageous over CT because it differentiates between soft tissues and outlines structures more clearly.

- Positron emission tomography (PET)/CT with [^{18}F] fluorodeoxyglucose (FDG) has a high sensitivity for the detection of affected lymph nodes because of the affinity of the majority of anal carcinomas to FDG. In approximately 20 % of cases an FDG PET/CT alters the staging, with a trend toward upstaging, as shown in several studies. Treatment intent is altered as a result in approximately 3–5 % of cases [21]. The US National Comprehensive Cancer Network currently recommends FDG PET/CT in their treatment recommendations.

Table 27.1 TNM classification of anal cancer

Primary tumor (T)			
Tis	Carcinoma in situ		
T1	Tumor invades ≤2 cm at the largest dimension		
T2	Tumor >2 cm but not >5 cm at the largest dimension		
T3	Tumor >5 cm at the largest dimension		
T4	Tumor of any size invades an adjacent organ (e.g., the vagina, urethra, bladder – but not the anal sphincter, perirectal skin, or subcutaneous tissue)		
Regional lymph nodes (N)			
N0	No regional lymph node metastasis		
N1	Metastasis in perirectal lymph nodes		
N2	Metastasis in unilateral internal iliac and/or inguinal lymph nodes		
N3	Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes		
Distant metastasis (M)			
M0	No distant metastasis		
M1	Distant metastasis		
Anal cancer stage grouping			
Stage	*T*	*N*	*M*
0	Tis	N0	M0
I	T1	N0	M0
II	T2–3	N0	M0
IIIA	T1–3	N1	M0
	T4	N0	M0
IIIB	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
IV	Any T	Any N	M1

27.7 Treatment

- The therapeutic management of AIN is controversial because of the largely unknown biological development of anal dysplasia. There are two different ways to handle a detected AIN: either watchful waiting with intensive patient surveillance for early diagnosis of anal carcinoma, or an aggressive strategy of destroying all dysplastic areas with the aim of preventing anal carcinoma. Against the watchful waiting strategy is the fact that chemoradiotherapy is poorly tolerated by and is associated with high morbidity and mortality in HIV-positive patients with anal carcinoma. Underlying this, a Markov model showed an increase in life expectancy in annually screened HIV-positive men and HIV-negative men who were screened every 2–3 years when this screening was accompanied by early destruction of all possible dysplastic areas [23, 24].
- Possible ablative treatments include infrared coagulation, carbon dioxide (CO_2) laser ablation, and destruction using electrocautery, cryoablation, or surgical excision. Cryoablation is especially advantageous in small perianal or intra-anal findings and can be used in the outpatient setting. Furthermore, it does not require general anesthesia but often has to be repeated. As soon as larger peri- and intra-anal areas are affected, infrared coagulation, CO_2 laser ablation, or electrocoagulation, which are more destructive, are better suited. Because of the low depth of penetration of the laser, CO_2 laser ablation does not cause scarring, and a combination with HRA leads to the more tar-

geted destruction of suspicious areas. Therefore, CO_2 laser ablation is a better treatment option than a wide surgical excision that causes extensive scarring.

- It is mandatory to take biopsies of suspicious areas and exclude anal carcinoma before performing any ablative therapy. It is also important to closely monitor patients after ablative therapy because of the high recurrence rate of dysplasia (especially in HIV-positive MSM) and the lack of histological confirmation of a complete removal.
- Topical treatment using imiquimod or podophyllin is suitable for perianal lesions, but the chances of success are low. A meta-analysis of patients treated with imiquimod showed that only 48 % of the patients achieved full remission, with a relapse rate of 36 % [26]. As a result, imiquimod should only be used in combination with an ablative treatment [27]. Another alternative for topical use is 5-fluorouracil [28]. The topical application of imiquimod or 5-fluorouracil for endoanal lesions is not well established since it is an "off-label" use.
- Within the past 20 years there has been a major change in the treatment of anal caner. Today, the primary treatment consists of chemoradiotherapy, whereas surgery plays a minor role, resulting in fewer permanent colostomies.
- Primary chemoradiotherapy is recommended in all four stages of squamous cell carcinoma of the anus, with the exception of tumors with a T1 anal margin. If the lesion is smaller (T1; <2 cm in diameter) it may be treated by primary surgery, providing it is localized on the anal margin and well differentiated. The local excision must allow for a margin >5 mm and sphincter function cannot be affected.
- The combination of 5-fluorouracil and mitomycin-C in addition to radiotherapy is the standard treatment. Adhering to this regimen can result in colostomy-free survival and local control rates of 83.7 % and 83.9 %, respectively, and a favorable toxicity profile [29].
- The complexity of radiotherapy treatment in anal cancer is increased by the variable size of the tumor and the fact that several critical structures near the tumor are dose-sensitive, such as the small bowel, rectum, bladder, femoral heads, perineum, and external genitalia. Because of new and improved treatment using CT-guided or three-dimensional radiotherapy, treatment accuracy and delivery have been greatly improved. These treatments allow radiation oncologists to differentiate between normal tissue and the soft-tissue targets using axial CT.
- Salvage surgical treatment should be considered in patients with locally persisting tumors after chemoradiation (CRT) and recurrent or progressive disease after previous CRT. As the achievement of negative resection margins is absolutely necessary, an abdominoperineal resection is recommended in most cases. Other options are posterior or total pelvic exenteration. Because of the wider involved area and the intensively irradiated area in perineal resection of anal carcinoma compared with rectal cancer, postoperative complications such as problems with wound healing can have an enormous impact. If curative resection can be carried out, abdominoperineal resection can achieve local control in about 50–60 % of patients, which corresponds to a 5-year survival rate of approximately 30–60 %. A radical groin dissection combined with pre- and postoperative irradiation of the groin should be considered if inguinal lymph nodes are involved. Nodal involvement is seen in 20 % of patients with T3 disease.
- Nodal involvement is seen in 20 % of patients with T3 disease.

27.8 Follow-Up

- After completion of CRT, anal carcinoma continues to slowly regress. A DRE is used to evaluate complete response after treatment is completed. *Complete response* refers to a total absence of tumors and/or ulcerations. If pain is still present or the treatment result is unclear, it is recommended to do the examination under general anesthesia. Clinical examination of the inguinal regions together with

radiographic exams (if possible, a comparison of PET/CT is the best option, otherwise pelvic MRI and CT) are mandatory.

- It is difficult to differentiate scar tissue, edema, and residual fibrosis from persistent active disease. However, there is no recommendation for routine biopsies of persistent clinically suspicious lesions 8–12 weeks after completed treatment, as complete regression may take up to 6 months. This can be monitored by close follow-up to evaluate good partial regression on radiography. Before proceeding to radical surgery, residual or recurrent tumors must be histologically confirmed.
- MRI has the advantage of complementing the clinical assessment and documenting response, whereas with endoanal ultrasound it is difficult to differentiate edema and scar tissue from a persisting tumor. FDG PET/CT scans currently play only a minor role in assessing response to treatment, but they are superior in the detection of residual lymph node metastasis.
- It is recommended that patients who have achieved complete remission after 8 weeks should be evaluated every 3–6 months for 2 years, and then every 6–12 months until the 5-year mark is reached. Evaluation should include a clinical examination using DRE and palpation of the inguinal lymph nodes. Anoscopy and proctoscopy are additional options, but these may be poorly tolerated and often too painful following CRT. Some recommend MRI semiannually for 3 years in addition to the clinical evaluation. A biopsy should be taken if any suspicious progressing lesions are found. Data from the ACT II trial show that the majority (>99 %) of relapses occur within 3 years; therefore extended imaging surveillance is only recommended within this time period [30].

27.9 Recurrence

- In 10–20 % of cases, patients relapse at distant sites, meaning that the majority of relapses are locoregional. When the metastasis occurs at a distant site, the most commonly affected organs are the paraortic nodes, liver, lungs, and skin. However, regular CT for metastatic surveillance are not recommended outside of clinical trials; unlike for colorectal cancers, there is a lack of evidence to support metastatic resection.
- The mortality rate associated with distant metastatic disease is very high: only 10 % of patients survive 2 years or more.

27.10 Special Considerations

- After treatment of HPV-associated high-grade dysplasia or anal cancer, patients still have to be considered high risk. Surveillance on a regular basis is mandatory. DRE, HRA, and brush cytology are recommended every 3 months in the first year after treatment. Thereafter, follow-up may be extended to yearly examinations. If no lesions reoccur, brush cytology should be performed every year and HRA every 2–3 years.
- A biopsy should be performed on any unusual or suspect anal lesion, especially in high-risk patients (MSM, HIV-positive, women with cervical dysplasia). Also, histological investigation of every tissue sample that is removed in the anal region is recommended since HPV-associated lesions are mostly asymptomatic and discreet.

References

1. Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, Snijders PJ, Meijer CJ, International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003;348(6):518–27.
2. Palefsky JM, Holly EA, Ralston ML, Da Costa M, Greenblatt RM. Prevalence and risk factors for anal human papillomavirus infection in human immunodeficiency virus (HIV)-positive and high-risk HIV-negative women. J Infect Dis. 2001;183(3):383–91.
3. Palefsky JM, Holly EA, Ralston ML, Jay N, Berry JM, Darragh TM. High incidence of anal high-grade squamous intra-epithelial lesions among HIV-positive

and HIV-negative homosexual and bisexual men. AIDS. 1998;12(5):495–503.
4. Scholefield JH, Castle MT, Watson NF. Malignant transformation of high-grade anal intraepithelial neoplasia. Br J Surg. 2005;92(9):1133–6.
5. Watson AJ, Smith BB, Whitehead MR, Sykes PH, Frizelle FA. Malignant progression of anal intraepithelial neoplasia. ANZ J Surg. 2006;76(8):715–7.
6. Kreuter A, Potthoff A, Brockmeyer NH, Gambichler T, Swoboda J, Stücker M, Schmitt M, Pfister H, Wieland U. Anal carcinoma in HIV-positive men: results of a prospective study from Germany. Br J Dermatol. 2010;162:1269 [Epub ahead of print].
7. Palefsky JM, Holly EA, Efirdc JT, Da Costa M, Jay N, Berry JM, Darragh TM. Anal intraepithelial neoplasia in the highly active antiretroviral therapy era among HIV-positive men who have sex with men. AIDS. 2005;19(13):1407–14.
8. Hessol NA, Holly EA, Efird JT, Minkoff H, Schowalter K, Darragh TM, Burk RD, Strickler HD, Greenblatt RM, Palefsky JM. Anal intraepithelial neoplasia in a multisite study of HIV-infected and high-risk HIV-uninfected women. AIDS. 2009;23:59–70.
9. Johnson LG, Madeleine MM, Newcomer LM, Schwartz SM, Daling JR. Anal cancer incidence and survival: the surveillance, epidemiology, and end results experience, 1973–2000. Cancer. 2004;101:281–8.
10. Cress RD, Holly EA. Incidence of anal cancer in California: increased incidence among men in San Francisco, 1973–1999. Prev Med. 2003;36(5):555–60.
11. Melbye M, Rabkin C, Frisch M, Biggar RJ. Changing patterns of anal cancer incidence in the United States, 1940–1989. Am J Epidemiol. 1994;139(8):772–80.
12. D'Souza G, Wiley DJ, Li X, Chmiel JS, Margolick JB, Cranston RD, Jacobson LP. Incidence and epidemiology of anal cancer in the multicenter AIDS cohort study. J Acquir Immune Defic Syndr. 2008;48:491–9.
13. Diamond C, Taylor TH, Aboumrad T, Bringman D, Anton-Culver H. Increased incidence of squamous cell anal cancer among men with AIDS in the era of highly active antiretroviral therapy. Sex Transm Dis. 2005;32(5):314–20.
14. Adami J, Gäbel H, Lindelöf B, Ekström K, Rydh B, Glimelius B, Ekbom A, Adami HO, Granath F. Cancer risk following organ transplantation: a nationwide cohort study in Sweden. Br J Cancer. 2003;89(7):1221–7.
15. Moscicki AB, Schiffman M, Kjaer S, Villa LL. Chapter 5: updating the natural history of HPV and anogenital cancer. Vaccine. 2006;24S3:42–51.
16. Chin-Hong PV, Vittinghoff E, Cranston RD, Browne L, Buchbinder S, Colfax G, Da Costa M, Darragh T, Benet DJ, Judson F, Koblin B, Mayer KH, Palefsky JM. Age-related prevalence of anal cancer precursors in homosexual men: the EXPLORE study. J Natl Cancer Inst. 2005;97:896–905.
17. Nyitray AG, Smith D, Villa L, Lazcano-Ponce E, Abrahamsen M, Papenfuss M, Guiliano AG. Prevalence of and risk factors for anal human papillomavirus infection in men who have sex with women: a cross-national study. J Infect Dis. 2010;201:1498–508.
18. Hernandez BY, McDuffie K, Zhu X, Wilkens LR, Killeen J, Kessel B, Wakabayashi MT, Bertram CC, Easa D, Ning L, Boyd J, Sunoo C, Kamemoto L, Goodman MT. Anal human papillomavirus infection in women and its relationship with cervical infection. Cancer Epidemiol Biomarkers Prev. 2005;14:2550–6.
19. Moscicki AB, Hills N, Shiboski S, Powell K, Jay N, Hanson E, et al. Risks for incident human papillomavirus infection and low-grade squamous intraepithelial lesion development in young females. JAMA. 2001;285:2995–3002.
20. Dindo D, Nocito A, Schettle M, Clavien PA, Hahnloser D. What should we do about anal condyloma and anal intraepithelial neoplasia? Results of a survey. Colorectal Dis. 2011;13(7):796–801.
21. Glynne-Jones R, Northover JMA, Cervantes A. Anal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010;21 suppl 5:v87–92.
22. Mathews C, Caperna J, Cachay ER, Cosman B. Early impact and performance characteristics of an established anal dysplasia screening program: program evaluation considerations. Open AIDS J. 2007;1:11–20.
23. Goldie SJ, Kuntz KM, Weinstein MC, Freedberg KA, Welton ML, Palefsky JM. The clinical effectiveness and cost-effectiveness of screening for anal squamous intraepithelial lesions in homosexual and bisexual HIV-positive men. JAMA. 1999;281(19):1822–9.
24. Goldie SJ, Kuntz KM, Weinstein MC, Freedberg KA, Palefsky JM. Cost-effectiveness of screening for anal squamous intraepithelial lesions and anal cancer in human immunodeficiency virus-negative homosexual and bisexual men. Am J Med. 2000;108(8):634–41.
25. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;17(6):1471–4.
26. Mahto M, Nathan M, O'Mahony C. More than a decade on: review of the use of imiquimod in lower anogenital intraepithelial neoplasia. Int J STD AIDS. 2010;21(1):8–16.
27. Hoyme UB, Hagedorn M, Schindler AE, Schneede P, Hopfenmüller W, Schorn K, Eul A. Effect of adjuvant imiquimod 5% cream on sustained clearance of anogenital warts following laser treatment. Infect Dis Obstet Gynecol. 2002;10(2):79–88.
28. Richel O, Wieland U, de Vries HJ, Brockmeyer NH, van Noesel C, Potthoff A, Prins JM, Kreuter A. Topical 5-fluorouracil treatment of anal intraepithelial neoplasia in human immunodeficiency virus-positive men. Br J Dermatol. 2010;163(6):1301–7.
29. Gilbert DC, Glynne-Jones R. Intensity-modulated radiotherapy in anal cancer – where do we go from here? Clin Oncol. 2013;25(3):153–4.

30. Glynne-Jones R, James R, Meadows H, et al. Optimum time to assess complete clinical response (CR) following chemoradiation (CRT) using mitomycin (MMC) or cisplatin (CisP), with or without maintenance CisP/5FU in squamous cell carcinoma of the anus: results of ACT II. 2012 ASCO Annual Meeting (abstr 4004). J Clin Oncol. 2012;30(Suppl.):abstr 4004.
31. Kreuter A, et al. J Invest Dermatol. 2008;128:2078–83.

28 Peritoneal Malignancies and Colorectal Peritoneal Metastases

Sanjeev Dayal, Lily Maguire, and Brendan Moran

28.1 Introduction

Advanced primary or recurrent colorectal cancer (CRC) commonly involves the peritoneum via a process best described as synchronous or metachronous colorectal peritoneal metastasis. Synchronous colorectal peritoneal metastases (CPMs) occur in approximately 5–10 % of patients undergoing CRC resection [1]. Twenty to 50 % of patients who have undergone curative surgery for CRC go on to develop metachronous intraperitoneal recurrence [2].

Conventional treatment of these patients using systemic chemotherapy with or without palliative surgery has been reported to result in a poor median survival of 5–7 months [1]. The more recent addition of modern chemotherapeutic agents, such as oxaliplatin and irinotecan, at best improves this median survival to approximately 12.6 months [3]. A recent report showed that the addition of biological agents in a select group of patients improved overall survival to 22.4 months [4].

There is emerging evidence that select patients with colorectal peritoneal metastatic disease may be cured by a combination of what is termed *cytoreductive surgery* (CRS) and *hyperthermic intraperitoneal chemotherapy* (HIPEC). For these patients, the concept of "peritoneal metastases" (Fig 28.1a, b) as a subset of diffuse "peritoneal carcinomatosis" (Fig 28.2) helps to define future directions in this complex field [5].

- The incidence of resectable synchronous or metachronous peritoneal metastases without extra-abdominal spread is unknown and can only be estimated at approximately 3 % of all patients with CRC [1]. This can be extrapolated to approximately 1,000 of the ~30,000 cases of CRC per year in England, though many patients are too unhealthy, or are unwilling, to undergo the complex strategy of CRS and HIPEC [5].

28.2 Pathophysiology and the "Redistribution Phenomenon"

The fundamental basis of metastatic peritoneal spread within the abdomen revolves around the pathophysiology of intraperitoneal fluid dynamics by a process called the "redistribution phenomenon" [6]. A fundamental knowledge of this phenomenon is central not only to the understanding of the surgery required in managing peritoneal malignancy but also the sites to focus on during noninvasive abdominal imaging or laparoscopic assessment of any patient with suspected or actual peritoneal malignancy.

S. Dayal, MD • L. Maguire, MD • B. Moran, MD (✉)
Peritoneal Malignancy Institute,
Basingstoke RG24 9NA, UK
e-mail: brendan.moran@hhft.nhs.uk

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_28

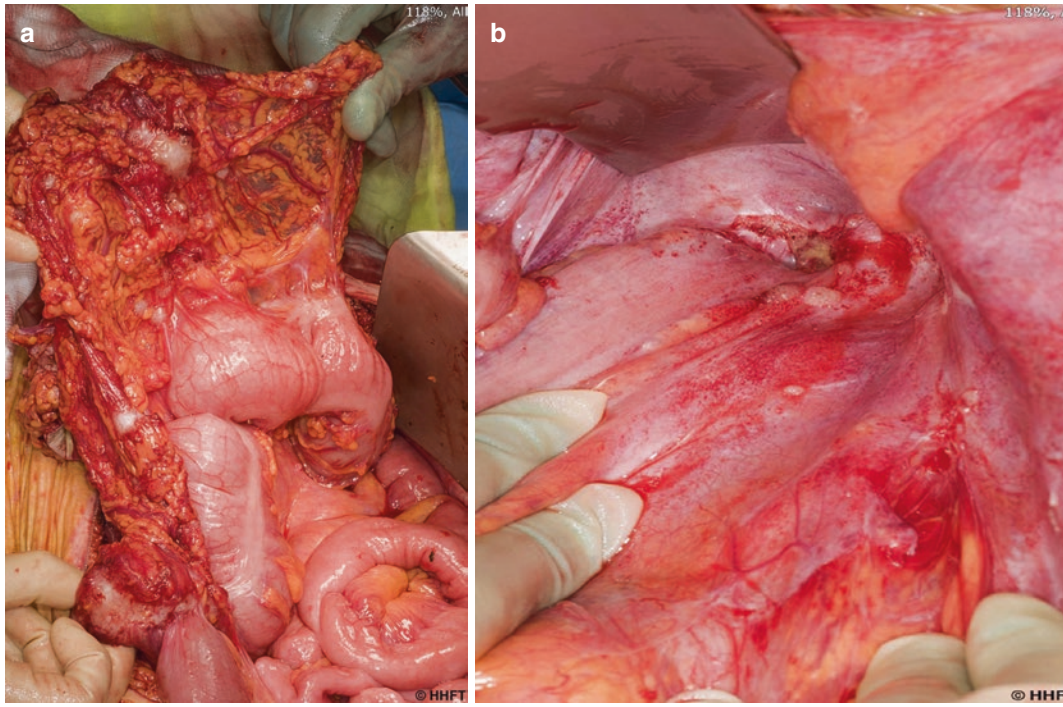


Fig. 28.1 Colorectal peritoneal metastases of the (**a**) omentum and (**b**) rectovesical pouch

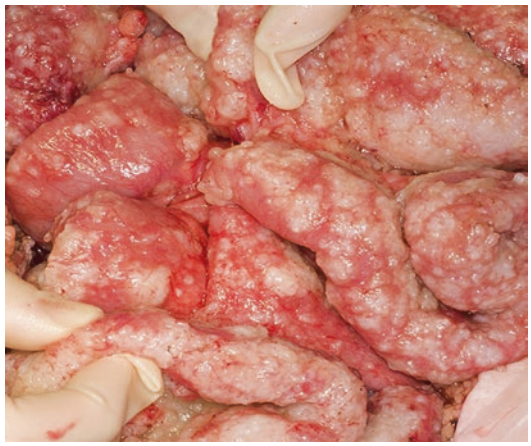


Fig. 28.2 Colorectal carcinomatosis

The redistribution of abdominal free-floating cells occurs via two main mechanisms – namely, gravity and a concentration of tumor at sites of peritoneal fluid absorption. The peritoneal cavity is a highly sophisticated, flexible container that allows the mobility of the motile contents, particularly the gastrointestinal tract. Physiologically it has a fluid interface between the parietal and visceral peritoneum, analogous to lubricating oil in a combustion engine. A mechanism to absorb and filter this physiological fluid, akin to an oil filter in an engine, incorporates the greater and lesser omentum and lacunae on the undersurface of the diaphragm, predominantly on the right side. Thus "redistribution" of peritoneal malignant cells occurs by gravitational forces, resulting in tumor accumulation in the pelvis, paracolic gutters, and subphrenic spaces and by a "filtration" and concentration effect in the omentum and undersurface of the diaphragm, predominantly on the right side.

Tumor biology is also pivotal, and the "invasive" potential of the cells determines whether peritoneal malignancy is confined to the peritoneum or invades vital abdominal viscera. The motility of the intra-abdominal organs, particularly the small bowel, is protected from involvement by relatively noninvasive tumor cells (classically pseudomyxoma peritonei [PMP]) and may similarly apply to some patients with CPMs.

Extensive prior surgery, with resulting inevitable adhesions, can interfere with bowel motility

and can affect tumor spread. This may result in tumor concentration in and infiltration of the small bowel, potentially affecting resectability.

28.3 Evidence to Support CRS and HIPEC

The treatment strategy of CRS and HIPEC has evolved predominantly from the work of various researchers, initially in the field of PMP [7] and subsequently extrapolated to other peritoneal malignancies. Animal studies [8], a randomized controlled trial [9], numerous case series, and two meta-analyses [10, 11] support the benefits of CRS and HIPEC.

An elegant animal model of peritoneal carcinomatosis, randomizing to surgery alone (CRS) or CRS and HIPEC, demonstrated a reduction in peritoneal tumor volume and a prolonged survival in the group treated by a combination of CRS and HIPEC [8].

In humans, the landmark randomized controlled trial by Verwaal et al. [9] reported that CRS and HIPEC significantly improved survival compared with the best systemic chemotherapy, with acceptable toxicity. In an updated report of this study, which included 103 patients, at a median follow-up of 96 months there was an improvement in the median disease-free survival – from 12.6 to 22.2 months – favoring the group receiving CRS and HIPEC[12]. To date, criticisms of this unique randomized controlled trial have been the relatively small number of patients; the inclusion of some cases with appendiceal carcinomatosis, which is known to have a more favorable outcome than CPMs; and the now outdated systemic chemotherapy. Nevertheless, the findings are valid and a credit to the Dutch investigators in such a complex field.

- A number of publications on nonrandomized comparative case-control studies report improved survival in patients with CPMs who underwent CRS and HIPEC. Elias et al. [13] studied a series of 96 patients with CPM in a case-control study comparing CRS and HIPEC with systemic chemotherapy. They reported superior median survival (62.7 vs. 23.9 months), 2-year survival (81 % vs. 51 %), and 5-year survival (51 % vs. 13 %) in the CRS and HIPEC group.
- Franko et al. [14] similarly reported on 105 patients and documented improved 1-, 3-, and 5-year survival of 90 %, 50 %, and 25 %, respectively, in the CRS and HIPEC group compared with the group receiving only systemic chemotherapy (55 %, 12 %, and 7 %, respectively)
- Mahteme et al. [15] studied 36 patients and compared CRS and early postoperative intraperitoneal chemotherapy versus systemic chemotherapy alone. They found improved overall survival in the CRS + early postoperative intraperitoneal chemotherapy group (5-year survival: 28 % vs. 5 %).
- A publication reporting on 107 patients who had CRS and intraperitoneal chemotherapy for CPM reported overall 5- and 10-year survival rates of 35 % and 15 %, respectively. In the subset who had complete cytoreduction and HIPEC, 16 % were regarded as cured, with a disease-free interval of at least 5 years [16].
- The original systematic review in 2006 [10] concluded that available evidence in favor of CRS and HIPEC for the treatment of CPMs was weak. An updated analysis and systematic review in 2014 by Mirzenami et al. [11] concluded that "enhanced survival times can be achieved for CPM after combined treatment with CRS and intraperitoneal chemotherapy."

While many criticize the concept of CRS and HIPEC, evidence to support its use may in fact exceed the well-accepted role of surgical resection of pulmonary and hepatic metastases from CRC, which have never been subjected to randomized controlled trials. Part of the problem has been terminology; "diffuse colorectal carcinomatosis" is an exclusion criterion, and the recent concept of "resectable CPM" helps to focus attention on suitable cases for this novel strategy [5].

There has also been an overview of published evidence by the United Kingdom's National Institute of Health and Clinical Excellence, which concluded that the overall 5-year survival

was 19% and that CRS plus HIPEC was an appropriate strategy in select patients [5].

The associated morbidity and mortality need to be taken into account when performing CRS and HIPEC. In their systematic review, Mirzenami et al. [11] found that mortality ranged from 0% to 12% and morbidity from 21.8% to 62%. The most common complications encountered were wound related (3–12%), fistulas (1–11%), intra-abdominal abscess (1.8–14%), reoperation rate (4–20.8%), and chemotherapy-related hematological toxicity (2–52%) [11]. The importance of the "learning curve" is now well recognized in this complex procedure, and most centers have reported a decline in the overall complication rate as the number of cases performed increased [17]. Moreover, improvements in anesthesia, operative technique, critical care, and both diagnostic and interventional radiology have all added to the early recognition and active treatment of complications [18]. Recent large-scale studies are now reporting acceptable morbidity and mortality rates following CRS plus HIPEC [19, 20].

28.4 Technical Aspects of CRS and HIPEC

The concept of CRS and HIPEC was initially popularized by Sugarbaker [21] and was subsequently adopted globally (a "global learning curve") [22]. The techniques have been developed and refined in PMP. Patients with extensive PMP may require all five primary, and two secondary, peritonectomies together with organ resections. The fundamental basis for CRS is the distribution of an abdominal tumor via the "the redistribution phenomenon," described earlier.

CRS involves a series of "peritonectomy procedures" in addition to the resection of involved nonvital organs such as the spleen, gallbladder, right colon, and rectosigmoid. Peritonectomy consists of resection of the parietal peritoneum lining the abdominal cavity in the relatively avascular subperitoneal plane.

- The five primary peritonectomy procedures are (1) right parietal, (2) left parietal, (3) right diaphragmatic, (4) left diaphragmatic, and (5) pelvic. The liver and spleen are enveloped by the peritoneum, and peritonectomy of the right and left liver involves capsulectomy of the right and left liver to complete the total of seven peritonectomy procedures.
- Peritonectomy, particularly liver capsulectomy, is facilitated by the use of high-powered electrosurgery using "rolly ball" diathermy with "cut" and "coag" at the highest settings. At these settings substantial smoke is produced, and a high-powered smoke extractor is mandatory to reduce smoke contamination.
- Both peritonectomy and organ resectional procedures in CRS for PMP have applications in other peritoneal malignancies, including CPMs. However, it is pertinent to note that patients with CPM who benefit from CRS and HIPEC should have localized disease and will never require the same extent of surgery as patients with extensive PMP.
- A radical greater omentectomy (inside the gastroepiploic vessels) is performed and the spleen is carefully assessed. If it is involved by disease, the splenic artery and vein are clamped, transfixed, and ligated, and a splenectomy is performed, taking great care to avoid damage to the tail of the pancreas. The lesser omentum is removed and dissection is carried upward in the aortocaval groove behind the caudal lobe of the liver. The gallbladder is removed and the portal structures identified, removing any peritoneal disease in this area.
- Pelvic dissection is commenced by rectal mobilization in the total mesorectal excision plane posteriorly, with full mobilization of the rectum. The peritoneal mobilization is carried anteriorly toward the bladder, and the peritoneum is carefully dissected off its posterior surface. The rectum and sigmoid colon can usually be preserved, but prior pelvic surgery (especially major gynecological surgery such as hysterectomy and salpingo-oophorectomy) may mean that the tumor has infiltrated the anterior rectal wall, and an anterior resection may be needed.
- In women, the ovaries are routinely removed; removal of the uterus may or may not be required.

Table 28.1 Completeness of cytoreduction

CC0	No visible residual tumour
CC1	Largest residual tumor <2.5 mm in size
CC2	Largest residual tumor 2.5–2.5 cm in size
CC3	Largest residual tumor >2.5 cm in size

- In many patients with PMP, appendicectomy alone may suffice to resect the tumor, but a right hemicolectomy is required if there is extensive peritoneal involvement of the cecum and/or terminal ileum, or if there are suspected involved nodes on the ileocolic chain. If right and left colectomies are performed, then anastomoses are generally performed after completing HIPEC. If a low colorectal anastomosis is needed, consideration should be given to performing a proximal temporary defunctioning loop ileostomy, which is our usual practice.

At the end of CRS, the completeness of cytoreduction (CC) is measured using the CC score. This ranges from CC-0 (no visible tumor), CC-1 (tumor nodules <2.5 mm), CC-2 (tumor nodule between 2.5 and 2.5 cm), and CC-3 (tumor nodule >2.5 cm) (Table 28.1). CC-0 and CC-1 are classed as "complete cytoreduction," since intraperitoneal chemotherapy penetrates to a depth of 3 mm. Patients with PMP after CC-0 and CC-1 cytoreduction have shown similar long-term, disease-free outcomes.

28.5 Hyperthermic Intraperitoneal Chemotherapy

After completion of CRS, a closed or open (coliseum) technique is used to administer HIPEC for 60–90 min at 42° C. The intraoperative chemotherapeutic agents commonly used for PMP or CPM are mitomycin-C (10 mg/m^2) or oxaliplatin (460 mg/m^2). The concept of HIPEC is that cytotoxic drugs penetrate to a depth of approximately 3 mm [23]. Hyperthermia enhances this penetration, and the drug's effectiveness and the hyperthermia induce tumor cell destruction as a result of the formation of heat shock proteins [24]. An additional benefit of hyperthermia is that the heat corrects the patient's physiology. A prolonged laparotomy usually results in hypothermia; HIPEC reverses this hypothermia, avoiding adverse effects and facilitating hemostasis. In our experience, HIPEC reduces secondary hemorrhage requiring reintervention, probably by restoring hemostasis and providing a long interval in which to detect bleeding points.

Once HIPEC is completed, the abdominal cavity is washed out with copious volumes of water or saline and low-suction abdominal drains are inserted into the four quadrants of the abdomen.

28.6 Patient Selection

With increasing awareness among oncologists of CRS and HIPEC as a treatment option for selected patients with CPM, there has been an increase in referrals to peritoneal malignancy treatment centers. The challenge still remains in selecting those patients who would benefit from CRS and HIPEC in terms of longer survival and improved quality of life. The best results occur in patients with limited disease (usually confined to one or two quadrants of the abdomen and with a minimum of ~200 cm of uninvolved small bowel), where complete tumor removal is achieved, ideally at the time of primary colorectal tumor resection in patients with synchronous disease [25].

The Peritoneal Carcinomatosis Index (PCI) is the most widely accepted quantitative prognostic indicator in selecting and treating CPMs [26]. The PCI is an intraoperative assessment that quantifies the extent of peritoneal disease distribution in combination with the size of tumor nodules (Table 28.2).

The numeric score ranges from 0 to 39, with a higher score indicating a greater tumor load. The abdomen and pelvis are divided into nine regions and the small bowel into four. If the lesion size is >5 cm in a region, the region is given a score of 3. If the lesion size is up to 5 cm, the region is given score of 2, and if it is up to 0.5 cm, it is given a score of 1. If no tumor is seen in a particular region ,it is scored as 0. The maximum PCI score

Table 28.2 Regions and scoring used for calculating the Peritoneal Carcinomatosis Index

Regions of the abdomen
Central
Right upper
Epigastrium
Left upper
Left flank
Lower left
Pelvis
Right lower
Right flank
Upper jejunum
Lower jejunum
Upper ileum
Lower ileum

Lesion size	Score
No tumor seen	0
Tumor ≤0.5 cm	1
Tumor ≤5.0 cm	2
Tumor >5.0 cm or confluence	3

Total number of regions	13
Maximum PCI score	39

that can be calculated is 39. In a French multicentre study including 523 patients with CPM, Elias et al. [26] found that survival at 4 years in patients with a PCI score <6 was 44 %; for a score between 7 and 12 4-year survival was 22 %, and with a score >19 it was 7 %. It has since been recommended that CRS and HIPEC should be avoided in patients with CPM with a PCI score >20. A more recent study of 180 patients by Goere et al. [27] suggested that this threshold may be lowered further to a PCI score >17. Ideally, a preoperative PCI score would help select patients for surgery; work is ongoing in this field using a combination of cross-sectional imaging (predominantly computed tomography [CT]) and selective use of laparoscopy. The problem is that imaging tends to underestimate the extent of low-volume peritoneal disease, and neither CT, magnetic resonance imaging, nor positron emission tomography (PET)/CT is sufficiently accurate in determining disease extent.

In the event that imaging predicts a high PCI and possible incomplete resection, optimal maximal palliative tumor debulking may be beneficial, particularly in patients with less aggressive tumours [17].

Nomograms to assess the suitability of patients for CRS and HIPEC are complex and not widely used. They serve more as guidelines as opposed to absolute recommendations.

- The Peritoneal Surface Disease Severity Score is calculated on the basis of clinical symptoms, the extent of peritoneal metastases, and tumor histology [28]. Esquivel et al. [29], in a study of 1,013 patients, concluded that the Peritoneal Surface Disease Severity Score can be used as a useful adjunct in decision making when considering patients with CPM for CRS and HIPEC, and for stratification within clinical trials.
- Verwaal et al. [30] calculated a Prognostic Score based on the location of the tumor, tumor differentiation, the presence of signet ring cells, and the number of regions affected. They found that a higher score was associated with decreased overall survival.
- Corep (COloREctal Ps) is another score based on histology, hematological status, serial tumor markers, and changes in tumor markers over time that can be used to assess the suitability of patients with CPM for CRS and HIPEC. A score >6 of 18 can predict short-term (<12 months) cancer-specific survival, but further validation of this score is required [31].

While patients should be reasonably healthy to undergo CRS and HIPEC, older age per se is not an absolute contraindication. However, older patients must be carefully assessed on the basis of their performance status [17]. Preoperative use of the Functional Assessment of Cancer Therapy questionnaire combined with Eastern Cooperative Oncology Group Performance may allow further enhanced prediction of treatment-related morbidity and mortality [32].

Not surprisingly, lymph node involvement is a poor independent prognostic factor [25]. However, surgery may still be of benefit if the tumor is limited and complete cytoreduction can be achieved [17].

As a general rule, if patients show disease progression while receiving current optimal systemic chemotherapeutic treatment, cytoreductive surgery is unlikely to be beneficial in improving long-term outcomes [17]. On the other hand, patients who have had a complete response to neoadjuvant chemotherapy may also benefit less from CRS and HIPEC compared with those who have had a partial response to systemic treatment. Passot et al. [33] reported on 115 patients with CPM and concluded that the degree of pathological response to neoadjuvant chemotherapy may represent a new outcome for prognosis following treatment with curative intent.

28.7 Imaging

The staging, management plan, and follow-up to detect recurrence of CRC have been revolutionized by advances in cross-sectional, noninvasive imaging, particularly CT and more latterly magnetic resonance imaging and PET/CT. Overall, CT has been the core imaging technique in CRC staging and has been central to an multidisciplinary team approach to optimize outcome. Likewise, in peritoneal assessment, CT remains the mainstay in diagnosing suspected synchronous or metachronous peritoneal spread, and an awareness of the redistribution phenomenon, as outlined earlier, is helpful in image analysis. CT clearly identifies patients with distant metastases; high-volume, widespread colorectal peritoneal carcinomatosis; and poor prognostic factors such as large-volume ascites and small-bowel obstruction. However, its sensitivity in detecting peritoneal implants is influenced by lesion size. Small nodules (<0.5 cm) are visualized only with a sensitivity of 11 %, in contrast to 94 % for lesions >5 cm [34]. Chang-Yun et al. [35] also showed that CT has a lower detection rate and a higher rate of underestimating of small-bowel lesions compared with overall assessment of the abdominopelvic region. It is well known that preoperative CT does not reliably predict resectability in peritoneal metastases, but interestingly, Rivard et al. [36] showed that while a single concerning radiological feature may not be associated with unresectability, patients who had two or more concerning radiologic features had a higher risk of unresectability (87.5 % vs. 36.4 %; $P = 0.035$). Concerning radiological features have been described as more than three resectable parenchymal hepatic metastases, evidence of biliary or ureteral obstruction, evidence of intestinal obstruction at more than one site, evidence of gross disease in the mesentery with several segmental sites of partial small-bowel obstruction, large-volume disease in the gastrohepatic ligament, and retroperitoneal lymphadenopathy [36, 37]. There is some evidence to suggest that combining PET and contrast-enhanced CT may yield better results and may prove to be a useful tool in selecting patients with CPM for CRS and HIPEC [38].

28.8 Laparoscopy

The main ongoing problem with CPM is the difficulty in preoperatively detecting diffuse, low-volume peritoneal disease, where extensive involvement of the small bowel results in unnecessary laparotomy. For this reason, there has been an increasing interest in using laparoscopy to assess the abdominal cavity when cross-sectional imaging is either equivocal or suggests that a patient may have resectable peritoneal metastases. A good correlation between open surgery data and a laparoscopic PCI score has been reported [39]. A recent paper by Iverson et al. [40] showed the benefits of laparoscopic staging in patients with colorectal carcinomatosis in reducing ineffectual laparotomy and aiding in the selection of those most likely to benefit. Laparoscopy is theoretically attractive, but almost all patients will have already had a bowel resection with subsequent adhesions, thereby increasing the risks and limiting views of the peritoneal cavity. Experienced units can balance the benefits against the risks, however, and marginal cases should be discussed with a peritoneal malignancy unit; laparoscopy is best performed in such a unit.

28.9 CPM and Liver Metastases

Extra-abdominal metastases limit the role of CRS and HIPEC. However, select patients with resectable peritoneal and liver metastases may be treated with curative intent. Elias et al. [41] concluded that combined treatment of liver metastases and peritoneal metastases is feasible and beneficial in highly selected patients presenting with three or fewer liver metastases. Maggiori et al. [42] also confirmed in their case-control study that patients with a PCI score <12 and three or fewer synchronous liver metastases had improved survival when synchronous liver resection was performed at the time of CRS and HIPEC.

28.10 What of the Future?

The increasing use of laparoscopic CRC resection presents new opportunities in patients with low-volume CPMs that are not detected during preoperative staging. In this situation, if the disease is limited and the tumor asymptomatic, surgery can be deferred and the patient referred to a peritoneal malignancy treatment center. The initial ports should be inserted in the midline if there is any suspicion of peritoneal disease on CT, and ideally only midline ports are inserted if there are metastases because ports at this site can easily be resected during a subsequent laparotomy to treat or prevent port-site metastases.

A patient with a symptomatic primary obstruction, for example, and localized peritoneal disease of course requires defunctioning or primary tumor resection. Timely advice from a peritoneal malignancy center is recommended in these scenarios, and in many such cases systemic chemotherapy, a "trial of time," and subsequent reassessment may help to clarify a way forward in this dynamic evolving field.

Another emerging concept is that of a "second look" procedure for patients at risk of peritoneal metastases. Elias et al. [42] reported on 41 patients who had "second look surgery" for a high risk of peritoneal disease based on three factors – namely, a perforated tumour, Krukenberg ovarian metastases, or limited peritoneal disease at the primary operation. All 41 underwent systemic chemotherapy after the primary operation and had normal CT scans before the second look surgery. Peritoneal metastases were found in 60 % in the initial limited peritoneal carcinomatosis group, 62 % in patients with Krukenberg tumors, and 37 % in the group with primary tumor perforation. The overall and 5-year disease-free survival rates were 90 % and 44 %, respectively, suggesting that this strategy may be beneficial. The downside was a 2 % mortality and 9.7 % major morbidity in the 41 patients, despite treatment in an experienced, high-volume center. A randomized French trial of this second look strategy is underway.

Current HIPEC systems are expensive and complex in design and application, both of which are major barriers to routine availability. One possibility is that there will be an effective "off-the-shelf" intraperitoneal chemotherapy agent readily available for any patient found to have unexpected resectable peritoneal metastases or any of the other high-risk factors described in this chapter.

Health care organizations all over the world are increasingly accepting the role and benefits of CRS and HIPEC in selects cases with peritoneal malignancy, particularly CPMs. The recent UK National Institute of Health and Clinical Excellence recommendation on colorectal carcinomatosis [5] resulted from an independent review of the available literature and is an excellent source of information for those wishing to explore the evidence base.

There is an ongoing need to establish training programs for centers embarking on CRS and HIPEC. Initiatives previously developed for CRC may be required. The United Kingdom has demonstrated an ability to address these challenges with initiatives such as the multidisciplinary team total mesorectal excision development program and Low Rectal Cancer national development

Table 28.3 Peritoneal malignancy tumor types and selection criteria for complete cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC)

Tumor type	Approximate incidence	Selection criteria for complete CRS + HIPEC	Importance of tumor markers	HIPEC	Overall 5-year survival
Pseudomyxoma peritonei from appendiceal primary	2–4 per million per year	PCI is not a prognostic indicator if the small bowel is disease free. Histology of low-grade carcinoma peritonei is favorable, high-grade carcinoma less so, and appendix adenocarcinoma behaves more like a primary colon cancer.	Surveillance In patients with low-grade histology, high preoperative tumor markers predict recurrence.	Mitomycin	60–80 %
CPMs	Colorectal cancer: 600 per million per year Resectable CPM 18 per million per year	PCI score ˂20 Small bowel is disease free on laparoscopy Generally, a CPM that has not progressed while receiving chemotherapy or when there is a time lapse between the development of resectable peritoneal disease and treatment of the primary tumor Poorly differentiated adenocarcinoma with signet cells have a poor outcome	Surveillance	Mitomycin or oxaliplatin	20–30 %
Peritoneal mesothelioma	1 per 5 million per year	If complete cytoreduction is feasible on laparoscopy The multicystic variant has the best outcome. Some patients with epithelioid mesothelioma may be suitable but those with biphasic and sarcomatoid variants are unlikely to benefit.	Surveillance	Cisplatin + doxorubicin	30–40 %

program [5] focusing on rectal cancer, and the National Training Program in Laparoscopic Colorectal Surgery [44]. A similar initiative is required to help establish and train peritoneal malignancy units to provide optimal care for appropriate patients.

The search continues for novel approaches to the management of the challenging problem of CPMs in advanced and recurrent CRC and peritoneal mesothelioma. Recent reports are encouraging, justifying hope for select patients (Table 28.3).

References

1. Jayne DG, Fook S, Loi C, Seow-Choen F. Peritoneal carcinomatosis from colorectal cancer. Br J Surg. 2002;89(12):1545–50.
2. Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, et al. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. Cancer. 2000;88(2):358–63.
3. Koppe MJ, Boerman OC, Oyen WJ, Bleichrodt RP. Peritoneal carcinomatosis of colorectal origin: incidence and current treatment strategies. Ann Surg. 2006;243(2):212–22.
4. Klaver YL, Leenders BJ, Creemers GJ, Rutten HJ, Verwaal VJ, Lemmens VE, et al. Addition of biological therapies to palliative chemotherapy prolongs survival in patients with peritoneal carcinomatosis of colorectal origin. Am J Clin Oncol. 2013;36(2):157–61.
5. Moran BJ, Cecil TD. Treatment of surgically resectable colorectal peritoneal metastases. Br J Surg. 2014;101(2):5–7.
6. Sugarbaker PH. Pseudomyxoma peritonei. A cancer whose biology is characterized by a redistribution phenomenon. Ann Surg. 1994;219(2):109–11.
7. Youssef H, Newman C, Chandrakumaran K, Mohamed F, Cecil TD, Moran BJ. Operative findings, early complications, and long-term survival in 456 patients with pseudomyxoma peritonei syndrome of appendiceal origin. Dis Colon Rectum. 2011;54(3):293–9.
8. Klaver YL, Hendriks T, Lomme RM, Rutten HJ, Bleichrodt RP, de Hingh IH. Intraoperative hyperthermic intraperitoneal chemotherapy after cytoreductive surgery for peritoneal carcinomatosis in an experimental model. Br J Surg. 2010;97(12):1874–80.
9. Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. J Clin Oncol: Off J Am Soc Clin Oncol. 2003;21(20):3737–43.
10. Yan TD, Black D, Savady R, Sugarbaker PH. A systematic review on the efficacy of cytoreductive surgery and perioperative intraperitoneal chemotherapy for pseudomyxoma peritonei. Ann Surg Oncol. 2007;14(2):484–92.
11. Mirnezami R, Moran BJ, Harvey K, Cecil T, Chandrakumaran K, Carr N, et al. Cytoreductive surgery and intraperitoneal chemotherapy for colorectal peritoneal metastases. World J Gastroenterol: WJG. 2014;20(38):14018–32.
12. Verwaal VJ, Bruin S, Boot H, van Slooten G, van Tinteren H. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. Ann Surg Oncol. 2008;15(9):2426–32.
13. Elias D, Lefevre JH, Chevalier J, Brouquet A, Marchal F, Classe JM, et al. Complete cytoreductive surgery plus intraperitoneal chemohyperthermia with oxaliplatin for peritoneal carcinomatosis of colorectal origin. J Clin Oncol: Off J Am Soc Clin Oncol. 2009;27(5):681–5.
14. Franko J, Ibrahim Z, Gusani NJ, Holtzman MP, Bartlett DL, Zeh 3rd HJ. Cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion versus systemic chemotherapy alone for colorectal peritoneal carcinomatosis. Cancer. 2010;116(16):3756–62.
15. Mahteme H, Hansson J, Berglund A, Pahlman L, Glimelius B, Nygren P, et al. Improved survival in patients with peritoneal metastases from colorectal cancer: a preliminary study. Br J Cancer. 2004;90(2):403–7.
16. Goere D, Malka D, Tzanis D, Gava V, Boige V, Eveno C, et al. Is there a possibility of a cure in patients with colorectal peritoneal carcinomatosis amenable to complete cytoreductive surgery and intraperitoneal chemotherapy? Ann Surg. 2013;257(6):1065–71.
17. Riss S, Mohamed F, Dayal S, Cecil T, Stift A, Bachleitner-Hofmann T, et al. Peritoneal metastases from colorectal cancer: patient selection for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Eur J Surg Oncol:J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2013;39(9):931–7.
18. Mirnezami R, Mehta AM, Chandrakumaran K, Cecil T, Moran BJ, Carr N, et al. Cytoreductive surgery in combination with hyperthermic intraperitoneal chemotherapy improves survival in patients with colorectal peritoneal metastases compared with systemic chemotherapy alone. Br J Cancer. 2014;111(8):1500–8.
19. Canda AE, Sokmen S, Terzi C, Arslan C, Oztop I, Karabulut B, et al. Complications and toxicities after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol. 2013;20(4):1082–7.
20. Bakrin N, Bereder JM, Decullier E, Classe JM, Msika S, Lorimier G, et al. Peritoneal carcinomatosis treated with cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for advanced ovarian carcinoma: a French multicentre retrospective cohort study of 566 patients. Eur J Surg Oncol: J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2013;39(12):1435–43.
21. Sugarbaker PH. Peritonectomy procedures. Cancer Treat Res. 1996;82:235–53.
22. Mohamed F, Cecil T, Moran B, Sugarbaker P. A new standard of care for the management of peritoneal surface malignancy. Curr Oncol. 2011;18(2):e84–96.
23. El-Kareh AW, Secomb TW. A theoretical model for intraperitoneal delivery of cisplatin and the effect of hyperthermia on drug penetration distance. Neoplasia. 2004;6(2):117–27.
24. Pelz JO, Vetterlein M, Grimmig T, Kerscher AG, Moll E, Lazariotou M, et al. Hyperthermic intraperitoneal chemotherapy in patients with peritoneal

carcinomatosis: role of heat shock proteins and dissecting effects of hyperthermia. Ann Surg Oncol. 2013;20(4):1105–13.
25. Elias D, Gilly F, Boutitie F, Quenet F, Bereder JM, Mansvelt B, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. J Clin Oncol: Off J Am Soc Clin Oncol. 2010;28(1):63–8.
26. Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res. 1996;82:359–74.
27. Goere D, Souadka A, Faron M, Cloutier AS, Viana B, Honore C, et al. Extent of colorectal peritoneal carcinomatosis: attempt to define a threshold above which HIPEC does not offer survival benefit: a comparative study. Ann Surg Oncol. 2015;22:2958–64.
28. Pelz JO, Stojadinovic A, Nissan A, Hohenberger W, Esquivel J. Evaluation of a peritoneal surface disease severity score in patients with colon cancer with peritoneal carcinomatosis. J Surg Oncol. 2009;99(1):9–15.
29. Esquivel J, Lowy AM, Markman M, Chua T, Pelz J, Baratti D, et al. The American Society of Peritoneal Surface Malignancies (ASPSM) Multiinstitution Evaluation of the Peritoneal Surface Disease Severity Score (PSDSS) in 1,013 patients with colorectal cancer with peritoneal carcinomatosis. Ann Surg Oncol. 2014;21(13):4195–201.
30. Verwaal VJ, van Tinteren H, van Ruth S, Zoetmulder FA. Predicting the survival of patients with peritoneal carcinomatosis of colorectal origin treated by aggressive cytoreduction and hyperthermic intraperitoneal chemotherapy. Br J Surg. 2004;91(6):739–46.
31. Cashin PH, Graf W, Nygren P, Mahteme H. Patient selection for cytoreductive surgery in colorectal peritoneal carcinomatosis using serum tumor markers: an observational cohort study. Ann Surg. 2012;256(6):1078–83.
32. Ihemelandu CU, McQuellon R, Shen P, Stewart JH, Votanopoulos K, Levine EA. Predicting postoperative morbidity following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CS+HIPEC) with preoperative FACT-C (Functional Assessment of Cancer Therapy) and patient-rated performance status. Ann Surg Oncol. 2013;20(11):3519–26.
33. Passot G, You B, Boschetti G, Fontaine J, Isaac S, Decullier E, et al. Pathological response to neoadjuvant chemotherapy: a new prognosis tool for the curative management of peritoneal colorectal carcinomatosis. Ann Surg Oncol. 2014;21(8):2608–14.
34. Koh JL, Yan TD, Glenn D, Morris DL. Evaluation of preoperative computed tomography in estimating peritoneal cancer index in colorectal peritoneal carcinomatosis. Ann Surg Oncol. 2009;16(2):327–33.
35. Chang-Yun L, Yonemura Y, Ishibashi H, Sako S, Tsukiyama G, Kitai T, et al. Evaluation of preoperative computed tomography in estimating peritoneal cancer index in peritoneal carcinomatosis. Gan to kagaku ryoho Cancer Chemother. 2011;38(12):2060–4.
36. Rivard JD, Temple WJ, McConnell YJ, Sultan H, Mack LA. Preoperative computed tomography does not predict resectability in peritoneal carcinomatosis. Am J Surg. 2014;207(5):760–4; discussion 4–5.
37. Esquivel J, Sticca R, Sugarbaker P, Levine E, Yan TD, Alexander R, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of peritoneal surface malignancies of colonic origin: a consensus statement. Society of surgical oncology. Ann Surg Oncol. 2007;14(1):128–33.
38. Pfannenberg C, Konigsrainer I, Aschoff P, Oksuz MO, Zieker D, Beckert S, et al. (18)F-FDG-PET/CT to select patients with peritoneal carcinomatosis for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol. 2009;16(5):1295–303.
39. Valle M, Garofalo A. Laparoscopic staging of peritoneal surface malignancies. Eur J Surg Oncol: J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2006;32(6):625–7.
40. Iversen LH, Rasmussen PC, Laurberg S. Value of laparoscopy before cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis. Br J Surg. 2013;100(2):285–92.
41. Elias D, Benizri E, Pocard M, Ducreux M, Boige V, Lasser P. Treatment of synchronous peritoneal carcinomatosis and liver metastases from colorectal cancer. Eur J Surg Oncol: J Eur Soc Surg Oncol Br Assoc Surg Oncol. 2006;32(6):632–6.
42. Maggiori L, Goere D, Viana B, Tzanis D, Dumont F, Honore C, et al. Should patients with peritoneal carcinomatosis of colorectal origin with synchronous liver metastases be treated with a curative intent? A case-control study. Ann Surg. 2013;258(1):116–21.
43. Elias D, Honore C, Dumont F, Ducreux M, Boige V, Malka D, et al. Results of systematic second-look surgery plus HIPEC in asymptomatic patients presenting a high risk of developing colorectal peritoneal carcinomatosis. Ann Surg. 2011;254(2):289–93.
44. Coleman MG, Hanna GB, Kennedy R, National Training Programme L. The national training programme for laparoscopic colorectal surgery in England: a new training paradigm. Colorectal Dis: Off J Assoc Coloproctol G B Irel. 2011;13(6):614–6.

Retrorectal Tumors

29

N. Chéreau and Y. Parc

29.1 Anatomy

The retrorectal space is limited by the posterior surface of the rectum, the sacrum, the line of peritoneal reflection, and the levator ani. Laterally, the area is bounded by the ureters, iliac vessels, and sacral nerves.

During the embryonic period, multiple tissues (neuroectoderm and ectoderm) grow in the retrorectal space. In the case of abnormal development of these different germ layers, retrorectal tumors (RRTs) can develop. Consequently, the retrorectal space may contain a heterogeneous group of benign and malignant tumors derived from embryological residues.

29.2 Pathology

The first case of an RRT, reported by Middeldorf [6] in 1885, involved a cystic RRT, corresponding to a rectal duplication, in a 1-year-old child. Many classifications have been proposed, including one described by Uhlig and Johnson [7], distinguishing four etiological groups of RRT: congenital, neurogenic, bone, and various tumors. Dozois et al. [8] subdivided these categories into benign and malignant tumors (Table 29.1).

29.2.1 Congenital Tumors

Congenital tumors are the most common RRT: 79 of every 120 (66%), in the experience of the Mayo Clinic [1]. The classification described by Malafosse et al. [9] in 1977, then reviewed and corrected by Barthod et al. [10] in 1996, is used by the majority of authors:

- *Vestigial tumors*: cystic (epidermoid, dermoid, enteroid; e.g., hamartomas or rectal duplications) and noncystic (teratomas)
- *Nonvestigial tumors*: chordomas, hemangiomas

29.2.1.1 Vestigial Tumors

(a) Dermoid and epidermoid cysts

Dermoid and epidermoid cysts (Fig. 29.1a) are typically benign and are frequently observed in women aged 40–50 years. The main risk is infection (30%) and can then be difficult to distinguish from peri rectal abscess. Epidermoid and dermoid cysts tend to be well circumscribed, with a thin outer layer. They contain stratified squamous cells and skin appendages [8, 11]. Unlike tailgut

N. Chéreau • Y. Parc (✉)
Department of Digestive Surgery,
Hôpital Saint-Antoine, Université Pierre et Marie Curie, Paris VI, 184 rue du faubourg Saint-Antoine, 75012 Paris, France
e-mail: nathalie.chereau@psl.aphp.fr; yparc1@gmail.com; yann.parc@aphp.fr

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_29

Table 29.1 Classification of retrorectal tumors by Dozois et al. [8]

	Benign	Malignant
Congenital tumors	Developmental tumors: tailgut cyst (cystic mucinous hamartoma), teratoma, rectal duplication, epidermoid cyst, dermoid cyst Anterior sacral meningocele	Chordoma Teratocarcinoma
Neurogenic tumors	Neurofibroma	Neuroblastoma Ependymoma Schwannoma
Osseous tumors	Giant-cell tumor	Ewing sarcoma Chondrosarcoma
Miscellaneous tumors	Lipoma, leiomyoma, desmoid tumor Hemangioma	Liposarcoma Fibrosarcoma

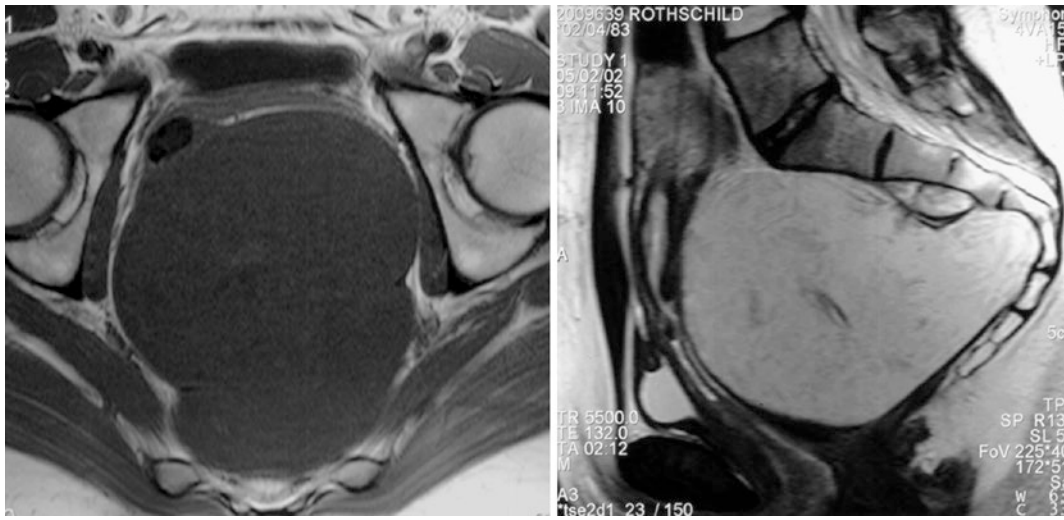


Fig. 29.1 Epidermoid cyst on T1 axial and T2 sagittal sections on magnetic resonance imaging

cysts, they do not contain transitional or glandular epithelium. They are usually unilocular, filled with a clear liquid.

(b) Enteroid (tailgut) cysts

Retrorectal hamartomas (tailgut cysts) or mucoepidermoid cysts (Fig. 29.2) are the most common cysts derived from endoderm and mesoderm. They are embryonic remnants of the terminal portion of the primitive hindgut, located after the cloacal membrane (tailgut). The distal portion of the primitive hindgut is temporary and should fully regress at the seventh week of gestation. Failure to regress is one origin of tailgut cysts. The second possible source of a hamartoma is persistence of the neurenteric canal, which is formed from the union of the endoderm and mesoderm. This canal is formed the 19th day of gestation and is obliterated when the caudal part of the notochord is completely formed. Persistence of this canal can be observed above the S2–S3 vertebrae in adults and may be the source of a congenital cyst. Histologically, the wall of these cysts can form from one or multiple types of epithelium normally found in the gastrointestinal tract of adults and fetuses [8]. These cysts are defined by the presence of at least transitional cells or cylindrical epithelium. Squamous epithelium is present in 75 % of cases, possibly as a result of metaplasia induced by inflammation [10, 11].

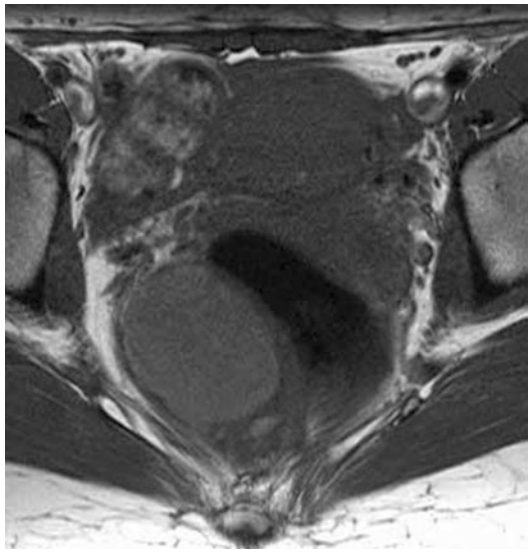


Fig. 29.2 Tailgut cyst onT1 and T2 axial sections on magnetic resonance imaging

Enteric cysts occur predominantly in middle-aged woman and present with pain (often during defecation) or symptoms related to a mass in 50 % of cases. Rectal exam may identify an extrinsic mobile or fixed fluctuating lesion. The location is predominantly in retrorectal space, although tailgut cysts have been described in the perianal space, the buttocks, the postsacral space, and even anterior to the rectum. Macroscopically, most have multicystic locules (80 %) and are well circumscribed but unencapsulated, usually starting in the retrorectal space. They rarely reach the rectal wall. The cysts can contain amorphous debris, keratin, or mucus (in the presence of mucus-secreting cells). Unlike teratomas, no calcifications are found. Inflammation is often present, whether acute or chronic (especially after trauma with cyst rupture), but it does not correlate with clinical symptoms. Malignancy is possible, in the form of adenocarcinoma or squamous cell carcinoma (occurs in 7 % of enteric cysts) [7]. Various findings are usually seen on magnetic resonance imaging (MRI):

- Median lesion in the retrorectal space, with possible forward and lateral development
- Multilocular cyst and the presence of variably sized satellite cysts
- Wall that is often visible, which can be enhanced with gadolinium
- Varied signal: homogeneous, either a hyper signal relative to T1 and T2, or either an iso signal T1 and hyper or iso signal T2

Tailgut cysts differ from duplication cysts in that they do not have a well-defined muscular wall, myenteric plexus, or serosa, although smooth muscle fibers can be found in a single layer.

Duplication cysts can occur throughout the digestive tract, with a predilection for the small bowel. Cystic rectal duplication represents 5 % of all developmental cysts. They occur solely or in combination with different abnormalities (lumbosacral, urogenital, and/or digestive). They can present either as a cyst (90–95 %) or a secondary bowel parallel to the normal digestive tract. Only the mesenteric edge of the duplication is in close contact with the main digestive wall. In 80 % of cases, however, the lumen does not communicate with the primary gastrointestinal tract (noncommunicating duplications). Retrorectal duplication cysts are usually not communicating. They must have two smooth muscular layers and a mucosa that is similar to the rectal mucosa, and they sometimes contain ectopic tissue (e.g., gastric mucosa in 25 %, pancreatic tissue). Malignant transformation has been described [8].

(c) Teratomas

Teratomas are the most common tumors in children. These are diagnosed in half of cases during the antenatal period using ultrasonography. Teratomas are characterized by a combination of differentiated tissues derived from the three germ layers: ectoderm (squamous and pilosebaceous annexes, brain and nervous tissue, glia, retina, and choroid plexus ganglion), endoderm (mucous, gastrointestinal, and lung, thyroid, salivary

glands), and mesoderm (bone, cartilage, smooth muscle, fibrous and fatty tissue) [8, 12, 13]. They can become malignant (10 %), forming teratocarcinomas, choriocarcinomas, and dysgerminomas [14].

29.2.1.2 Nonvestigial Tumors

(a) Chordoma
Chordomas are the most common malignancies of the retrorectal space [1, 15–18]. They develop from embryonic remnants of the notochord. Fifty to 60 % of chordomas are located in the sacrococcygeal region, but they can be located all along the spine. These tumors are rare (2–4 % of malignant bone tumors), frequently diagnosed in patients between 40 and 70 years old, and are more common among males (male-to-female ratio, 2:1). These tumors have a low possibility for malignancy, with approximately 20 % metastatic risk, but they can be very aggressive locally. They grow slowly and often are fortuitously discovered during a routine rectal or pelvic exam. Chordomas are lobulated gelatinous masses that invade and destroy adjacent bone structures, requiring radical resection to prevent recurrence. Computed tomography (CT) can show a large osteolytic soft-tissue mass in the sacrum and allow evaluation of the locoregional invasion. MRI characterizes this tumor with a hypo signal or intermediate signal in T1 and an hypersignal in Fig. 29.3. Enhancement of the tissue component varies but is often moderate. Their prognosis is poor, and important sequelae occur after surgical resection according to the level of the bone and sacral nerve resection.

(b) Meningocele
Meningoceles are rare, sporadic, and more common in women than men. The anterior sacral meningocele is the result of a herniated dural sac in the presacral space, caused by a bony defect of the anterior wall of the sacrum. The sac communicates with the spinal canal and is filled with cerebrospinal fluid. Patients can present with headache exacerbated by defecation, urinary symptoms, constipation, sacral pain, and sometimes meningitis. Other bone defects occur in 50 % of cases. CT reveals a well-circumscribed tumor and a watery, uniform cyst and confirms the bone defect.

29.2.2 Neurogenic and Bone Tumors

Neurogenic and bone tumors each represent approximately 10 % of RRTs.

29.2.2.1 Neurogenic Tumors

The main neurogenic tumors are mostly benign: solitary neurofibromas, schwannomas, and ganglioneuromas. Presacral plexiform neurofibromas can be part of the lesions observed in Recklinghausen type 1 disease. Malignant transformation is rare but can occur in 8–10 %. Surveillance with MRI is usually advised.

Schwannomas develop at the expense of the Schwann cells of the sacral nerve roots. They are rarely located in the presacrum. These are slow-growing tumors and are usually discovered fortuitously. Schwannomas are mainly solitary but can be part of neurofibromatosis type 1 in 5–15 %. Malignancy is rare. CT shows a well-demarcated oval or spherical mass with sharp contours in the presacral space. Cystic alterations or intratumoral calcifications are possible. A schwannoma can present as an extension through a foramen that seems enlarged. On MRI, the tumor is typically hypointense in T1, hyperintense in T2, and takes contrast. The signal may be heterogeneous in the case of a calcification or the presence of a cyst.

29.2.2.2 Bone Tumors

The most common bone tumors are benign giant-cell tumors characterized by hypervascularization and local aggressiveness. Malignant tumors include mainly sarcomas [19] and, especially in children, osteochondrosarcoma, chondrosarcoma, and Ewing sarcoma. Because of their relatively rapid growth, these tumors often reach a considerable size. The lungs are the preferential sites of metastasis.

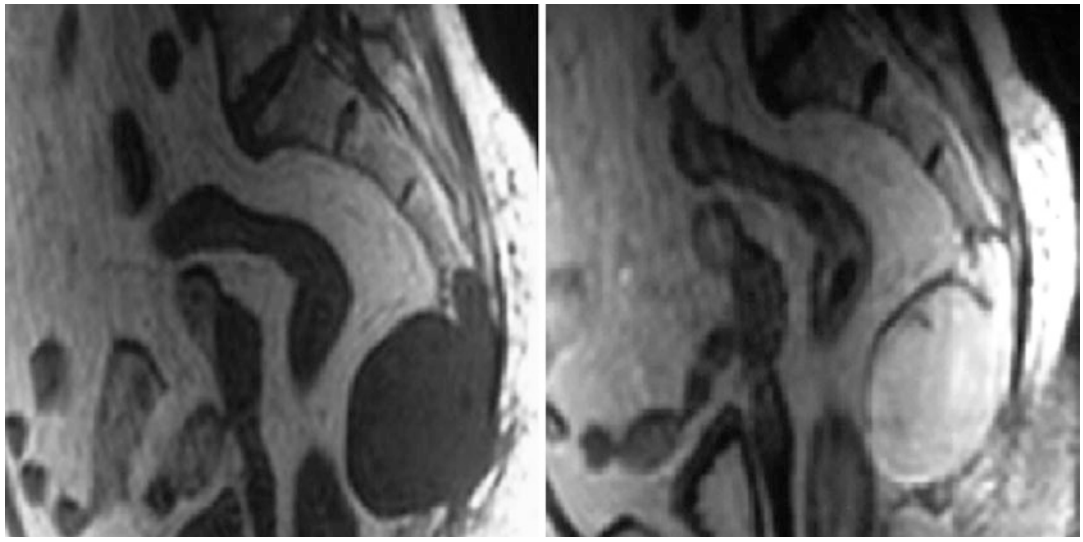


Fig. 29.3 Sacral chordoma on T1 and T2 sagittal sections on magnetic resonance imaging

29.2.3 Mixed Tumors

Gastrointestinal stromal tumors, liposarcomas, extraabdominal desmoid tumors, adenocarcinomas, fibrosarcomas, and hemangiomas represent various mixed tumors. Fibromatosis (desmoid tumor) is also part of this mixed-tumor classification. The natural history varies from spontaneous regression to aggressive growth. The treatment objective for these lesions is not to resect at all costs but to stabilize the lesion.

29.3 Diagnosis

The incidence of RRT is difficult to estimate because only small population a few articles with low numbers have been reported [2–5]. A general surgeon practicing outside a specialized center can expect to see just one RRT throughout his or her entire career. Table 29.2 summarizes the results of the main studies of RRTs.

29.3.1 Symptoms

Although the majority of RRTs are congenital, patients rarely have a family history of RRT (except for those with Currarino syndrome; see below). Asymptomatic for long time, RRTs are often discovered late, incidentally during a pelvic exam. Rectal examination can identify a retrorectal mass (97 % of lesions in a series from the Mayo Clinic [1]). They are more common among middle-aged woman (25–45 years). This sex difference might be explained by the gynecologic surveillance of women.

The most common symptom is pelvic pain [20], which is sometimes increased by sitting and relieved by standing up. The rapid appearance of symptoms favors malignant transformation [1]. An RRT may also be revealed by signs of compression of the adjacent organs (rectal fullness, constipation, tenesmus, dysuria, urinary frequency, urinary retention, dyspareunia) or nerve root (sciatic pain). Another common presentation is fistula (30 % cases) [2, 20], which may then lead to a diagnosis of anal fistula or pilonidal disease and results in iterative procedures. In cases of recurrent perianal abscesses, clinicians should suspect an RRT and request MRI. Some lesions are responsible for dystocia; this is one reason to recommend resection of all RRTs – even benign and asymptomatic ones – in young woman. These RRT cysts (anterior sacral meningocele, teratoma, tailgut or dermoid cyst, or a combination of these) are rarely part of Currarino syndrome (the association of an anorectal malformation or imperforate

Table 29.2 Results of the main studies of retrorectal tumors

Series, year	Study period	Participants, *n*	Malignant tumors, *n* (%)	Kraske procedure/ abdominal approach/Kraske and abdominal mixed	Morbidity, n (%)	Recurrence, %
Grandjean, 2008 [5]	1989–2005	30	0 (0)	23	6 (20)	7
Gao, 2011 [35]	2001–2009	36	6 (17)	26/8/2	8 (22)	11
Glasgow, 2005 [3]	1981–2003	34	8 (24)	11/14/9	5 (15)	24
Woodfield, 2007 [4]	1998–2006	27	7 (26)	12/11/4	4 (15)	11
Buchs, 2007 [28]	1994–2003	16	0 (0)	16/0/0	1 (6)	6
Localio, 1979	1964–1979	20	12 (60)	4/3/13	5 (25)	5
Westbrook, 1982 [29]	1972–1981	19	6 (32)	19/0/0	8 (42)	0
Chereau, 2013	1997–2011	47	9 (19)	42/3/2	4 (9)	6

anus, a sacral bone defect, and a presacral mass). A genetic mutation for this autosomal-dominant disorder, located on the *HLXB9* gene on chromosome 7q36, is found in 50 % of cases.

29.3.2 Radiology and Biopsy

Radiology has an important role in the diagnosis of RRTs, which are frequently found incidentally. CT usually shows a well-defined, unilocular or multilocular lesion dense with fluid, with thin walls, and no enhancement after contrast injection, allowing the diagnosis of a cyst. However, CT does not always distinguish between an RRT and a perirectal abscess (CT had 70 % accuracy in the series by Chéreau et al. [21]). MRI is the most efficient radiologic exam for the diagnosis of RRT, with a positive predictive value of 100 %. Compared with CT, MRI also provides more accurate preoperative assessment of the nature and morphology of a lesion.

- Yang et al. [22] conducted a retrospective study of 21 patients and proposed specific MRI criteria to distinguish benign and malignant tumors. Cystic benign tumors (14 patients) had the following characteristics: hypoT1, hyperT2 (sometimes hyperT1 if mucus is present), circumscribed, regular limits, uni- (dermoid or epidermoid lesions) or multi-locular (hamartomas). Malignant tumors (seven patients) were solid small lesions with a heterogeneous or hyper signal in T2, and irregular boundaries invading adjacent structures with contrast enhancement after gadolinium injection.

These data were confirmed by Chéreau et al. [21; a high density (solid), irregular contours, a heterogeneous signal extending above S3, contrast enhancement after gadolinium injection, and invasion of adjacent structures were also associated with malignancy.

Proctoscopy highlights the extrinsic compression of the posterior wall of the rectum but has little value in the diagnosis of RRT. However, it is useful to rule out rectal mucosal involvement or communication of the lesion with the rectal lumen, as occurs in rectal duplication. A fistula with a cyst may be seen on proctoscopy, but CT will give the most valuable information in such cases. Echo-endoscopy can provide a histological orientation (fluid or solid content) and clarify the relationship of the lesion with the rectum.

The role of preoperative biopsy is controversial. Although some investigators reported no complications following biopsy, recent studies suggest that the risk of a disseminating malignant lesion and of infection results in a significant increase in morbidity after resection [1]. In cases of meningocele, biopsy can lead to life-threatening meningitis. Biopsies should be performed only if the lesions seem to be unresectable and have a potential pathological diagnosis that requires consideration of radiotherapy or chemotherapy.

Apart from this indication, performing a biopsy on RRT is not recommended [20].

29.4 Treatment

With the risk of chronic pain, bleeding, infection, compression of adjacent organs, and especially the risk of malignant transformation, the current consensus is to propose complete surgical excision of all RRTs. A multidisciplinary team (colorectal surgeon, orthopedic surgeon, plastic surgeon, neurosurgeon, radiologist, oncologist, and radiation oncologist) should evaluate and treat large tumors with local invasion.

29.4.1 Surgical treatment

Since the Mayo Clinic report [1], treatment has been based on complete surgical excision of any RRT to avoid the risk of complications and recurrence. However, this is an unusual surgery, with specific risks because of anatomic relationships, the risk of rectal bleeding (presacral veins), and sometimes the risk of mutilation when a large excision is required for malignant tumors. An R0 resection with negative resection margins is the primary goal. This may require multivisceral en-bloc resection when malignancy is suspected.

A surgical approach should be planned based on preoperative imaging. Two approaches are possible: posterior or anterior. The choice is determined by the size and position of the tumor, its morphology, and signs of possible malignancy (invasion of the sacrum or adjacent organs) [23–30].

- Indications for the posterior (transsacral) approach (Kraske procedure) [27–30] are limited to RRTs in the lower part of the presacral space, below S2 (Fig. 29.4).
- The abdominal approach is reserved for high tumors or if an invasion of the rectum or adjacent organs is suspected [30]. Woodfield et al. [4] proposed an algorithm for a surgical approach based on the position and size of the tumor, its neoplastic nature, and invasion of adjacent structures, all of which are determined by preoperative MRI. In their series of 27 patients, 11 lesions located at or below S3 without local invasion required only a perineal incision. When the lesion was larger than 10 cm or difficult to access, an S4–S5 coccygectomy was performed. An abdominal approach was used for lesions above the S3 or with adjacent organ invasion. In cases of invasion of the sacrum, a combined approach was preferred. However, Chéreau et al. [21] reported total resection of lesions above the S3 using the Kraske procedure in five patients. Thus an upper limit of the tumor above S3 does not seem to be an absolute contraindication for a Kraske incision. An abdominal approach is reserved for high lesions and malignancies, for which a wider excision seems necessary.

The Kraske procedure allows better exposure of the tumor, if necessary, with a coccyx resection. Complete excision of cysts is associated with less risk of tumor rupture [21]. Specific postoperative morbidities after a Kraske procedure include [29, 30] pain when sitting (in relation to a sacral osteitis) (5–10 %) [21], especially after resection of a large malignant tumor, anal or urinary incontinence (lesions of the ventral roots of the third and fourth sacral nerves), and abscess (4.8 %) [21]. The risk of recurrence varies greatly depending on the study and the histology of the lesion (2.6 % are benign and 22.2 % are malignant [21]), with overall survival close to 100 %; however, adequate resection margins are essential [21, 33]. This observation reinforces the need for optimal surgical technique and wide excision. Several authors recommend a systematic coccygectomy [32], but increased risk of recurrence in the absence of coccygectomy has not been demonstrated, and most authors consider a lack of adhesion of the tumor to the coccyx requires consideration of resection without excision of the coccyx [21, 31]. Moreover, it should be noted that coccygectomy is not associated with a higher risk of postoperative pain [21].

The contribution of laparoscopy [23–26] to the removal of an RRT, particularly to reduce postoperative pain, deserves to be studied in large series. However, the risks of tumor rupture and

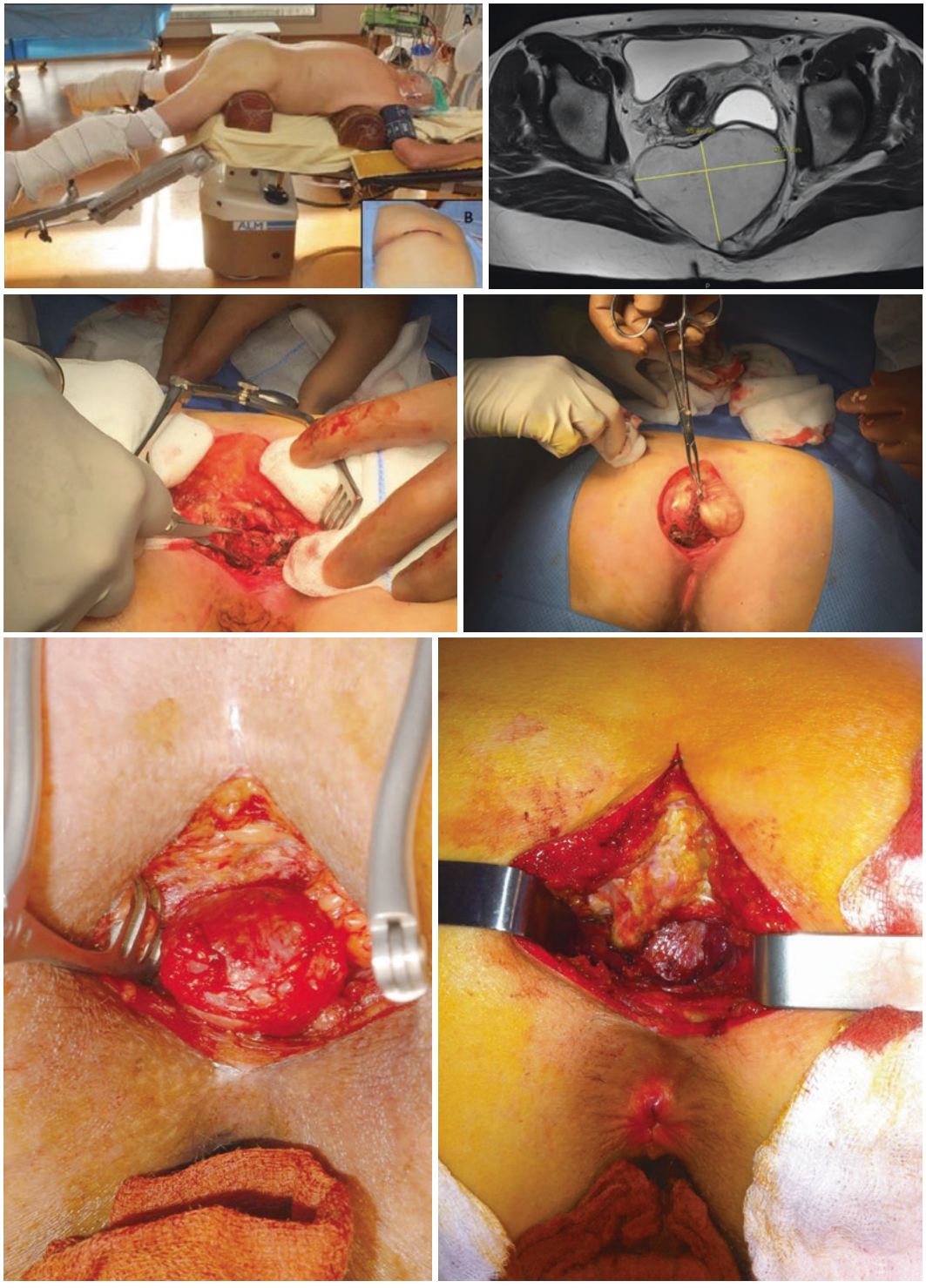


Fig. 29.4 Posterior approach. (**a**) Position. (**b**) Coccygectomy. (**c**) Rectal dissection

incomplete resection, especially for large tumors or tumors low in the presacral space, can increase the risk of recurrence. Similarly, the intimate contact of an RRT with the posterior wall of the rectum increases the risk of rectal perforation. Duclos et al. [34] recently reported a series of 12 patients undergoing laparoscopic resection (including two malignant tumors) with low morbidity, with two conversions and one ileostomy performed for rectal perforations.

29.4.2 Chemotherapy and Radiotherapy

Some larger solid tumors, such as sarcomas, are at high risk of metastatic disease, and neoadjuvant chemotherapy is indicated. Approximately 33 % of patients respond with reduced tumor volume, facilitating more conservative surgery [8].

Postoperative irradiation may be considered to reduce the incidence of local recurrence after sarcoma resection [8]. If the initial surgery was macroscopically incomplete, extended resection (most often associated with anterior resection) can be discussed before irradiation. Similarly, postoperative radiotherapy reduces the risk of local recurrence for chordoma. In the case of a retrorectal gastrointestinal stromal tumor near the sphincter, neoadjuvant initamib treatment can be discussed.

29.5 Prognosis

Overall survival for a benign RRT is close to 100 % in most studies. Recurrence and malignant transformation are possible, requiring a long follow-up, particularly for multilocular cysts. The Mayo Clinic study [1] estimated the risk of recurrence at 15 % after a follow-up of 10 years. One recurrence (2.6 %) after excision of a developmental cyst was seen by Chéreau et al. [21] after 71 months (range, 2–168 months) of follow-up; this occurred after four recurrences (11 %) in the study by Hjermstad et al. [2] and in 7 % in the study by Grandjean et al. [5].

The risk of local recurrence for malignant tumors reached 50 % in some studies [15], with a disease-free survival of 17 % at 5 years. Two malignant lesions recurred (22 %) at 3 and 9 months and were treated by chemotherapy in the study by Chéreau et al. [21]. Chordomas are among the most aggressive tumors. About a third of patients develop distant metastases. Early studies reported a 10-year survival of less than 20 % and a 96 % risk of recurrence [16].

With advances in the diagnosis and therapeutic management of RRTs, including a more aggressive surgical strategy (bloc resection, coccygectomy), the prognosis for patients with chordomas has improved significantly. Bergh et al. [17] reported a series of 39 patients, a survival rate of 84 % at 10 years and a recurrence rate of 44 %. The largest study to date, involving 400 chordomas [18], found a 5-year survival of 67 % and a 10-year survival of 40 %.

References

1. Jao SW, Beart RW, Spencer RJ, Reiman HM, Ilstrup DM. Retrorectal tumors: Mayo clinic experience, 1960–1979. Dis Colon Rectum. 1985;28:644–52.
2. Hjermstad BM, Helwig EB. Tailgut cysts. Report of 53 cases. Am J Clin Pathol. 1988;89(2):139–47.
3. Glasgow SC, Birnbaum EH, Lowney JK, Fleshman JW, Kodner IJ, Mutch DG, Lewin S, Mutch MG, Dietz DW. Retrorectal tumors: a diagnostic and therapeutic challenge. Dis Colon Rectum. 2005;48:1581–7.
4. Woodfield JC, Chalmers AG, Phillips N, Sagar PM. Algorithms for the surgical management of retrorectal tumours. Br J Surg. 2008;95:214–21.
5. Grandjean JP, Mantion GA, Guinier D, Henry L, Cherki S, Passebois L, Chalabreysse P, Viennet G, Pujol B, Chabanon J. Vestigial retrorectal cystic tumors in adults: a review of 30 cases. Gastroenterol Clin Biol. 2008;3:769–78.
6. Middeldorf K. Zur Kenntnis der angeborden Sacralgeschwulste. Virchow's Arch Pathol Anat. 1885;101:37–44.
7. Uhlig BE, Johnson RL. Presacral tumors and cysts in adults. Dis Colon Rectum. 1975;18:581–96.
8. Dozois EJ, Jacofsky DJ, Dozois RR. Presacral tumors. In: Wolff BG, Fleshman JW, Beck DE, et al., editors. The ASCRS textbook of colon and rectal surgery. New York: Springer; 2007. p. 501–14.
9. Malafosse M, Gallot D, Douvin D, Herve de Sigalony JP. Kystes et tumeurs péri-ano-rectaux d'origine vestigiale chez l'adulte. J Chir (Paris). 1977;113:351–60.
10. Barthod F, De Sigalony JPH, Parc R. Les formations kystiques rétrorectales de l'adulte. Ann Chir. 1996;50:906–12.

11. Dahan H, Arrivé L, Wendum D, Docou le Pointe H, Djouhri H, Tubiana JM. Retrorectal developmental cysts in adults: clinical and radiologic-histopathologic review, differential diagnosis, and treatment. Radiographics. 2001;21:575–84.
12. Chêne G, Voitellier M. Tératome bénin mature présacré et formations kystiques vestigiales rétro-rectales chez l'adulte. J Chir. 2006;143:5.
13. Head HD, Gertein JD, Muir RW. Presacral teratoma in the adult. Am Surg. 1975;41:240–8.
14. Glasgow SC, Dietz DW. Retrorectal tumors. Clin Colon Rectal Surg. 2006;19:61–8.
15. Cody HS, Marcove RC, Quan SH. Malignant retrorectal tumors: 28 years' experience at Memorial Sloan-Kettering Cancer Center. Dis Colon Rectum. 1981;24:501–6.
16. Gray SW, Singhabhandhu B, Smith RA, Skandalakis JE. Sacrococcygeal chordoma: report of a case and review of the literature. Surgery. 1975;78:573–82.
17. Bergh P, Kindblom LG, Gunterberg B, Remotti F, Ryd W, Meis-Kindblom JM. Prognostic factors in chordoma of the sacrum and mobile spine: a study of 39 patients. Cancer. 2000;88:2122–34.
18. McMaster ML, Goldstein AM, Bromley CM, Ishibe N, Parry DM. Chordoma: incidence and survival patterns in the United States, 1973–1995. Cancer Causes Control. 2001;12:1–11.
19. Dozois EJ, Jacofsky DJ, Billings BJ, Privitera A, Cima RR, Rose PS, Sim FH, Okuno SH, Haddock MG, Harmsen WS, Inwards CY, Larson DW. Surgical approach and oncologic outcomes following multidisciplinary management of retrorectal sarcomas. Ann Surg Oncol. 2011;18:893–8.
20. Hobson KG, Ghaemmaghami V, Roe JP, Goodnight JE, Khatri VP. Tumors of the retrorectal space. Dis Colon Rectum. 2005;48:1964–74.
21. Chéreau N, Lefevre JH, Meurette G, Mourra N, Shields C, Parc Y, Tiret E. Surgical resection of retrorectal tumours in adults: long-term results in 47 patients. Colorectal Dis. 2013;15:476–82.
22. Yang BL, Gu YF, Shao WJ, Chen HJ, Sun GD, Jin HY, Zhu X. Retrorectal tumors in adults: magnetic resonance imaging findings. World J Gastroenterol. 2010;16:5822–9.
23. Bax NM, Van der Zee DC. The laparoscopic approach to sacrococcygeal teratomas. Surg Endosc. 2004;18:128–30.
24. Konstandinis K, Theodoropoulos GE, Sambalis G, Georgiou M, Vorias M, Anastassakou K, Mpontozoglou N. Laparoscopic resection of prescacral schwannomas. Surg Laparosc Endosc Percutan Tech. 2005;15:302–4.
25. Murdock J, Abbou MA. Laparoscopic abdominoparacoccygeal resection of anorectal cystic teratoma. JSLS. 2010;14:583–6.
26. Gunkova P, Martinek L. Laparoscopic approach to retrorectal cyst. World J Gastroenterol. 2008;14:6581–3.
27. Kraske P. Zur extirpation hochsizenden mastdarmkrebs verhandle deutsch gesellsch. Verh Otsch Gs Chir. 1885;14:464–74.
28. Buchs N, Taylor S, Roche B. The posterior approach for low retrorectal tumors in adults. Int J Colorectal Dis. 2007;22:381–5.
29. Westbrook KC, Lang NP, Broadwater JR, Thompson BW. Posterior surgical approaches to the rectum. Ann Surg. 1982;195:677–85.
30. Abel ME, Nelson R, Prasad ML, Pearl RK, Orsay CP, Abcarian H. Parasacrococcygeal approach for the resection of retrorectal developmental cysts. Dis Colon Rectum. 1985;28:855–8.
31. Bohm B, Milsom JW, Fazio VW, Lavery IC, Church JM, Oakley JR. Our approach to the management of congenital presacral tumors in adults. Int J Colorectal Dis. 1993;8:134–8.
32. Wolpert A, Beer-Gabel M, Lifschitz O, Zbar AP. The management of retrorectal tumors in the adult. Tech Coloproctol. 2002;6:43–9.
33. Mathis KL, Dozois EJ, Grewal MS, Metzger P, Larson DW, Devine RM. Malignant risk and surgical outcomes of presacral tailgut cysts. Br J Surg. 2010;97:575–9.
34. Duclos J, Maggiori L, Zappa M, Ferron M, Panis Y. Laparoscopic resection of retrorectal tumors: a feasibility study in 12 consecutive patients. Surg Endosc. 2014;28:1223–9.
35. Gao, Xian H, ZHANG, W, FU, Chuan G, et al. Local recurrence after intended curative excision of presacral lesions: causes and preventions. World Journal of Surgery. 2011;35(9):2134–42.

Stomas and Stomatherapy

30

Harald R. Rosen

30.1 Introduction

Fecal diversion by constructing a stoma is a common procedure in colorectal surgery. While a permanent stoma as a treatment for rectal cancer has decreased markedly since the introduction of sphincter-saving techniques, a variety of indications still lead to the construction of intestinal stomas. While the first historical reports about the treatment of penetrating abdominal injuries date back to the thirteenth century, the eighteenth and nineteenth centuries saw a change from mere exteriorizations of intestinal lacerations to elective formations of ileostomies, cecostomies, and left inguinal colostomies for large bowel obstructions [1]. Following the next "milestone" of a rod introduced by Maydl, which led to the creation of the loop colostomy in 1884, it took more than 60 years until mucocutaneous sutures and the immediate opening of a stoma were accepted as the method of choice [11]. At the same time, Koernig, a German student studying chemistry and suffering from the side effects of an ileostomy performed because of ulcerative colitis, developed a bag made of rubber and fixed to the skin with a latex preparation, thus leading to the emergence of modern stoma appliances. While the principle of the "Koernig bag" remained a standard for many years, more effective sealing materials – first karaya gum and later Stomahesive and similar hydrocolloids – have led to the present state of the art of stoma appliances.

H.R. Rosen, MD, FEBSQ
Chair of Surgical Oncology, Sigmund Freud Medical School, Freudplatz 1, 1020 Vienna, Austria
e-mail: rosensurg@csi.com

30.2 Definitions and Indications

Stomas may be *permanent* or *temporary* and can be created either as a *loop*, *double barrel*, or *end stoma* using a part of the small (*ileostomy*) or large (*colostomy*) bowel.

30.2.1 Indications for a Permanent Stoma

- Abdominoperineal excision of the rectum for rectal cancer, recurrent anal cancer, or severe inflammatory bowel disease of the anorectum
- Untreatable persistent fecal incontinence

30.2.2 Indications for a Temporary Stoma

Contrary to previous applications, when a temporary stoma was used as the first step of treatment in emergency situations (colonic obstruction, acute diverticulitis, fulminant ulcerative colitis), most patients today will be treated

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_30

by definitive surgical resection immediately [12, 13]. Therefore, forming a temporary stoma as a sole procedure should be reserved only for those few patients with a massive obstruction and in such a general condition that they cannot tolerate a resection.

Formation of a temporary stoma is limited to those patients in whom either a *primary anastomosis* might be *not desirable* (Hartmann procedure, double-barrel stoma following resection in selected patients) or in whom it would serve as a so-called *protective or covering stoma*. However, stoma reversion should be feasible within an acceptable time period [2].

- Protection of low rectal or anal anastomoses
- Need to delay primary anastomoses until a later time (Hartmann procedure, double-barrel stoma)
- Complicated perianal and/or rectal fistula
- Penetrating colorectal injuries
- Extensive trauma to the pelvic floor
- Congenital malformations (anal atresia)

30.2.2.1 Efficacy of a Protective Stoma

There is controversy regarding the *efficacy of a protective stoma* today. Experimental and clinical data show evidence that the fecal stream has an important beneficial effect on anastomotic healing, leading to a higher anastomotic strength and increased collagen synthesis [6]. It is widely accepted that loop stomas in particular do not result in a complete fecal exclusion of the bowel, which should be covered; therefore the use of a temporary stoma for protective purposes is being questioned. Furthermore, recent data show the safety of elective colorectal surgery, even without bowel preparation, with the introduction of early feeding and activation of peristalsis [14, 15].

In contrast to these observations, low rectal anastomoses are regarded as being at higher risk for leakage. Data from randomized trials suggest that although covering stomas do not influence the insufficiency rate, serious life-threatening infections might be prevented [2, 4, 8].

However, it must be taken into account that in large series only two-thirds of all temporary stomas were closed, whereas more than 30 % of all patients kept their stoma permanently (e.g., because of the underlying primary disease, old age, a poor general condition) or died before closure [2]. In addition, closure of a stoma is not a procedure devoid of problems; the complication rate ranges form 16 to 35 %, with a mortality of 0–4 % [16, 21]. The most common complications are wound infections, fistulas, and incisional hernia; bowel obstruction and peritonitis have also been observed.

In general defunctioning, although the role of stomas in preventing anastomotic dehiscence is still controversial, they are regarded as being able to reduce the clinical consequences following anastomotic leakage (sepsis, peritonitis) [17, 18].

30.2.2.2 Loop Ileostomy or Loop Colostomy?

In the 1980s many surgeons started to favor loop ileostomies to avoid problems associated with colostomies (i.e., higher incidence of parastomal hernias and/or stoma prolapse, incisional hernias following stoma closure, easier application of appliances with ileostomies). While some controlled studies with a limited number of patients showed evidence of a lower complication rate associated with the formation and subsequent closure of ileostomies (lower rates of infections and incisional hernias) [3], other data show a decrease in the number of obstruction problems following reversal of colostomies [7]. Furthermore, it must be emphasized that for the mere decompression of an obstructing process in the colon or rectum, an ileostomy (if the ileocecal valve is still competent) can sometimes be insufficient. However, construction of a transverse loop colostomy or loop sigmoidostomy is technically so difficult – especially in obese patients – that an ileostomy is preferable.

The choice of the type of loop stoma is therefore influenced by individual patient factors: anatomy, weight and size, indication(s) for the formation of a loop stoma, and time until stoma closure [8, 19].

30.3 Stoma Construction

30.3.1 Stoma Site and Preoperative Counseling

The optimal location for a stoma is a prerequisite for satisfying function and an acceptable application of stoma appliances. The site depends on the anatomic position and type of stoma, scars, and the patient's build and dressing habits.

Anatomic sites of stomas (present surgical standard):

Ileostomy: over the right rectus muscle, halfway between the umbilicus and the anterior superior iliac spine, lying just below the midline and well away from the symphysis pubis and costal margin. If the right side is not accessible (e.g., scars after previous operations), a trephine can be performed in the left rectus muscle.

Transverse colostomy: usually brought through the rectus muscle just right of the midline, well above the umbilicus but a safe distance from the costal margin.

Sigmoidostomy: Through the left rectus muscle away from the inguinal ligament, midway between the umbilicus and the anterior superior iliac spine.

In elective stoma formation (or even when there is a possibility for the need of a stoma), it is mandatory to define the site preoperatively using ink and a stoma bag.

The optimal position should be marked while the patient is sitting and standing, and with regard to the patient's usual clothing. A specialized stoma therapist should counsel the patient and the surgeon during this step to achieve an optimal position.

Preoperative counseling by a stoma therapist who also follows the patient postoperatively and after hospital discharge is mandatory to reduce the negative effects of a stoma on quality of life (QOL). This includes introducing stoma appliances, irrigation sets (if applicable), and dietary recommendations to the patient and his/her relatives as well as communicating with the patient, the family doctor, and the surgeon during follow-up. Organized "patient stoma groups" are also available in some countries and have been proven to be beneficial to allay patients' concerns and fears preoperatively and to reduce postoperative problems, especially with regard to health care providers (e.g., insurance problems).

30.3.2 Surgical Techniques

30.3.2.1 Conventional (Open) Surgery

- Insert a straight trephine through the abdominal wall (dimensions: one thumb for an end stoma, two fingers for a loop stoma).
- Excise a cylinder of subcutaneous fat together with skin.
- Divide the rectus sheath and the rectus muscle (parallel to the muscle fibers). For colostomies, a cruciate incision of the rectus sheath may be advisable to create sufficient space for the sometimes bulky bowel. Avoid pulling the stoma lateral of the rectus muscle (increased risk of parastomal hernia).
- Divide the posterior rectus sheath and the peritoneum.
- Dissect the ileum as close as possible to the ileocecal valve for an end ileostomy (avoids a large volume of secretions)
- Mobilize the stoma and its mesentery (vascular supply) through the abdominal wall without any tension.
- Close the lateral gutter with sutures between the bowel wall, mesentery, and lateral peritoneum to prevent the formation of an inner hernia (however, this is not uniformly accepted practice).
- Fixate the stoma with absorbable mucocutaneous sutures and with a rod for loop stomas (all sutures – even if absorbable – must be removed after a period of 7–10 days to avoid an inflammatory peristomal reaction as well as the formation of granulomas). Stoma rods in loop stomas can lead to pressure ulcers and/or necrosis of the posterior wall, especially in

obese patients. In this context, the placement of a subcutaneous 16 or 18 F suction drain with the points of entry and exit just beyond the circumference of the flange seems to be an interesting approach. Using this easy method, the stoma flange can be applied immediately after the operation, thus preventing skin problems during the early postoperative period [20].

30.3.2.2 Laparoscopic Surgery

Laparoscopic stoma formation might be indicated either as part of a laparoscopically performed colorectal resection or (in rare cases) as a therapy on its own [5]. (The Hartmann procedure can be used for complicated fistula disease, fecal exclusion for severe pelvic soft-tissue infections, and palliative treatment for malignant colorectal obstructions). If indicated, however, laparoscopically constructed stomas have been shown to be beneficial with regard to a short hospital stay an easier reversion of the stoma (if possible).

- A pneumoperitoneum can be created either by a conventional technique (Veress needle) or by preparing the trephine for an "open" approach.,
- Trocars are placed for laparoscopic colorectal surgery (usually three 10- to 12-mm trocars or the single-indication laparoscopic technique)
- Ileostomies can be easily produced after identifying the terminal ileum by grabbing the bowel with an atraumatic Babcock clamp and pulling it through the abdominal wall while the trocar is retracted. Special caution must be used to ensure the trocar channel is sufficiently wide for a loop ileostomy as there is a risk of stenosis.
- Colostomies need more surgical preparation in terms of either mobilization and/or dissection of the mesocolon to achieve stoma formation without tension.
- The Hartmann procedure requires the additional use of a laparoscopic stapling device to close the rectal stump.

30.4 "Continent" Stomas

There has been no discussion that a stoma will lead to a significant impairment of QOL, and various studies have shown its negative impact on the different domains of daily life [9, 10]. Depending on individual factors (social status, geographic origin, religion, lack of stoma therapists), this can lead to a complete deterioration of a patient's QOL. Therefore there have been continuous efforts to create stomas in which the evacuation of the bowel content can be voluntarily controlled by the patient; however, only those that have gained some prominence in the literature and in routine practice are mentioned here.

30.4.1 Stoma Irrigation

While irrigation of a colostomy has been controversial among patients in the past, introduction of an easy-to-handle device has led to the increased popularity of this method in some countries. The great advantage of irrigation is that bulky appliances are not needed (the stoma is simply covered by a cap), and it enhances the patient's body image, leading to an improvement in QOL. It does, however, require a certain level of intelligence, toilet facility, and stoma design, as well as a certain training period with the assistance of a specialized stoma therapists. Therefore the acceptance of this effective method of bowel control varies among European countries.

30.4.2 Colostomy Plug

A recently developed two-piece occlusive device is supposed to be able to occlude a stoma sufficiently and even absorb flatus. After initial enthusiastic reports, this method has been accepted mainly by patients who undergo irrigations achieve control of flatus (in more than 90 %).

30.4.3 Total Anorectal Reconstruction

The construction of a perineal colostomy ("neoanus") is a possibility [9], especially for patients whose body image ("abdomen without a bag") is of the utmost importance. Various procedures have been described in the literature, including a simple stoma implanted into the perineum, the construction of a colonic conduit, and the formation of a muscle wrap ("neosphincter") around the perineal colostomy using skeletal muscles (the gracilis or gluteus muscle). To achieve acceptable continence, these muscles have also been stimulated by an implanted neuromuscular stimulation system connected to a subcutaneous implanted pulse generator (dynamic graciloplasty). Because the major problem in patients following total anorectal reconstruction was the problem of voluntarily emptying their neorectum, almost all patients have to undergo regular irrigations, either retrograde via the perineal colostomy or antegrade via an appendicostomy or a colonic conduit (Malone procedure). Despite these and other problems (soiling, need for a pad), patients with a functioning total anorectal reconstruction report a high degree of satisfaction and a marked improvement of their QOL.

30.4.4 Kock Ileostomy

In most patients surgical therapy aims to preserve the anal canal, thus leaving the possibility for reconstruction by ileal pouch anal anastomosis. Still, some patients have to undergo the formation of a permanent ileostomy. For these, the Kock ileostomy provides the possibility to overcome many of the problems associated with a permanent ileostomy. However, the construction is a technically demanding operation; revision rates for valve slippage range from 7 % to 25 %, and serious complications such as obstruction, sepsis, and fistula have been reported. Although QOL (especially in young patients) is significantly improved by a functioning Kock stoma, metabolic problems, valve slippage, and inflammation of the pouch are potential problems with this method.

30.5 Stoma Complications

30.5.1 Early Complications

30.5.1.1 Stoma Necrosis

Stoma necrosis is usually caused by an impaired vascular supply due to technical problems during stoma formation or high tension and occurs within the first days following surgery. It must be distinguished from superficial focal necrotic areas around some mucocutaneous sutures in the mucosa of the stoma, which have no clinical significance. However, total wall necrosis of a stoma is a major problem because it can lead to retraction of the bowel wall into the abdominal wall or even into the peritoneum. Early diagnosis and the formation of a new, well-vascularized stoma are the only therapeutic options.

30.5.2 Late Complications

30.5.2.1 Skin Excoriation and Infection

Skin excoriation is associated with liquid stomal effluent and/or badly fitting appliances (sometimes as a result of a bad stoma site). Patients with skin problems should be managed by cutting the wafer as close as possible to the circumference of the stoma in order to avoid any contact of the skin with bowel content. Sometimes it is also necessary to selectively fill existing skin depressions with the wafer, thus preventing leakage.

A peristomal skin infection must be managed depending on the extent of the problem: local antibiotic ointments, local drainage, resitting the stoma, or forming a more proximal "covering" stoma.

30.5.2.2 Stenosis

Stenosis rarely responds to dilatation. Refashioning is the only solution over the long term.

30.5.2.3 Parastomal Hernia

A wide trephine to achieve a loop colostomy (especially in obese patients), obesity, and/or an increase in intra-abdominal pressure; a stoma site lateral to the rectus muscle; and delaying stoma closure in temporary loop stomas are the common reasons why parastomal hernias develop. In temporary stomas, stoma closure should be achieved as the most effective therapy. In permanent stomas, parastomal hernias must be treated if appliances do not fit appropriately anymore or if obstruction problems arise. The most successful strategy is resitting the stoma on the contralateral abdominal side; however, local repair might be indicated in patients who are not candidates for a laparotomy or in whom the contralateral side is not appropriate for stoma placement (scars, infection). Direct repair of the abdominal wall defect as well as mesh repair have been reported, with varying results. Recent reports suggest the use of a reinforcing mesh during the formation of a permanent stoma to reduce the rate of parastomal hernia [22, 23].

30.5.2.4 Prolapse

The etiology of prolapse is not completely understood, but it is thought to occur mainly in patients in whom the bowel was significantly dilated during stoma formation (e.g., because of obstruction). After reducing the bowel size, a defect remains in the abdominal wall, which allows the stoma to slip. While manual reposition might be necessary in the acute situation, definitive surgical treatment is indicated in most patients over the long term. Local reduction of the prolapsed bowel (amputation, colopexy) should be reserved only for unfit patients or those willing to undergo new stoma formation, for whom the long-term results are unsatisfying.

30.5.2.5 Ileostomy Flux

Ileostomy flux is characterized by water/fluid discharge of a total volume more than 1.5 L in 24 h and requires repeated emptying of the stoma bag to avoid leakage. The etiology of ileostomy flux can be a too-proximal small-bowel stoma (jejunostomy), short bowel syndrome, intra-abdominal sepsis, gastroenteritis, intestinal obstruction, or– in many patients – completely unknown. Since this complication can quickly become life-threatening because of dehydration and insufficient absorption of necessary medications, early admission and intravenous fluid replacement are recommended. Oral intake of water, sweet drinks, and salt aggravates secretion, and therefore the consumption of isotonic electrolyte drinks up to a total volume of 1L/day is recommended. In addition, drugs such as codeine and somatostatin analogues are helpful in special situations.

References

1. Hardy KJ. Evolution of the stoma. Aust N Z J Surg. 1989;59:71–7.
2. Kairaluoma M, Rissanen H, Kultti V, Mecklin JP, Kellokumpo I. Outcome of temporary stomas. Dig Surg. 2002;19:45.
3. Gooszen AW, Geelkerken RH, Hermans J, et al. Temporary decompression after colorectal surgery: randomized comparison of loop ileostomy and loop colostomy. Br J Surg. 1998;85:76–9.
4. Pakkastie TE, Ovaska JT, Pekkala ES, et al. A randomised study of colostomies in low colorectal anastomoses. Eur J Surg. 1997;163:929–33.
5. Oliveira L. Laparoscopic stoma creation and closure. Sem Laparosc Surg. 2003;10:191–6.
6. Uden P, Blomquist P, Jiborn H, et al. Influence of proximal colostomy on healing of a left colon anastomosis: an experimental study in the rat. Br J Surg. 1988;75:325–30.
7. Williams NS, Nasmyth DG, Jones D. Defunctioning stomas: a prospective controlled trial comparing loop ileostomy with loop transverse colostomy. Br J Surg. 1986;73:566–72.
8. Rosen HR, Schiessel R. Das Deviationsstoma. Chirurg. 1999;70:650–5.
9. Lasser P, Dube P, Guillot JM, Elias D. Pseudocontinent perineal colostomy following abdominoperineal resection: technique and findings in 49 patients. Eur J Surg Oncol. 2001;27:49–53.
10. Sprangers MAG, Taal BG, Aaaronson NK, et al. Quality of life in colorectal cancer: stoma vs nonstoma patients. Dis Colon Rectum. 1995;38:360–9.
11. Patey DH. Primary epithelial apposition in colostomy. Proc R Soc Med. 1951;44:423–9.

12. Gonzales R, Falimirski M, Holevar M. Further evaluation of colostomy in penetrating colon injury. Am Surg. 2000;66:342–6.
13. Deen K, Madoff R, Goldberg S, et al. Surgical management of left colonic obstruction: the University of Minnesota experience. J Am Coll Surg. 1998;187:573–6.
14. Miettinen R, Laitinen S, Makela J. Bowel preparation with oral polyethylene glycol electrolyte solution vs. no preparation in elective open colorectal surgery. Prospective, randomised study. Dis Colon Rectum. 2000;43:669–75.
15. Kehlet H, Willmore DW. Fast-track surgery. Br J Surg. 2005;92:3–4.
16. Livingstone DH, Miller FB, Richardson JD. Are the risks after colostomy closure exaggerated? Am J Surg. 1989;158:17–20.
17. Hüser N, Michalski CW, Erkan M, Schuster T, et al. Systematic review and meta-analysis of the role of defunctioning stoma in low rectal cancer surgery. Ann Surg. 2008;248:52–60.
18. Chude CG, Rayate NV, Patris V, et al. Defunctioning loop ileostomy with low anterior resection for distal rectal cancer: should we make an ileostomy as a routine procedure? A prospective randomized study. Hepatogastroenterology. 2008;55:1562–7.
19. Güenaga KF, Lustosa SA, Saad SS, et al. Ileostomy or colostomy for temporary decompression of colorectal anastomosis. Cochrane Database Syst Rev. 2007;24:1.
20. Harish K. The loop stoma bridge – a new technique. J Gastrointest Surg. 2008;12:958–61.
21. Boman-Sandelin K, Fenyo G. Construction and closure of the transverse loop colostomy. Br J Surg. 1985;69:19–22.
22. Fleshman JW, Beck DE, Hyman N, Wexner SD, Bauer J, George V, PRISM Study Group. A prospective, multicenter, randomized, controlled study of non-cross-linked porcine acellular dermal matrix fascial sublay for parastomal reinforcement in patients undergoing surgery for permanent abdominal wall ostomies. Dis Colon Rectum. 2014;57(5):623–31.
23. Gardner B. Mesh prophylaxis to prevent parastomal hernia. J Am Coll Surg. 2014;218:1083–4.

31 Endoscopy: Diagnostics, Therapeutics, Surveillance, New Techniques

Søren Meisner and Evangelos Kalaitzakis

31.1 Introduction

Endoscopy means "to look inside" and refers to an examination of the interior of a canal or hollow organ by means of an endoscope using a light delivery system to illuminate the organ under inspection. The light source is outside the body and the light is directed via a fiber optic system. Then, the image is transmitted through a lens system and in flexible systems through a fiberscope to the viewer. a camera at the distal end of the optical system was recently developed to project findings onto a monitor or screen. Therapeutic endoscopes have an additional channel to allow the entry of instruments used for biopsy or therapy.

Flexible endoscopy of the colon and rectum was introduced in 1963. The procedure is a primary diagnostic and therapeutic tool for the evaluation and treatment of colorectal diseases.

Endoscopy of the colon and rectum has become a discipline with an infrastructure built upon many areas of medicine, including internal medicine, general practice, gastroenterology, surgery, pathology, radiology, and pediatrics.

S. Meisner, MD (✉) • E. Kalaitzakis, MD, PhD
Endoscopy Unit, Digestive Disease Center,
Bispebjerg Hospital, University of Copenhagen,
Bispebjerg Bakke 23, Entr. 7 J, 2400 Copenhagen,
Denmark
e-mail: soeren.Meisner@regionh.dk;
kalvag@hotmail.com

31.2 Diagnostic Endoscopy of the Colon and Rectum

31.2.1 Sigmoidoscopy

Sigmoidoscopy is the direct examination of the rectum, sigmoid colon, and descending colon (≤70 cm) using a flexible fiber optic endoscope [1–3].

31.2.1.1 Indications

Common indications include:

- Screening for colorectal cancer
- Evaluation of patients with lower gastrointestinal (GI) bleeding
- Evaluation of suspected lower GI pathology
- Evaluation of suspected inflammatory disease of the colon and rectum
- Decompression of sigmoid volvulus
- Cancer surveillance after surgical resection/endoscopic resection (to rule out local intraluminal recurrence)

31.2.1.2 Contraindications

Few absolute contraindications exist. Sigmoidoscopy should be avoided in high-risk situations, including

- Severe diverticulitis (unless carcinoma is highly suspected)
- Acute peritonitis
- Toxic megacolon/toxic colitis

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_31

- Severe cardiopulmonary disease (acute or recent myocardial infarction)
- Signs of intestinal perforation
- Massive GI bleeding (in an unstable patient)
- Severe coagulopathy

Sigmoidoscopy is also not indicated if there is a clear indication for colonoscopy or if the patient refuses.

31.2.1.3 Patient Preparation

On the basis of information given to the patient, informed consent must be received. Key points when explaining the investigation cover goals, technique, risks, and alternatives.

Several options are available for bowel preparation; 90 % adequate bowel preparation can be obtained by a single phosphosoda enema several minutes before the procedure. Sedatives, narcotics, or anesthetics are not necessary in the majority of cases, and after the examination patients can resume their prior level of activity.

31.2.1.4 Complications

Sigmoidoscopy is very safe and complications are rare. Occasionally reported adverse events include local pain, bleeding, bacteremia, cardiac arrhythmia, and bowel perforation (in <0.01 %).

31.2.1.5 Report Chart

Endoscopy report should include various pieces of information:

- Indication
- Type of instrument
- Adequacy of bowel preparation
- Premedication used, antibiotic prophylaxis (if given)
- Most proximal bowel segment examined
- Appearance of the mucosa
- Abnormalities
  - Polyps (number, size, appearance) (Fig. 31.1)
  - Pseudopolyps
  - Hemorrhagic areas
  - Ulcers
  - Neoplastic or obstructing lesions (Fig. 31.2)
  - Diverticula (Fig. 31.3)
  - Friable regions
  - Lipomas
  - Angiodysplasia (Fig. 31.4)
  - Spasms
  - Fissures
  - Hemorrhoids (Fig. 31.5)
  - Blood
  - Pus
  - Others
- Therapeutic procedures performed
- Biopsy sites
- Complications
- Recommendations/plan

31.2.2 Colonoscopy

The designation of a "diagnostic" or "therapeutic" procedure can only be assigned after the procedure. It is generally unacceptable to perform diagnostic procedures without the skill to also perform the therapeutic maneuvers that are likely to be indicated. All colonoscopists must be trained in polypectomy and must perform colonoscopy with the intent to clear the colon of polyps at the initial examination [1–3].

31.2.2.1 Indications

In clinical practice, opinions differ regarding indications for colonoscopy. Standard indications are:

- Evaluation of an abnormality seen on barium enema or virtual colonoscopy

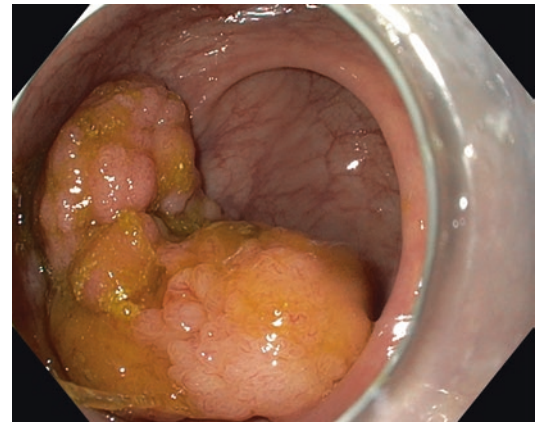


Fig. 31.1 Large rectal polyp

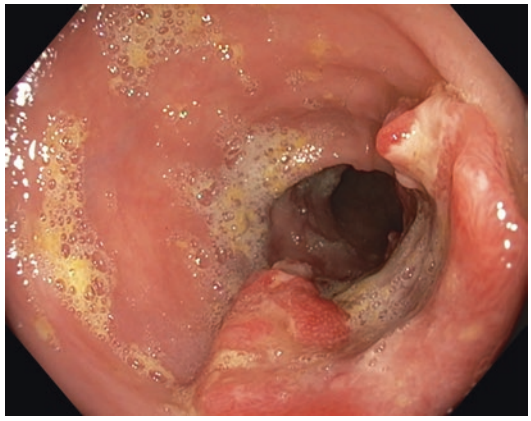


Fig. 31.2 Colon cancer

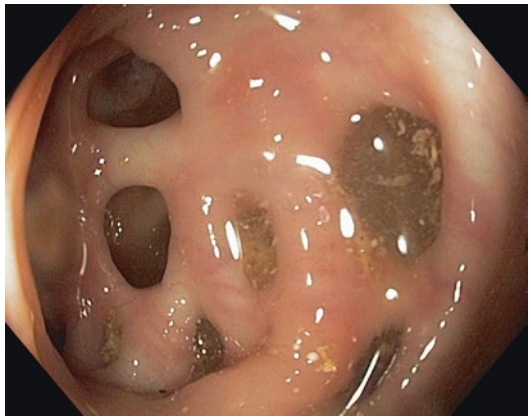


Fig. 31.3 Colonic diverticula

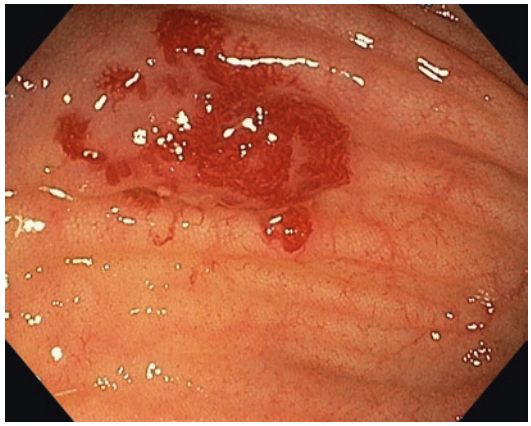


Fig. 31.4 Angiodysplasia

- Evaluation of unexplained GI bleeding
  - Melena after an upper GI source has been excluded by gastroscopy
  - Presence of fecal occult blood (positive fecal occult blood test)
  - Unexplained iron-deficiency anemia
- Follow-up/surveillance after polypectomy for adenomas
- Follow-up/surveillance after colorectal cancer resection
- Clearing the colon of synchronous neoplasia (polyps or cancer) in patients with colorectal cancer
- After identification of adenomas on sigmoidoscopy
- Follow-up/surveillance of ulcerative colitis
- Follow-up/surveillance of Crohn's colitis
- Colorectal cancer screening
- Chronic inflammatory bowel disease of the colon (to make a more precise diagnosis or determine the extent and activity of disease)
- Significant diarrhea of unexplained origin
- Intraoperatively to identify a lesion that is not apparent during surgery

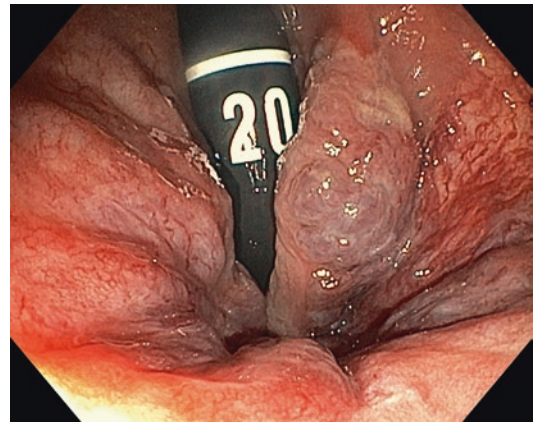


Fig. 31.5 Hemorrhoids

31.2.2.2 Generally Accepted Nonindications/Relative Indications

- Irritable bowel syndrome
- Acute self-limited diarrhea
- Stable inflammatory bowel disease (except in cancer surveillance)
- Melena with clear suspicion of an upper GI source
- Hematochezia with an anorectal source clearly seen on sigmoidoscopy

- Surveillance after curative resection for colon cancer, to rule out a cancer recurrence on the suture line
- Routine evaluation before elective noncolonic abdominal surgery with no symptoms related to the colon or rectum

31.2.2.3 Contraindications

- There are similar to those for sigmoidoscopy but also include situations where the patient is unable to cooperate and/or cannot be adequately sedated.

31.2.2.4 High-Risk Situations (Relative Contraindications)

- Uncontrolled lower GI bleeding (hemodynamic instability)
- Recent colorectal surgery/immediate postoperative stage
- Multiple pelvic surgeries in the past
- Severe chronic obstructive pulmonary disease or severe arteriosclerotic heart disease
- Acute or recent myocardial infarction/pulmonary embolism
- Very large and/or symptomatic abdominal aortic aneurysm
- Pregnancy in the second or third trimester

31.2.2.5 Patient Preparation

Informed Consent on the Basis of Information Given to the Patient

- Patient preparation is similar to that for sigmoidoscopy and includes providing the patient with a description of the technique and information about the possibility of biopsy, polypectomy, and other applicable procedures.

Bowel Preparation

Thorough bowel cleaning is mandatory. A wide variety of methods use dietary restrictions with various purgatives and laxatives. Diet and cathartics, gut lavage, and phosphates are three commonly used options.

Diet and Cathartics

The patient should ingest clear liquids for 72 h or a low residual diet for 1–3 days. Cathartics such as magnesium citrate and bisacodyl should be used. A tap-water enema should be administered the evening or morning before the procedure.

Gut Lavage

Peroral gut lavage with osmotically balanced electrolyte solutions such as polyethylene glycol electrolyte lavage solution (volume, 2–4 L; lavage rate, 1.5 L/h) should be performed. Several adverse experiences have been reported, including disagreeable taste, hypothermia, feeling of fullness, nausea, bloating, aspiration, reactivation of bleeding, esophageal tear, perforation, pill malabsorption, and allergic reaction (angioedema, urticaria, anaphylaxis).

Phosphates

Phosphates are available as solutions or tablets – an attractive alternative because of the lower volume that must be ingested. Oral sodium phosphates (45 mL) diluted with water (to 90 mL) should be administered the evening before and repeated 4 h before colonoscopy. The solution is very hypertonic. Adverse experiences have been reported and include electrolyte disturbances, hyperphosphatemia, hypocalcemia, vomiting, dehydration, colonic aphthous ulcerations, and seizures.

Contraindications for colonoscopy bowel preparation

- Preparation should not be performed if there is a contraindication for colonoscopy or if a gastric or bowel obstruction is suspected. Gut lavage should be avoided in gastroparesis.

An increased risk to bowel preparation exists in patients with congestive heart failure, ascites, renal insufficiency, dehydration, debility, GI obstruction, gastric retention, colitis, megacolon, and ileus; those who are unable to take oral fluid; and those taking diuretics or medications that affect electrolytes.

Premedication and Sedation

Based on tradition, culture, and economics, acceptance of colonoscopy can differ from

country to country. Sedation and analgesia are commonly provided for colonoscopy. The goal is to increase the patient's tolerance for the procedure and to increase the satisfaction of both the patient and endoscopist. Standard sedation (a combination of a narcotic and benzodiazepine) is safe and effective when administered by the endoscopist. Propofol provides excellent patient and endoscopist satisfaction. It can cause profound apnea, however, and needs to be administered by an anesthesiologist or others with special/similar training. Colonoscopy can be done without sedation in selected patients.

31.2.2.6 Special Considerations

The risk for bacteremia during colonoscopy is low. There is not complete consensus on antibiotic prophylaxis for bacterial endocarditis in patients undergoing colonoscopy. It is common to administer antibiotics to patients with prosthetic valves or a history of endocarditis. Several accepted regimens can be used, depending on local guidelines.

31.2.2.7 Complications

Major Complications

- Perforation (estimated at 0.14–0.8 %)
- Hemorrhage (negligible; 0–0.5 %)
- Respiratory depression (oversedation, especially in patients with chronic lung disease)
- Bacteremia (incidence varies from 0% to 0.5 %)

Other Complications

- Vasovagal reactions
- Splenic laceration
- Transient electrocardiography changes
- Dehydration resulting from bowel cleansing
- Volvulus
- Explosion of combustible gases in the colon (hydrogen, methane) when in contact with an electric spark

31.2.2.8 Report Chart

The report chart for colonoscopy is similar to that for sigmoidoscopy (refer to the "Report Chart" section related to sigmoidoscopy earlier in this chapter).

31.2.2.9 Alternatives to Diagnostic Colonoscopy

Virtual Colonoscopy

Computed tomography (CT) is the preferred method for image acquisition. Some centers use magnetic resonance imaging. Bowel preparation with complete cleansing of the colon together with colonic insufflation of gas is required for "virtual" colonoscopy using CT.

Virtual colonoscopy has several indications/clinical roles:

- Evaluation of the colon after incomplete conventional colonoscopy
- Evaluation of the colon secondary to an obstructing neoplasm
- Evaluation in patients who are not fit for conventional colonoscopy (chronic obstructive lung disease, bleeding diathesis, allergic reactions to sedation)
- Contribute to colorectal screening
- Patients who refuse colonoscopy

Double-Contrast Barium Enema

- A double-contrast barium enema has a higher risk of missing colorectal cancer than colonoscopy. It has a sensitivity of about 50 % for adenomas. This procedure does not allow for biopsy or treatment.

A double-contrast barium enema is most appropriate for low-prevalence populations and indications if imaging of the colon is necessary (patients younger than 50 without a family history of colorectal cancer and nonbleeding symptoms for instance).

31.3 Therapeutics

31.3.1 Polypectomy

The ability to find and remove colon polyps is one of the major reasons for colonoscopy. Removal of polyps has affected the incidence, morbidity, and mortality of colorectal cancer [1–3]. A safe polypectomy is one that:

- Removes the polyp through transection with a snare loop
- Achieves hemostasis using heat/coagulation
- Maintains the integrity of the colon wall

31.3.1.1 Snare Loops

Snare loops are available in a wide variety of shapes and sizes. Colonoscopists should be familiar with a few types.

Polypectomy Technique

Anyone undertaking colonoscopy with polypectomy is recommended to read dedicated textbooks describing therapeutic endoscopy in detail. One should be aware of a few important steps:

- Mark the handle at the point where the snare is just closed at the tip. This makes it possible to estimate the tissue volume in the closed snare.
- Check for a smooth "feel" when moving the handle to open and close the snare. Provide maximum feedback to the assistant controlling the snare.
- Be aware of the thickness of the snare wire; this greatly affects the speed of electrocoagulation and transection of the polyp.
- Be aware of the squeeze pressure. If it is inadequate, transection will rely on high-power cutting, increasing the risk of bleeding due to insufficient coagulation of stalk vessels.

31.3.1.2 Additional Devices

Hot Biopsy Polypectomy Forceps

These forceps are used to destroy small polyps (≤5 mm in diameter), enabling simultaneous cautery of a polyp base while obtaining a biopsy specimen.

Polyp Retrieval

Polyps can be retrieved using various tools:

- Nylon net
- Multiprong grasping forceps
- Polyp suction trap

Injection Needles

Needles can be used to inject various fluids:

- Saline
- Adrenaline-saline
- India ink (to tattoo a polypectomy site)

Dye-Spray Cannulas

- Dye-spray cannulas are requested for chromoendoscopy (CE) (see Sect. 5.3)

Clipping Devices

Clipping devices are used for a few indications:

- Hemostasis after polypectomy
- Prevent bleeding

Nylon-Loop Devices

Nylon-loop devices can be used in various circumstances:

- Strangulation of a polyp stalk (to prevent bleeding)
- Treatment of bleeding after polypectomy

31.3.1.3 Complications of Polypectomy

Bleeding

Immediate Bleeding

Immediate bleeding is usually a slow ooze but it can be an arterial spurt. This is usually treated by injection of adrenalin-saline solution. Stalk bleeding can also be treated by resnaring the remnant stalk. Hemostatic clips can be applied to the polyp transection area.

Secondary (Delayed) Hemorrhage

Delayed bleeding can occur up to 2 weeks after polypectomy, particularly after the removal of larger polyps. It usually is self-limiting but may require re-endoscopy and hemostatic treatment.

"Post-Polypectomy Syndrome"

This syndrome is characterized by fever, pain, and localized signs of peritonitis/peritonism. It represents a "closed perforation," with full-thickness heat damage to the bowel wall. Conservative treatment with bed rest and antibiotics is indicated, and the syndrome rarely requires surgical intervention.

Frank Perforation

Frank perforation is rare. Management is often conservative, depending on the area and localization of the polyp base. A surgeon should always be consulted.

31.3.2 Placement of Self-Expanding Metal Stents

Self-expanding metal stents (SEMSs) are used for the nonsurgical relief of a malignant colorectal obstruction [4]. Obstruction occurs in 8–25 % of patients with colorectal cancer. An emergency operation is associated with a high morbidity rate (up to 60 %) and a mortality rate up to 22 %, and often results in a temporary or permanent colostomy, which affects quality of life.

The need for alternative procedures is obvious. The placement of SEMSs is a procedure that has quickly become more widespread because it avoids a high-risk emergency operation and reduces the need for a colostomy.

31.3.2.1 SEMS: Two Main Techniques for Placement

Radiological Placement

The obstruction is located fluoroscopically using a water-soluble contrast medium. The stricture is then passed with a guide wire, over which the stent is inserted into the obstruction and released under fluoroscopic guidance. Depending on the outer diameter of the application system and the degree of the obstruction, some surgeons dilate the stricture with a balloon.

Combined Endoscopic/Fluoroscopic Placement

The distal/anal end of the obstruction is documented endoscopically and, if indicated, biopsy can be done. If the obstruction cannot be passed with the scope, the length and configuration of the stenosis are demonstrated fluoroscopically by injecting water-soluble contrast. After this, the obstruction is negotiated with a guide wire. The stent delivery system is then inserted through the scope, and the stent is released under both endoscopic and fluoroscopic guidance. If the application system cannot pass the working channel of the scope, it has to be removed after the guide wire is placed. The stent is then inserted under fluoroscopic control.

31.3.2.2 SEMS: Two Main Indications

Bridge to Surgery

Instead of emergency surgery, a SEMS is placed as a preoperative decompression, securing normal bowel function. It allows the patient to be clinically stabilized. The patient's comorbid illnesses and the extent of malignancy can be addressed. In addition, it allows preoperative chemoradiation therapy to be administered. If the patient is a candidate for elective surgical treatment, the stent remains in place until surgery, when the stent is resected en bloc with the tumor. If the patient is a poor candidate for surgical resection because of underlying illnesses or has unresectable or widely metastatic disease discovered by imaging studies, the SEMS can serve as the final palliative treatment.

Palliation

Palliation of patients with advanced malignancy can be a challenge. Surgery may be considered inappropriate in this group of patients, who are often frail and whose comorbid conditions may not be fully optimized preoperatively. Surgical palliative procedure has been shown to have a significant mortality rate. Candidates for colonic SEMS placement are patients with colorectal cancer who have extensive local or metastatic disease with a relatively short life expectancy. In addition, patients with large-bowel obstruction secondary to noncolonic pelvic malignancies (e.g., bladder, prostate, or ovarian carcinoma) or metastatic disease (e.g., breast carcinoma) can be palliated with a SEMS. Several series have demonstrated successful palliation of obstruction, avoiding colostomy in 85–100 % of patients. The stents effectively palliated obstruction for more than 1 year.

31.3.2.3 Complications of SEMS

Complications may occur during the procedure, either early or late after placement. Major early complications such as perforation (<4 %) and bleeding (<5 %) are rare. Two types of complications are mainly seen now: reobstruction (10 %) caused by tumor ingrowth, which can be treated with restenting, and distal stent migration (10 %), which may be completely asymptomatic; if obstructive symptoms occur, a new stent can be placed in the tumor stricture. The procedure-related mortality is very low (0.5–1 %).

31.4 Surveillance

31.4.1 Postpolypectomy Surveillance

Removal of colon polyps will, to a large extent, protect the patient from developing carcinoma by interrupting the adenoma-carcinoma sequence [5–9].

Not all patients have the same likelihood of developing metachronous adenomas. Therefore, follow-up colonoscopic examinations needs to take into account each patient's risk for developing metachronous advanced adenomas.

Postpolypectomy surveillance strategies should be tailored accordingly, and patients should be stratified into high- and low-risk groups after a high-quality baseline colonoscopy with complete removal of all detected neoplastic lesions (Table 31.1). The crude risk for advanced adenomas during follow-up is estimated to 15.5 % in the high-risk group compared with 6.9 % in the low-risk group.

31.4.1.1 Recommendations for Benign Polyps

High-quality complete colonoscopy should be performed at the time of the initial polypectomy to detect and resect all synchronous adenomas.

- Additional clearing colonoscopies may be required after resection of large sessile adenomas, or if the colonoscopist is not reasonably confident that all adenomas have been found and removed, as, for example, in the case of poor bowel cleansing.
- Surveillance colonoscopy is performed according to a risk stratification, see Table 31.1
- Endoscopic follow-up is recommended within 6 months following piecemeal resection of adenomas >10 mm in size, before initiating a surveillance program according to Table 31.1.
- In high-risk patients, after one negative follow-up surveillance examination, colonoscopy intervals may be increased to 5 years.
- If surveillance colonoscopy is not feasible/possible, flexible sigmoidoscopy followed by virtual colonoscopy may be an acceptable alternative.
- It is important to individualize follow-up surveillance according to the patient's age and comorbidities. It is considered reasonable to discontinue endoscopic postpolypectomy follow-up at age 80 years, or earlier, depending on life expectancy.

31.4.1.2 Recommendations for Malignant Polyps

Because the risk for local recurrence of or for lymph node metastasis by invasive carcinoma in an endoscopically resected polyp is less than the

Table 31.1 Surveillance strategies stratified according to risk level

High-risk group	Adenomas	Colonoscopy interval: 3 years
	Villous histology	
	High-grade dysplasia	
	≥1 cm in size	
	Multiple (≥3) Serrated polyp ≥ 10 mm in size and/or with dysplasia	
Low-risk group	Adenomas	Colonoscopy
	One or two small (<1 cm), tubular-type tumors	10 Years after the index colonoscopy (in or out of a national screening program)
	No low-grade dysplasia	
	Serrated polyp <10 mm in size and without dysplasia	

risk of death from colonic surgery, no further treatment is indicated after endoscopic resection of a malignant polyp if the endoscopic and pathological criteria listed in Table 31.2 are fulfilled.

All patients with malignant polyps should be discussed in multidisciplinary meetings per local guidelines. Follow-up endoscopic examination should be done in about 3 months to check for residual abnormal tissue at the polypectomy site (it can be useful to mark the polypectomy site with India ink). After one negative examination, standard surveillance, as recommended for benign polyps, must be established.

31.4.2 Colonoscopy Surveillance After Colorectal Cancer Resection

After a curative operative resection for colorectal cancer, colonoscopy follow-up is frequently performed with the intention of detecting cancer recurrence and removing new adenomas (to prevent metachronous cancers from developing) [10]. However, it is not certain that interval repeat colonoscopy following colon cancer resection indeed detects recurrence at a stage when a salvage operation can be performed successfully. The optimum intervals for colonoscopy have to be defined. The same questions are raised for metachronous carcinoma prevention in terms of effectiveness and optimum intervals.

In patients operated on to cure colorectal cancer, one-third to one-half will have recurrent cancer, but intraluminal recurrences (which can be seen on endoscopy) are relatively uncommon, occurring in only 3–14 % of cases.

Table 31.2 Endoscopic and histopathology criteria identifying excised malignant polyps with no need for further treatment

The polyp is considered completely excised by the endoscopist and is submitted in toto for pathological examination
It should be possible to accurately determine the depth of invasion, grade of differentiation, and completeness of excision of the carcinoma
The cancer is not poorly differentiated
There is no vascular or lymphatic involvement
The margin of the excision is not involved

Recommendations

All patients must have a full colonoscopy in the perioperative period. This examination detects synchronous cancers and adenomas. If it is normal, subsequent colonoscopy should be offered 1 year postoperatively and every 3–5 years thereafter. There is no evidence for shorter intervals, and it is not indicated to use colonoscopy to detect intraluminal local recurrent cancer. Anastomoses recur in only 2 % of colon cancers and are generally accompanied by intra-abdominal disease that cannot be resected as a cure.

31.5 Techniques in Endoscopic Imaging

Efforts have been directed toward the earlier diagnosis of GI neoplasia at the dysplasia level [11–17]. The limitation of previous conventional white-light endoscopy (WLE) was that it could not detect occult dysplasia, differentiate hyperplastic from adenomatous polyps, or easily detect recurrence at the scar site of previously snared, flat, spreading villous adenomas.

New endoscopic technology to improve mucosal visualization has recently been developed. The improved lesion detection allows the endoscopist to provide real-time visual diagnosis. Improvements in image resolution, software processing, and optical filter technology have resulted in high-definition endoscopy and optical contrast techniques such as narrow-band imaging, flexible spectral imaging color enhancement, and iScan. Table 31.3 gives an overview of commercially available imaging techniques and their clinical applications.

31.5.1 High-Definition White-Light Endoscopy

High-definition (HD) endoscopes produce images with a resolution of more than 1 million pixels compared with older standard-definition

Table 31.3 Commercially available imaging techniques and their clinical applications

Technique	Technology	Tissue target	Applications
High definition	High pixel density, fast line scanning (sharper images)	Surface enhancement, high image resolution, fewer artifacts	Comparable to other enhancement techniques (dye-based and computerized chromoendoscopy)
Magnification (zoom)	Optical magnification ×150	Detailed pit pattern, villous structure, vascular details	Neoplasia characterization
Electronic chromoendoscopy			
Narrow-band imaging	Filter reduces wavelength to 415 and 540 nm Improves contrast between vasculatures and mucosa	Improved vascular contrast of capillaries and enhanced mucosal structure	Neoplasia characterization
FICE/iScan	Proprietary image processing algorithm on white-light images (spectral emission methods)	Structural and vascular enhancement	Seems to have applicability similar to narrow-band imaging
Autofluorescence endoscopy	Excitation light (370–470 nm) and green light (540–560 nm) are radiated sequentially Activates endogenous fluorophores and light is selectively detected and displayed as a pseudo-color image	Red-flag technology for the detection of dysplasia or early cancer (displayed as magenta on the pseudo-color image)	Detection of neoplasia
Confocal laser endoscopy	Laser light is focused via a pinhole An image is produced by the same light reflected via the same pinhole	High image resolution to the level of subcellular structures	Identification of neoplastic lesions during endoscopy

FICE Fujinon intelligent chromoendoscopy

endoscopes, with a resolution of only 100,000–400,000 pixels. High-resolution endoscopes magnify the images about 30-fold, and zoom endoscopes can magnify the optics up to 150-fold while maintaining image display resolution. Digital zoom (electronic magnification) results in decreased image resolution. Most conventional endoscopes have a digital zoom up to twofold.

HD endoscopy enables the endoscopist to view finer mucosal and vascular details as a result of improved image resolution. It has yield rates comparable to those of other mucosal enhancement techniques, including dye-based and electronic CE.

31.5.2 Magnifying Endoscopy

Magnification colonoscopy allows visualization of the minute structures of the colonic surface. There are two types of magnifying colonoscopes:

- One with an adjustable focusing system that provides both a conventional image and a magnification factor of ×10 to ×35
- One with two separate optical systems manipulated by a control on the head of the scope: one system provides a conventional image, the other produces an ultrahigh magnification (×170)

The combination of CE and magnifying colonoscopy is used to classify and characterize neoplasia.

31.5.3 Chromoendoscopy

Chromoendoscopy (CE) is a technique in which tissue stains or dyes are applied to the gastrointestinal mucosa. It may or may not be combined with magnification endoscopy or high-resolution endoscopy. The purpose of using CE is threefold:

- To detect abnormalities that cannot be seen without it
- To characterize those abnormalities
- To delineate the margins of those abnormalities

Classification of Tissue Stains Used in CE
Tissue stains can be classified into three categories (Table 31.4):

- Absorptive stains (vital stains): identify specific epithelial cell types or cellular constituents by preferential entry into cells
- Reactive stains: identify cellular products (e.g., a change in the color of a pH indicator)
- Contrast stains: are not absorbed by epithelial tissue and highlight tissue topography by pooling in epithelial crevices and depressions

31.5.4 Computerized Virtual Chromoendoscopy

In contrast to dye-based CE, computerized virtual CR uses either real-time postprocessing filter algorithms or a rotating filter placed in front of the light source to enhance visualization of surface structures and vasculatures. Three different systems are commercially available: narrow-band imaging (NBI; Olympus Corp., Tokyo, Japan), FICE (Fujinon intelligent CE; Fujinon, Tokyo, Japan), and iScan (Pentax, Tokyo, Japan).

31.5.4.1 Narrow-band Imaging

Switching from WLE mode to NBI mode occurs by mechanically inserting the narrow-band filter in front of the xenon arc lamp. The final composite NBI image is displayed by feeding the 415-nm image into the blue and green channels and the 540-nm image into the red channel of the monitor. NBI thereby improves visualization of surface characteristics.

NBI can be used to characterize colorectal polyps. Training with NBI may improve the ability of endoscopists to identify more mucosal abnormalities than they can visualize with conventional WLE. Until recently there was not enough evidence to justify the routine use of NBI because of its relatively poor light intensity. A new generation of NBI processors (290 and 190 series) with a higher NBI light intensity is now available and might change this.

The use of NBI in dysplasia detection in patients with long-standing ulcerative colitis is not clear, and recent guidelines from the European Society of Gastrointestinal Endoscopy recommends HD WLE with dye-based CE.

31.5.4.2 FICE and IScan

FICE enhances the visualization of mucosal structures and microcirculation by selecting a spectral transmission with a dedicated wavelength. The FICE system is software driven and uses a proprietary image-processing algorithm based on spectral emission methods. It comes with ten presets that can be customized and configured from a large number of wavelength permutations.

iScan is a digital contrast method based on postprocessing algorithms applied on white-light images. It has three modes of image enhancement. Surface-enhancement mode improves structural appearance by recognizing edges, contrast enhancement mode augments differences between the structure and sections with depression, and tone enhancement mode helps enhance individual organ appearance by modifying the red, green, and blue components of each pixel.

The utility of FICE and iScan are still emerging, and it is likely that they will have the same applicability as NBI. Both FICE and iScan seem to be accurate for the characterization of colorectal lesions but do not enhance adenoma yield.

Table 31.4 Types of tissue stains

Category	Stain	Mechanism	Example
Absorptive	Lugol solution	Stains epithelial cells or cellular elements by preferential entry into cells	Stains glycogen in normal cells in the esophagus
	Methylene blue	Stains actively absorbing cells in the intestine and colon	Enters normal absorptive tissue
	Cresyl violet	Absorbed by the glands of Lieberkühn	Stains margins of pits on the mucosal surface of the colon
Reactive	Congo red	Identifies cellular products	Changes color from red to dark blue or black in an acidic environment (pH < 3) Combined with methylene blue it "bleaches" neoplastic cells
Contrast	Indigocarmine	Highlights tissue topography	Distinguishes diminutive polyps, detects flat lesions of the colonic mucosa

31.5.5 Autofluorescence Endoscopy

An autofluorescence endoscope has two separate charge-coupled devices (CCDs): one for WLE and one for autofluorescence imaging. WLE and autofluorescence imaging are turned on by a switch on the endoscope. Excitation light and green light are provided by a xenon arc lamp via a rotation filter. A barrier filter placed in front of the CCD removes reflected excitation light. The result is false-color image that shows normal mucosa as green and dysplastic/cancerous tissue as magenta.

Autofluorescence endoscopy has the potential to be used as a red-flag technique in the detection of neoplasia. Limiting factors are high false-positive rates in CE, low-resolution images and jerky video, the inability to visualize subsurface features, and false-positive artifacts in the colon caused by fecal remnants.

31.5.6 Confocal Laser Endomicroscopy

The Pentax confocal laser endomicroscopy (CLE) system is integrated into the tip of a conventional endoscope. They are still used but are not produced anymore. A probe-based CLE (Cellvizio; Mauna Kea Technologies, Paris, France) comes with different sizes of mini-probes that can be advanced through the working channel of endoscopes to examine the upper and lower GI tracts and can also be used in mini-scopes to visualize the pancreatobiliary duct systems.

CLE provides high-resolution microscopic images at a subcellular resolution (*confocal* means alignment of both the illumination and collection systems in the same focal plane: laser light is focused through a pinhole at the selected depth via the same lens). Intravenous fluorescein is used to contrast cellular, subcellular, and connective tissues and vessel architecture at a high resolution. Nuclei are not stained by fluorescein, and other dyes such as acriflavine or cresyl violet can be used as adjuncts to fluorescein to obtain better definition.

CLE is not in routine clinical use but is used in research protocols. A steep learning curve is associated with the use of this technology. Its limited field of view also makes it unsuitable as a red-flag technique. HD endoscopy and dye-based or virtual CE is needed to identify suspicious areas before CLE evaluation. Cost-effectiveness data for this technology are also awaited, and additional studies are needed before it can be applied in routine clinical practice.

31.5.7 Miscellaneous Imaging Techniques

31.5.7.1 Raman Spectroscopy

Raman spectroscopy (RS) is able to provide a biochemical "fingerprint" of tissue by measuring the molecule-specific inelastic scattering of light.

RS requires the illumination of a tissue sample with a monochromatic laser and subsequent collection and analysis of the scattered light to determine intensity and wavelength. The Raman spectrum is a direct function of the molecular composition of the interrogated volume within the tissue, producing a complex molecular fingerprint. The majority of biological molecules are Raman active, each with their own fingerprint. RS is highly sensitive to subtle biochemical and molecular changes, which is vital in the differentiation of tissue samples.

Raman probes small enough to fit down the biopsy channel of an endoscope and enabling rapid evaluation of tissue have been developed and tested. Experimental research has been performed to determine whether RS can be used to discriminate between normal colonic mucosa, hyperplastic polyps, adenomatous polyps, adenocarcinomas, and ulcerative colitis. Encouraging results have been achieved, but the technique is not yet ready for clinical use.

31.5.7.2 Light-Scattering Spectroscopy

An important pathological feature as tissue becomes dysplastic is an increase in nuclear size, nuclear density, and nuclear crowding. Light-scattering spectroscopy detects nuclear size using a point spectroscopy multifiber probe, which is touched lightly to the surface being tested. Light-scattering spectroscopy is a relatively simple optical spectroscopic technique that provides structural (morphology) information about tissue. It is based on white-light reflectance, in which incident photons on tissue are scattered back without a change in wavelength. Measurement of the relative backscattering intensity of light over the wavelength spectrum of visible light has been shown to be sensitive to both tissue scatterers, such as cell nuclei and mitochondria, and tissue absorbers such as hemoglobin. Because of the limited penetration depth of white light, morphological information is obtained primarily from the epithelial layers of tissue. Changes in the density and/or size of scatters associated with tissue transformation can be measured by light-scattering spectroscopy and correlated with corresponding histopathologic diagnosis. The main advantages over fluorescence arise from a significantly stronger signal and the use of white light instead of a laser. A simplified and less expensive spectroscopic detection system can thus be used. Similar to point fluorescence spectroscopy, the primary drawback is the limited volume sampled by the optical probe. Nevertheless, rapid (<1 s) spectroscopic readings can be obtained with light-scattering spectroscopy. Ongoing studies are promising, but the technique cannot yet be implemented in clinical use.

31.5.7.3 Optical Coherence Tomography

Optical coherence tomography (OCT) or volumetric laser endomicroscopy is a biomedical imaging technique that enables cross-sectional imaging of biological tissues with a high spatial resolution (7–10 μm) and in near real time. OCT is analogous to B-scan ultrasonography, but the images are formed by detecting light (as opposed to sound) that is reflected back from subsurface tissue microstructures. The resolution of current OCT systems is nearly tenfold greater than that of high-frequency endoscopic ultrasound – high enough to identify microscopic features such as villi, glands, crypts, lymphatic aggregates, and blood vessels. The price to be paid for this remarkable resolution is a limited imaging depth of about 2–3 mm. OCT probes 2.0 mm in diameter and similar to endoscopic ultrasound probes are passed down the biopsy channel of a conventional scope and placed near the tissue to be examined. In the GI tract, OCT has been used to image the esophagus, stomach, small and large intestines, and biliary and pancreatic ducts. However, much of the experience and practical utility with OCT has been with esophageal, biliary, and pancreatic duct imaging.

It has been shown that adenomas in the colon had significantly less structure and scattered light to a lesser degree than hyperplastic polyps, and that hyperplastic polyps were significantly closer in organization and light scattering to normal mucosa compared with adenomas. Other studies have characterized OCT findings in the normal colon, ulcerative colitis, Crohn's disease, and radiation proctitis. Since OCT gives an image of

all the layers of the colonic wall, it might be useful in diagnosing transmural inflammation in Crohn's disease and enable this to be differentiated from ulcerative colitis.

31.5.7.4 Endocytoscopy

Endocytoscopy (EC) is now commercially available. EC can provide cellular-level analysis with up to 1,400-fold magnification. The technology uses contact light microscopy and allows high-level magnification of the superficial layers of the mucosa to a depth of about 50 μm. A fixed-focus, high-power objective lens projects onto a CCD a highly magnified image from a 0.5-mm-diameter sample. Two types of systems are available: (1) a probe-based, handheld miniprobe, providing magnification up to ×570 and ×1,400, which can be passed through the working channel of a conventional endoscope, and (2) a system integrated into the distal tip of an endoscope, providing magnification up to ×580. The EC probe needs to be in contact with the tissue surface to acquire an image, and the system requires preparation of the mucosal layer with absorptive contrast agents such as methylene blue or toluidine blue. Some promising initial results have shown that EC can discriminate neoplastic from non-neoplastic tissue. The interest in EC has not really taken off, maybe because of the requirement for topical staining, the relative lack of axial discrimination, and the low-resolution images compared with other microscopy techniques such as CLE.

31.5.7.5 Molecular Imaging

Molecular imaging is a new technique in endoscopy. Work on developing safe biomarkers and probes to detect molecular changes in cells with high specificity and accuracy is ongoing. Most molecular imaging studies are in the developmental and preclinical stages. Future studies are needed to confirm the long-term safety and efficacy of these labeled molecular biomarkers.

Conclusion

Endoscopy of the lower GI tract is a safe and commonly used diagnostic and therapeutic modality in coloproctology. Examples of common indications for therapeutic colonoscopy include removal of polyps, treatment of angiodysplasias, and insertion of stents through malignant strictures, whereas colonoscopy has a major role in follow-up after endoscopic polypectomy and surgical resection for colorectal cancer. Although CE has been in use for several years to detect and characterize mucosal lesions, new endoscopic imaging technologies have recently emerged, such as computerized virtual CE, autofluorescence endoscopy, and CLE. Refinement of advanced imaging technologies is underway and, together with the development of new imaging techniques, holds promise for further improvement in the diagnosis of colorectal disease.

References

1. Waye JD, Rex DK, Williams CB, editors. Colonoscopy: principles and practice, 2nd ed. ISBN: 978-1-4051-7599-9.
2. Cotton PB, Williams CB with Hawes RH, Brian P. Practical gastrointestinal endoscopy: the fundamentals, 6th ed. Saunders: American Society for Gastrointestinal Endoscopy. ISBN: 978-1-4443-5654-0.
3. Ginsberg GG, Kochman ML, Norton ID, Gostout CJ. Clinical gastrointestinal endoscopy, 2nd ed. ISBN: 978-1-4377-1529-3.
4. van Hooft JE, van Halsema EE, Vanbiervliet G, Beets-Tan RGH, DeWitt JM, Donnellan F, Dumonceau JM, Glynne-Jones RGT, Hassan C, Jiménez-Perez J, Meisner S, Muthusamy VR, Parker MC, Regimbeau JM, Sabbagh C, Sagar J, Tanis PJ, Vandervoort J, Webster GJ, Manes G, Barthet MA, Repici A. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2014;46(11):990–1053.
5. Hassan C, Quintero E, Dumonceau JM, Regula J, Brandao C, Chaussade S, Dekker E, Dinis-Ribeiro M, Ferlitsch M, Gimeno-Garcia A, Hazewinkel Y, Jover R, Kalager M, Loberg M, Pox C, Lieberman D. Post-polypectomy colonoscopy surveillance: European society of gastrointestinal endoscopy (ESGE) guideline. Endoscopy. 2013;45:842–51.
6. Martinez ME, Baron JA, Lieberman DA, Schatzkin A, Lanza E, Winawer SJ, Zauber AG, Jiang R, Ahnen DJ, Bond JH, Church TR, Robertson DJ, Smith-Warner SA, Jacobs ET, Alberts DS, Greenberg ER. A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. Gastroenterology. 2009;136:832–41.

7. Khasab M, Eid E, Rusche M, Rex DK. Incidence and predictors of "late" recurrences after endoscopic piecemeal resection of large sessile adenomas. Gastrointest Endosc. 2009;70:344–9.
8. Pohl H, Srivastava A, Bensen SP, Anderson P, Rothstein RI, Gordon SR, Levy LC, Toor A, Marckenzie TA, Rosch T, Robertson DJ. Incomplete polyp resection during colonoscopy. Results of the complete adenoma resection (CARE) study. Gastroenterology. 2013;144:74–80.
9. Davila RE, et al. ASGE guideline: the role of endoscopy in the diagnosis, staging, and management of colorectal cancer. Gastrointest Endosc. 2005 61:1–7
10. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalá M, Cervantes A, Arnold D. Early colon cancer: ESMO clinical guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(S 6):vi64–72.
11. Coda S, Thillainayagam A. State of the art in advanced endoscopic imaging for the detection and evaluation of dysplasia and early cancer of the gastrointestinal tract. Clin Exp Gastroenterol. 2014;133.
12. Kallaway C, Almond LM, Barr H, Wood J, Hutchings J, Kendall C, et al. Advances in the clinical application of Raman spectroscopy for cancer diagnostics. Photodiagnosis Photodyn Ther. 2013;10(3):207–19.
13. Kamiński MF, Hassan C, Bisschops R, Pohl J, Pellisé M, Dekker E, et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European society of gastrointestinal endoscopy (ESGE) guideline. Endoscopy Maj. 2014;46(5):435–49.
14. Kirtane TS, Wagh MS. Endoscopic optical coherence tomography (OCT): advances in gastrointestinal imaging. Gastroenterol Res Pract. 2014;2014:376367.
15. Roy HK, Backman V. Spectroscopic applications in gastrointestinal endoscopy. Clin Gastroenterol Hepatol. 2012;10(12):1335–41.
16. Subramanian V, Ragunath K. Advanced endoscopic imaging: a review of commercially available technologies. Clin Gastroenterol Hepatol 1 Marts. 2014;12(3):368–76. e1.
17. Urquhart P, DaCosta R, Marcon N. Endoscopic mucosal imaging of gastrointestinal neoplasia in 2013. Curr Gastroenterol Rep. 2013;15(7):330.

Anal and Rectal Trauma

32

Donato F. Altomare

32.1 Introduction

Anal and rectal traumas are relatively rare (except as a result of iatrogenic damage) because of the anatomic position of the anorectum; it is protected by the pelvic bones, the sacrum, and the pelvic floor muscles. Owing to its relatively superficial position, the anus is injured more often than the rectum, but trauma involving the extraperitoneal rectum, although rare, are often more severe and extend to neighboring organs. As in any trauma, the aim of surgery is to preserve life, followed by controlling infections and, in these cases, preserving fecal continence and evacuation function.

32.2 Etiology

- *Blunt* (*closed*) *trauma*: Rarely affects the anus or the rectum without involving the pelvic bones and is usually a consequence of motor vehicle accidents or accidental falls down stairs and from scaffolding.
- *Childbirth*: Cephalopelvic disproportion during delivery can lacerate the vagina, tearing the perineal body. Midline episiotomy can facilitate the progress of the laceration through the sphincters, anal canal, and rectum and should be avoided. Although rare, wide laceration of the posterior midline of the vagina occurring during an unassisted delivery, particularly in rural environments, may create a cloacal deformity (Fig. 32.1); these are rarely repaired early, severely impairing the quality of sexual life and genitourinary infections.
- *Ingested foreign bodies*: Several small, sharp particles ingested voluntarily (such as nails eaten by psychiatric patients), or accidentally (fish or chicken bones, walnut husks, fragments of glass, toothpicks, dentures) can reach the rectum and become trapped in the rectal wall or sphincter muscles, leading to perforation or abscess. Drugs wrapped in plastic packets are a new type of ingested foreign body. The package may break during endoscopic or surgical attempts to remove it, possibly causing a life-threatening drug overdose.
- *Foreign bodies introduced through the anus*: An amazing variety of oblong (phallic-like) objects have been introduced into the rectum and remained trapped above the anal sphincters – the most frequently found are bottles, plastic dildos and vibrators, vegetables, electric light bulbs, pens, and glasses – usually in an attempt at autoerotism or during sexual assault. Sometimes thermometers can get lost in the rectum when measuring temperature in

D.F. Altomare, MD
Department of Emergency and Organ Transplantation, Azienda Ospedaliero Universitaria Policlinico Bari, Bari, Italy
e-mail: donatofrancesco.altomare@uniba.it

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_32

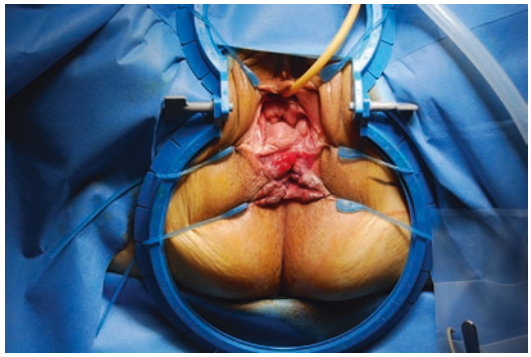


Fig. 32.1 Cloacal deformity of the perineum with an absence of the perineal body and large communication of the vagina with the anal canal

children and may break, causing penetrating injuries to the rectal wall.

- *Sexual assault via the anus*: In both men and women trauma may be the result of too vigorous anal sex acts voluntarily accepted by both partners or may be a criminal act sometimes performed on children (particularly young boys).
- *Pneumatic injuries*: Explosion of the rectum and colon, provoking severe abdominal pain and shock, can be caused by a sudden increase in intrarectal pressure if compressed air is injected through the anus; this may be done as a foolish and criminal joke.
- *Iatrogenic diagnostic/therapeutic injuries*: These can be the result of:
  - Enema (the enema nozzle may cause mucosal laceration and rectovaginal fistulas, or using water that is too hot can severely burn the mucosa)
  - Barium enema
  - Rectal biopsy, which can cause bleeding and perforation
  - Diathermy polypectomy, which can cause colonic gases (methane, hydrogen sulfide, hydrogen) to explode
  - Rectoscopy, sigmoidoscopy
  - Surgery for anal fissures, hemorrhoids, fistulas, and abscesses
  - Surgery for prostate, bladder, and uterine diseases
- *Penetrating injuries*: Sharp anorectal injuries caused by stab or gunshot wounds should be classified as intraperitoneal and extraperitoneal wounds; the former are more frequent than the latter.
  - Stab wounds involving the anus or the extraperitoneal rectum are rare in Western countries but may arise as part of a complex anoperineal trauma in car or motorcycle accidents. Penetrating stab wounds involving the intraperitoneal rectum may be produced by knives or daggers and need to be treated like any colonic injury.
  - Gunshot wounds are relatively frequent in wartime because of the prone position assumed by soldiers while firing, and the extent of rectal damage depends on the ballistic properties of the projectile. High-velocity bullets (military) produce a small entrance hole but extensive tissue damage, multiple perforations, and a large exit wound, whereas low-velocity bullets (civilian use) are often retained in the tissues.
- *Rectal impalement*: This was used to torture and kill enemies in ancient times, but today it can still occur following falls onto pointed objects. This may happen, for example, in agricultural workers who accidentally fall onto a tools or a fence post with the legs astride, or in an accidental fall by those participating in sports involving climbing or jumping. The penetrating trauma can involve the anus, the anal sphincters, and the rectal wall and may extend to the sacrum and coccyx, perineum, prostate, urethra, and bladder, as well as the intraperitoneal organs, especially the small and large bowels. Such severe trauma has also been described as the outcome of criminal acts.

32.3 Diagnosis

Inspection and digital exploration of the anal canal can easy demonstrate the outcome of an anal trauma (Figs. 32.2 and 32.3). Today, the use of 2D or 3D transanal ultrasound is a cornerstone in the diagnosis of any anal trauma and is most useful if shown in three dimensions.

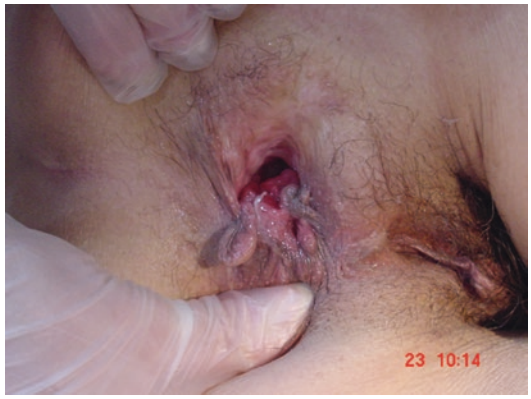


Fig. 32.2 Keyhole deformity of the anus following surgery for anal fistula

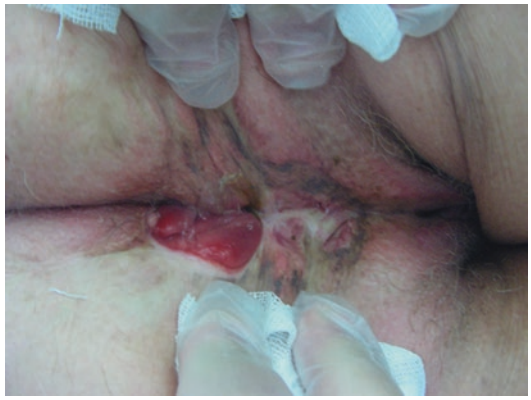


Fig. 32.3 Outcome of accidental anal trauma resulting in a prolapsed rectal mucosa, patulous anus, and a scar replacing the anoderm

- Enquiry about the patient's history and an exploration of the perineum and abdomen are the first steps in assessing any anorectal trauma. Sometimes patients are reluctant to admit anal intercourse or autoerotism resulting in retention of foreign bodies. Perianal ecchymosis or laceration are usually present after any sexual assault, and sperm may also be found. Because of legal issues, special care must be taken to prove the assault with photographs or stains, allowing eventual identification of the perpetrator after rape, for instance.
- A retained foreign body may be felt by lubrication anal digital exploration, although in most cases the foreign body migrates distally into the rectosigmoid colon. An abdominal radiograph can usually assist in the diagnosis. A colonoscopy could be necessary to diagnose and treat a retained foreign body.
- Abdominal pain, tenderness, ileus, and high temperature after a rectal trauma suggest perforation and peritonitis.
- Minor anorectal trauma and retention of foreign bodies may cause anal and abdominal pain, rectal bleeding, and reflex urinary retention. The formation of a perianal/perirectal abscess can cause fever and induce severe pain sometimes leading to general sepsis.

Management and prognosis depend on the severity of the trauma. The American Association for the Surgery of Trauma attempted to quantify the severity of anal trauma and proposed the Rectal Injury Scaling System comprising five degrees of severity. McGrath et al. created a simpler classification of rectal injuries, between intraperitoneal and extraperitoneal rectal trauma, on the basis of rectal anatomy.

32.4 Management

Management of anal trauma with a sphincter lesion includes several treatment options – from an overlapping sphincteroplasty to stimulated graciloplasty or artificial bowel sphincter– whereas cloacal deformity often requires the collaboration of plastic surgeons to re-create the posterior wall of the vagina using rotated cutaneous flaps (Fig. 32.4).

- Severe anorectal trauma must be managed as any other trauma (Fig. 32.5): control of bleeding and immediate resuscitation of the patient are the first steps in emergency treatment.
- Control of infection by the so-called 4-D treatment is mandatory in cases of severe penetrating (stab or gunshot) wounds; this is recommended during anorectal trauma examination under anaesthesia.
  - Distal rectal washout
  - Diversion of the faecal stream
  - Drainage
  - Damage repair

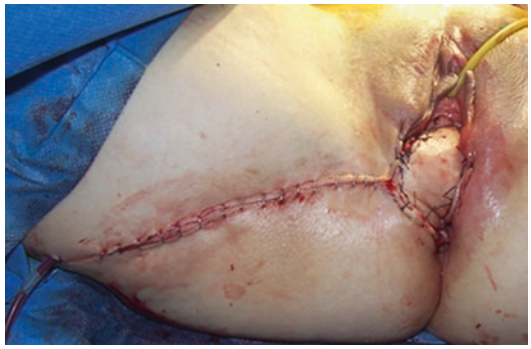


Fig. 32.4 Correction of cloacal deformity by reconstructing the posterior vaginal wall and perineum with a cutaneous flap and sphincteroplasty

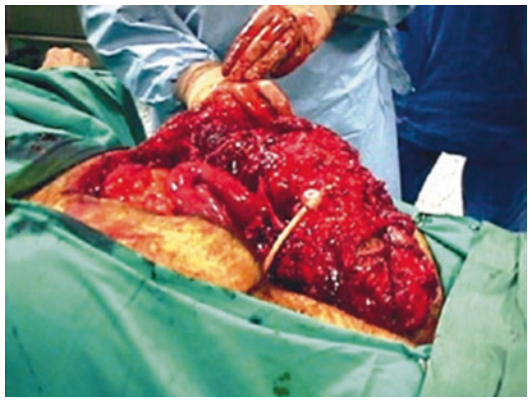


Fig. 32.5 Severe anoperineal trauma involving the anus, sphincters, rectum, prostate, and urethra, with a small-bowel herniation, following a car accident

- The necrotic tissue, foreign bodies, and feces must be accurately removed from the wounds, which also need to be irrigated with antiseptic solution. The perirectal spaces must be drained with a Penrose or a suction drainage, and a diverting left colostomy should be performed immediately.
- Full-dose antibiotic therapy, including anti–gram-negative anaerobe bacterial antibiotics (metronidazole, tobramycin) and tetanus antitoxin should be started as soon as possible because of the considerable risk of severe infection. Administration of general analgesics may be necessary.
- Major anorectal trauma with impalement or destruction of the perineum and external herniation of the small bowel (Fig. 32.2) may require complex reconstructive surgery with a left colostomy, anorectal resection, urinary tract repair, and complete closure of the perineum.
- Rectal perforation can be sutured, and a protective left colostomy should be performed. A distal rectal washout using a diluted povidone-iodine solution through a mucous fistula or the anus is recommended.
- Anorectal endoscopy is necessary in every case of anorectal trauma to evaluate and control rectal bleeding, to facilitate cleaning of damaged tissues and remove feces, and to locate foreign bodies. It should not, however, be performed if perforation of the extraperitoneal rectum is suspected.
- The patient should be positioned in the lithotomy position, except for selected cases of posterior trauma involving the sacrum and coccyx, where the prone position would provide better exposure of the traumatized area.
- Local anesthesia may be sufficient in patients with minor anal traumas, but spinal or general anaesthesia is generally preferred for most anorectal traumas.
- Placement of a urinary catheter is mandatory to exclude lesions of the urinary tract. Sometimes multislice magnetic resonance imaging, or, if that is not available, water-soluble contrast enema (diatrizoic acid [Gastrografin, Hypaque]), and intravenous urography may aid in the recognition of extrarectal organ and tissue involvement.
- In cases of suspected intraperitoneal perforation, laparoscopy (in stable patient) could be performed as a preliminary step.
- Laparotomy may be necessary in cases of disseminated peritoneal contamination, bleeding, and perforation. These complex cases may need a multidisciplinary approach that includes urologists, vascular surgeons, radiologists, and bone surgeons (for fixation of pelvic fractures).
- Isolated anal sphincter lesions could be managed by primary suture (using reabsorbable material such as polyglycolic acid sutures) if the risk of infection is low. Primary suture of the sphincter muscle seems to yield better functional results than delayed suture, provided infection can be prevented. In such cases, vigorous antibiotic prophylaxis should

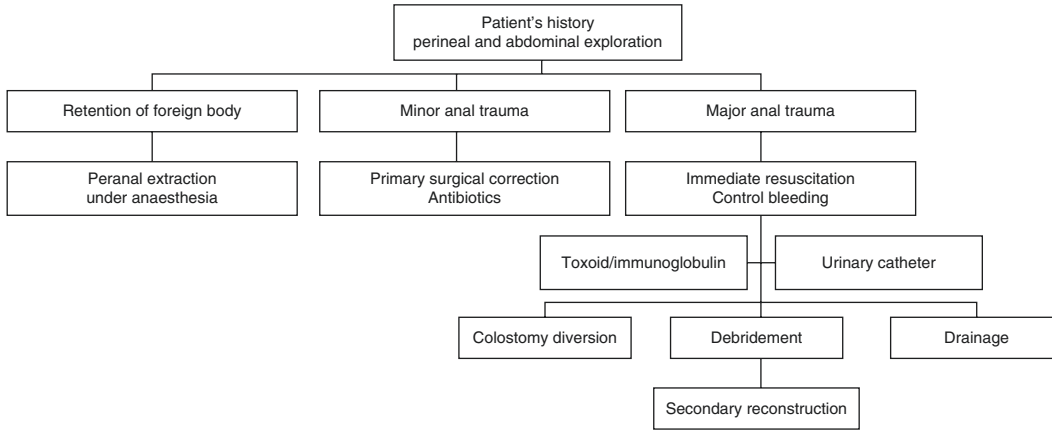


Fig. 32.6 Management of anorectal trauma

be administered and sigmoidostomy performed at the same time.
- Minor anal trauma can be managed conservatively with antibiotics, local medication, and analgesics.

32.4.1 Treatment of Foreign Bodies in the Rectum

- Foreign bodies should be extracted from the rectum through the anus whenever possible.
- After maximal anal dilation has been obtained under anesthesia, several instruments have been proposed to assist n extraction: a Foley catheter placed above the foreign body and pulled downward after inflation of the balloon, obstetric forceps, long hemostatic forceps, an endoscope.
- Rectosigmoidoscopy should be repeated after the foreign body is retrieved to evaluate any possible mucosal lesion or perforation.
- Laparotomy with a rectal opening to extract the foreign body should be performed only when transanal attempts fail (Fig. 32.6).

32.5 Functional Sequelae Following Anorectal Trauma

- Several disabling conditions can follow anorectal traumas, the most frequent of which is fecal incontinence. In addition, defecation problems can arise as a consequence of strictures or rectal denervation.
- Sexual assaults, particularly during childhood, usually leave profound psychological problems and frequently anismus or pelvic dyssynergia, causing obstructed defecation.
- The persistence of abdominal colostomy is not rare after these traumas and has obvious disabling consequences on a patient's social and emotional lives.
- Severe traumas involving the sacral nerves and the anterior perineum can lead to severe problems, including impotence, urinary incontinence, and urinary retention requiring a permanent catheter. Major surgery, using a multidisciplinary approach (urologist, plastic surgeon, colorectal surgeon, and neurologist), can sometime help these patients.

Suggested Reading

1. Anderson SW, Soto JA. Anorectal trauma: the use of computed tomography scan in diagnosis. Semin Ultrasound CT MR. 2008;29:472–82. Review.
2. Cleary RK, Pomerantz RA, Lampman RM. Colon and rectal injuries. Dis Colon Rectum. 2006;49:1203–22. Review.
3. Corman ML. Colon and rectal surgery, 5th ed. Lippincott Williams & Wilkins; 2005. p. 441–449.
4. Hasankhani EG, Omidi-Kashani F. Treatment outcomes of open pelvic fractures associated with extensive perineal injuries. Clin Orthop Surg. 2013;5:263–8.

5. Hellinger MD. Anal trauma and foreign bodies. Surg Clin North Am. 2002;82:1253–60. Philapelphia, PA, USA. Review.
6. Herzig DO. Care of the patient with anorectal trauma. Clin Colon Rectal Surg. 2012;25:210–3.
7. LaCross A, Groff M, Smaldone A. Obstetric anal sphincter injury and anal incontinence following vaginal birth: a systematic review and meta-analysis. J Midwifery Womens Health. 2015;60:37–47.
8. Larsen ML, Hilden M, Lidegaard Ø. Sexual assault: a descriptive study of 2500 female victims over a 10-year period. BJOG. 2015;122:577–84.
9. McGrath V, Fabian TC, Croce MA, Minard G, Pritchard FE. Rectal trauma: management based on anatomic distinctions. Am Surg. 1998;64(12):1136–41.
10. Moore EE, Cogbill TH, Malangoni MA, et al. Organ injury scaling, II: pancreas, duodenum, small bowel, colon, and rectum. J Trauma. 1990;30:1427–9.
11. Sy ED, Chiu YI, Shan YS, Ong RL. Pneumatic colon injury following high pressure blow gun dust cleaner spray to the perineum. Int J Surg Case Rep. 2015; 6C:218–21.
12. Thiagamoorthy G, Johnson A, Thakar R, Sultan AH. National survey of perineal trauma and its subsequent management in the United Kingdom. Int Urogynecol J. 2014;25:1621–7.
13. van Waes OJ, Halm JA, Vermeulen J, McAlister VC. Treatment of rectal war wounds. J R Army Med Corps. 2014;160:255–7.

Colonic and Rectal Obstruction

33

J. Pimentel

33.1 Introduction

Colorectal obstruction, also known as large-bowel obstruction (LBO), is the serious impairment or complete arrest of the passage of intestinal contents caused by a mechanical or functional blockage [1, 2]. It is an emergency condition that requires early recognition and prompt therapeutic intervention to obviate the potential risk of serious complications and death. It is much less common than small-bowel obstruction, representing less than 20 % of all cases of intestinal obstruction. According to its presentation, LBO can be classified in several ways:

- Acute or chronic
- Partial or complete
- Open or closed loop

The pathophysiology depends on the competence of the ileocecal valve. If competent, a closed loop obstruction occurs, with the risk of perforation and gangrene. If incompetent, the intestinal contents can reflux into the small intestine.

Recent technological innovations have changed the therapeutic strategy, with marked benefits for patient outcomes. Understanding these innovations in the light of the various etiological hypotheses, as well as the clinical presentation and the use of appropriate tests, make choosing the best treatment option possible [3].

33.2 Etiology

The etiology of obstruction may be mechanical or nonmechanical (Table 33.1). Mechanical factors can be anything that causes the large-bowel lumen to become more narrow and can be either intraluminal, mural, or extrinsic. Non-mechanical factors include those interfering with the peristaltic motor function or intrinsic innervation of the bowel.

33.3 Symptoms

Symptoms of LBO depend on a number of factors, in particular the etiology, the degree of obstruction (partial or total), and how it presents (acute or chronic, closed or open loop, with a competent or incompetent ileocecal valve). Symptoms may occur suddenly, suggesting an acute obstruction, such as that which occurs in

J. Pimentel, MD, PhD
Faculty of Medicine and University Hospital, Coimbra, Portugal

Department of Surgery B, University Hospital of Coimbra, 3000-075 Coimbra, Portugal
e-mail: joaopimentel@huc.min-saude.pt; j_m_pimentel@iol.pt

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_33

Table 33.1 Etiologies of colonic/rectal (large-bowel) obstruction

Mechanical	Non-mechanical
Tumor	Ogilvie syndrome
Volvulus	Paralytic ileus
Diverticulitis	Constipation
Fecal impaction	Dysfunction
Anastomotic stricture	
Ulcerative/Crohn's colitis	
Benign stenosis	
Ischemia, endometriosis, rare entities	

sigmoid or cecal volvulus, or they may be progressive, making colorectal cancer a more plausible cause. The most frequent clinical presentation may include a change in bowel habits, constipation, colicky abdominal pain and distension, nausea, and vomiting. Severe, continuous abdominal pain, especially in the right iliac fossa, increases the suspicion of gangrene, with imminent perforation.

Systemic symptoms may be present but are usually less serious than those of small-bowel obstruction; these include weight loss, fatigue, anorexia, and anemia – suggesting a neoplastic lesion – or fever, chills, and an unwell feeling, which are associated with an inflammatory disorder such as subacute diverticulitis or colitis. A history of chronic constipation, straining to defecate, pneumaturia, or fecaluria could reveal diverticulitis or carcinoma, and a change in stool caliber is indicative of the latter. In the case of colonic ischemia, signs and symptoms of acute toxicity may be found, and septic shock is possible.

33.4 Diagnosis

The initial physical examination must evaluate the severity of the patient's condition. Careful and comprehensive history-taking is required, along with a complete physical examination assessing vital signs, general physical appearance, and mental status.

A focused abdominal examination is required. Significant abdominal distention is found in the vast majority of patients. Colonic distension may be extremely large, as in the case of a closed-loop obstruction or with a competent ileocecal valve, in which the risk of ischemia or perforation (mainly cecal) is higher. Hyper-resonance is noted upon percussion. Palpation reveals tenderness; rebound tenderness in the right lower quadrant suggests ischemia or perforation of the cecum, which needs urgent surgical treatment. Perforation can also occur at the site of obstruction (tumors or diverticulitis). Eventually, a mass evoking a carcinoma or diverticulitis, or a markedly dilated caecum, can also be palpated. At auscultation, during the initial phase, bowel sounds may be hyperactive or normal, becoming diminished or absent in cases of long-standing obstruction, colonic ischemia, or colonic pseudo-obstruction. Digital rectal examination should always be performed to identify a rectal or lower pelvic mass and in some cases an impacted foreign body. The presence of blood suggests a carcinoma.

Routine laboratory studies are necessary to evaluate fluid and electrolyte imbalances, chronic blood loss, and/or sepsis, including blood for a complete blood count, prothrombin time, crossmatch, electrolyte concentrations, creatinine, and liver function tests. Arterial blood gas should also be determined. An elevated white blood cell count suggests bowel ischemia/necrosis or diverticulitis.

Computed tomography (CT), which is used expeditiously today, has progressively become the gold standard for the diagnosis of LBO; it is useful for a complete, one-venue assessment of a patient's condition, providing detailed information about the etiology and severity of an obstruction as well as complications such as perforation. If the cecal diameter is larger than 12 cm, there is a risk of rupture, and urgent surgery is indicated. CT can also be used as part of a therapeutic procedure (Fig. 33.1). When CT is unavailable, a plain abdominal series (flat and upright or left lateral decubitus films) may be used. This distinguishes small- from large-bowel obstruction, confirming the diagnosis in 60–80 % of cases. An erect chest radiograph or an upright abdominal film may reveal free air if a perforation has

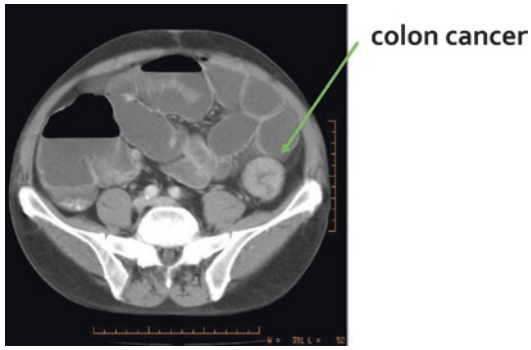


Fig. 33.1 Large-bowel obstruction (colon cancer)

occurred. If the diagnosis – whether a mechanical or nonmechanical obstruction – or the site of obstruction is in doubt, in the absence of signs of peritoneal irritation, a water-soluble contrast enema should be carried out. Ultrasound plays a limited role; it has low accuracy because of the presence of major gaseous distention.

Colonoscopy may help determine a diagnosis in this setting and also has a therapeutic role in reducing a sigmoid volvulus or in decompressing the colon in O'Gilvie syndrome. It has to be done carefully because of the risk of perforation.

33.5 General Management

A patient's resuscitation must begin immediately. This includes volume resuscitation, correction of electrolyte imbalances, and transfusion, if necessary. Because intravascular volume is usually depleted, early intravenous crystalloid fluid rehydration is required (isotonic saline or Ringer lactate solution), sometimes by means of a central venous catheter. A urethral catheter is inserted to monitor urinary output.

When bowel obstruction is partial, these measures should precede or accompany intestinal decompression efforts, which can be attempted by inserting a transanal large-bowel tube or by means of retrograde enemas. A nasogastric tube is also necessary if the patient is vomiting, in some cases revealing fecal content. Prophylactic antibiotics should be considered.

Appropriated treatment depends on the etiology of the colonic/rectal obstruction (Table 33.1). Each situation, including its prognosis, is described below.

Laparoscopic treatment of LBO is feasible and safe in the hands of highly experienced laparoscopic teams, who report results similar to those of elective colonic laparoscopic resection. Except in these situations, however, the abdominal approach continues to use an open approach [4].

A patient's informed consent about management options should be obtained whenever possible. In the case of potential stoma formation, patient consent should be obtained and the possible site marked before surgery (Fig. 33.2).

33.6 Neoplastic Colorectal Obstruction

33.6.1 Etiology-Epidemiology

Colorectal carcinoma is responsible for approximately one-third (in the United Kingdom) to one-half (in the United States) of all cases of colorectal obstruction. About 15 % of all patients with colorectal carcinoma present with obstruction. Most patients are older than 70 years. The risk of obstruction is greater in the left colon, most often in the sigmoid segment or at the splenic flexure, whereas rectal carcinomas are less prone to obstruction than other carcinomas. Cancers found with LBO are usually at an advanced stage of disease: 25 % are already metastatic when the diagnosis is made [5].

33.6.2 Symptoms

The onset of symptoms caused by an obstructive tumor may be insidious or acute. Most patients report symptoms evolving over a 3 to 6-month period, whereas acute obstruction occurs as the first symptom in 15–20 % of carcinomas of the left colon. Symptoms are actually nonspecific and often ignored until complete obstruction

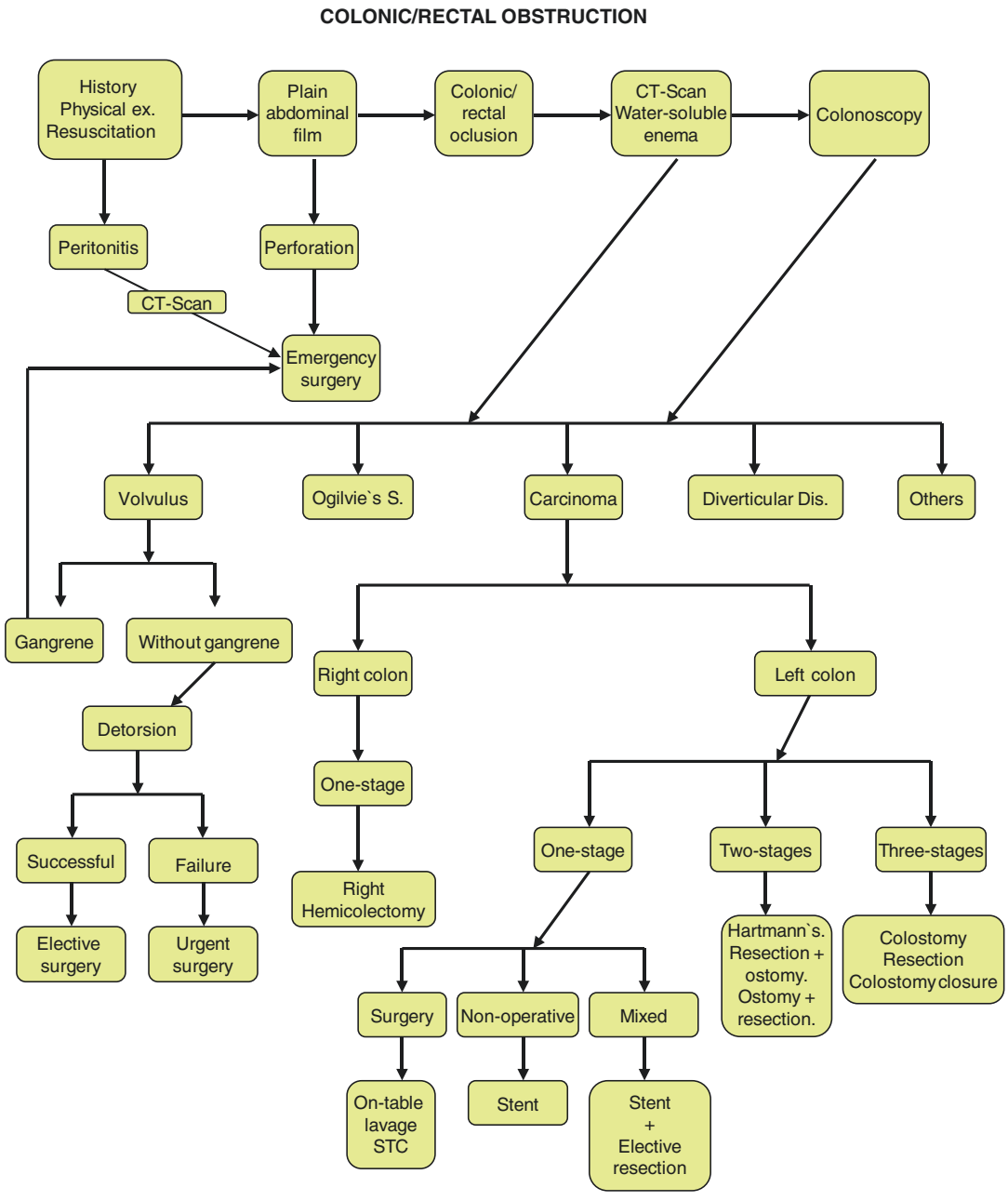


Fig. 33.2 Management of colorectal (large-bowel) obstruction

occurs. They include an inability to pass gas and feces, colicky abdominal pain and abdominal distension, anorexia, asthenia, bloody stool and rectal bleeding, changes in bowels habits and the diameter of feces, tenesmus, abdominal mass and/or marked weight loss, jaundice, ascites, and cough raising suspicion of a metastatic disease.

Whether the tumor is located in the right or left colon can also affect the clinical picture. The former presents with obstruction of the small bowel and the latter with obstruction of the large bowel.

33.6.3 Diagnosis

The stepped procedures mentioned above for a general diagnosis should be followed. A patient's history usually reveals a drawn-out evolution, with changes in bowel habits over several months. Results of the physical examination depend mainly on the tumor stage and duration of symptoms: signs of cachexia, malnutrition, and dehydration can be found, or, on the contrary, the patient's general health status may be preserved. Prompt resuscitation could be necessary.

Abdominal distension is usually present with loud borborygmus. In some cases a mass can be palpated, corresponding to the site of the tumor. Rebound tenderness in the right lower quadrant can be caused by a pre-perforated cecum or local gangrene. A digital rectal examination may identify and characterize the tumor.

Laboratory studies (including carcinoembryonic antigen) should be requested. CT is the most useful tool in the case of a large-bowel obstruction caused by a colorectal cancer (especially using triple contrast: intravenous, oral, and rectal), helping in the clinical staging or the differential diagnosis with diverticulitis [6] (Fig. 33.3). A water-soluble contrast enema could be considered if CT is not available or in cases of a dubious diagnosis. Flexible endoscopy may be useful if the colon distal to the obstruction can be prepped with enemas. It allows for biopsies.

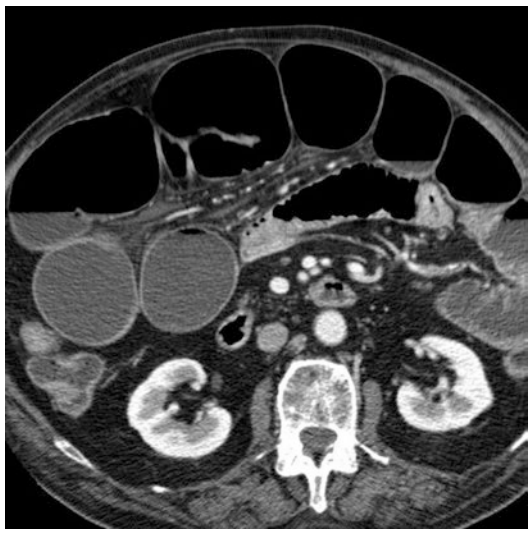


Fig. 33.3 Large-bowel obstruction (local recurrence of rectal cancer)

33.6.4 Treatment

In the case of a partial colonic/rectal obstruction caused by colorectal cancer, patients can be initially managed conservatively, with appropriate reanimation and bowel preparation, allowing an elective surgical procedure. Complete obstruction requiring early and urgent treatment has a higher morbidity and mortality and worse survival rates than partial obstruction [5]. Surgical procedures are mostly used, but nonsurgical procedures such as endoscopic stenting (introduced in the early 1990s) are also useful to relieve obstruction. Stent placement before elective surgery as a bridge to surgery is an alternative to emergent surgery in patients with acute left-sided malignant colonic obstruction. However, because its benefits are uncertain, there is no consensus about the most appropriate therapeutic options to select [7]. Several options are currently available to permit a one-stage procedure, avoiding the inconvenience directly related to multistaged procedures performed in the past, requiring at least one temporary stoma. These procedures are, however, far from being abandoned.

33.6.4.1 Conservative Treatment

To minimize the risks associated with surgical treatment of patients with LBO, there has been a trend toward decompressing the colon before surgery, allowing an emergency situation in an unstable patient to be converted into an elective one, and in the mean time avoiding the need for a stoma. This can be accomplished by laser tumor ablation or by endoscopic stent placement to canalize a neoplastic obstruction.

Stent insertion is today the most commonly used nonsurgical endoluminal technique [8]; the need for repeated treatment sessions and the risk of complications have limited the widespread acceptance of laser dilatation. Stents have been increasingly applied since their introduction in the early 1990s, bridging patients from emergency

to elective surgery [9] by reestablishing the intestinal lumen and allowing thorough bowel preparation before surgery. Bowel function is restored immediately after the stent is inserted. Despite its efficacy in resolving distal LBO (technical and clinical success rates of stent placement are around 70 %), the results of different randomized controlled trials, multicenter studies, meta-analyses, and systematic reviews comparing stent insertion and emergent surgery are conflicting [7, 10–15]. No firm conclusions can be drawn concerning morbidity, mortality, need for stomas, primary anastomosis, complications, oncological outcomes, and technical and clinical success rates. Further evaluation and studies are needed to elucidate which group of patients could benefit most from stent insertion or emergency surgery, since high-grade evidence is currently sparse [16]. As a whole, however, this technique seems to compare favorably with surgery [15]. Colonic stents are also used as a palliative and definitive treatment in patients in whom surgery should be avoided because of significant comorbidities, incurable malignancy, or nonresectable cancer. Although debatable, endoluminal stent insertion seems to be a cost-effective technology, especially when skills to implement this approach are present, with a high rate of successfully relieving obstruction in the vast majority of patients [15].

33.6.4.2 Surgical Treatment

Right-sided colonic obstructive cancers (cecal, ascending, and transverse colonic lesions proximal to the splenic flexure) are usually treated with resection and primary anastomosis (right hemicolectomy). This is the procedure of choice, except in cases of perforation or gangrene and peritonitis (a primary anastomosis is contraindicated in this setting) that are best managed by resection, end ileostomy, and exteriorization or closure of the proximal colon, with subsequent restoration of intestinal continuity (Table 33.2).

It is difficult to formulate recommendations for the surgical treatment of left-sided lesions. The discussion centers on multiple-staged operations versus one-stage procedures as the preferred approach (Table 33.2). LBOs in this location have been managed for years by multistaged (three- and two-stage) surgical procedures: initial diversion followed by a staged procedure or resection without primary anastomosis followed by the restoration of colonic continuity. There has recently been an increasing trend toward a single-stage procedure (segmental resection and primary anastomosis after colonic lavage or subtotal colectomy) – conceptually the ideal surgical strategy – if performed safely [14].

Three-Stage Procedure

Since a three-stage procedure involves three operations (construction of a defunctioning colostomy, resection with anastomosis, closure of the colostomy) and a prolonged hospital stay, its use has been almost abandoned. Eventually, however, this strategy could still play a role for high-risk patients or less experienced surgeons.

Two-Stage Procedure

A two-stage procedure always implies a stoma formation: primary resection with the creation of an end colostomy (the Hartmann procedure) followed by restoration of intestinal continuity [13], or primary resection with anastomosis and the creation of a defunctioning stoma, followed by closure of the stoma. As an alternative, a proximal diversion can be done (usually a transversostomy), allowing for adequate patient resuscitation and complete investigation followed by an early elective resection with a primary anastomosis [17]. Following this approach, however, intestinal continuity is restored in only 70 % of patients.

One-Stage Procedure

When a one-stage procedure is an option, the goal is best accomplished by on-table lavage followed by segmental resection and anastomosis [18]. Even under certain conditions this procedure can be done safely without intraoperative colonic irrigation [19]. A subtotal colectomy should be reserved for patients with cecal ischemia/perforation or with right-sided concomitant tumors because of the increased number of bowel movements that occur after such a procedure. It must be avoided in the case of compromised fecal continence [18]. The indications for a one-stage procedure remains debatable; multistage

Table 33.2 Current treatment recommendations for neoplastic colorectal obstruction

	Right-sided lesions	Left-sided lesions
One-stage procedure	Resection with primary anastomosis (right hemicolectomy)	Resection with primary anastomosis (on-table lavage)
		Resection with primary anastomosis (subtotal colectomy)
		Colonic stenting followed by elective surgery (resection with primary anastomosis)
Two-stage procedure	Resection with end ileostomy and secondary restoration of intestinal continuity (if gangrene or perforation are present)	Resection with colostomy, reestablishment of intestinal continuity (Hartmann procedure)
		Resection with anastomosis with diversion ostomy, closure of ostomy
		Initial proximal diversion, secondary bowel resection including tumour and stoma site, followed by primary anastomosis

procedures are still used mainly for severely ill patients, those with associated conditions, or in the case of bowel gangrene or fecal peritonitis (patients classified as having an ASA III or IV physical status).

33.6.5 Prognosis

Perioperative and long-term survival are both adversely affected in patients with LBO. Regardless of tumor stage at the time of surgery, perioperative mortality is higher in patients with LBO operated in emergency conditions (15–30 %) than in those with nonobstructive carcinomas (<10 %) as a consequence of increased surgical risk. The same is also true for the crude overall survival at 5 years, which is approximately 30 % (around 35 % after curative surgery). Only 40–50 % of obstructing tumors are operated on with an intent to cure – far from the 70 % of those without obstruction. Although acute complete LBO does not have a *major* impact on prognosis, it is nonetheless an independent prognostic factor to consider when deciding on postoperative chemotherapy. Other variables affect the prognosis for patients with LBO, some of which are common to nonobstructive colorectal carcinomas: colonic perforation, advanced-stage tumor, poor tumor differentiation, mucinous characteristics, and vascular and neural invasion.

33.7 Colonic Volvulus

33.7.1 Definition

Colonic volvulus is caused by an abnormal twisting of the affected segment of bowel along its longitudinal mesocolic axis. This creates a partial or total intestinal obstruction with significant vascular compromise, possibly leading to ischemia and gangrene of the colonic segment. It may occur in any part of the colon but is most commonly located in the sigmoid colon (75–80 %), followed by the cecum (15–20 %) and other, rarer sites (2–3 %) [20, 21].

33.7.2 Epidemiology-Etiology

Volvulus is an important cause of colonic occlusion worldwide [20, 21]. The incidence varies considerably, according to the population; it is extremely prevalent (50–80 %) in the Middle East, Africa, and parts of Europe and Brazil (the so-called Volvulus Belt), with a minor incidence in Western Europe and the United States (1–5 %). It is rare among children and adolescents; it is mostly a disorder of the elderly. Sigmoid volvulus occurs predominantly in patients who are 70 years of age and older, whereas cecal volvulus arises, on average, 10 years earlier. Fifty percent of concerned patients have had a previous episode.

There is no clear etiology, but certain factors are known to predispose to colonic volvulus. For a sigmoid volvulus, the presence of a long, mobile, redundant loop of sigmoid with a narrow mesocolic base is often found. It is usually acquired rather than congenital, and it facilitates the twisting of the mesocolon, usually clockwise. For a cecal volvulus, an incomplete or absent retroperitoneal fixation with a mobile cecum and ascending colon is usually found. This suggests a congenital defect that allows the mesentery to twist around the ileocolic artery axis or fold upward (cecal bascule). Other causative factors include a high-fiber diet (as consumed in the Volvulus Belt), constipation, a sedentary lifestyle, Parkinson disease, psychotropic drug use, internment in a psychiatric institution (or nursing home, for the elderly), Chagas and Hirschsprung diseases, and, in some cases, pregnancy (cecal volvulus).

33.7.3 Symptoms

Signs and symptoms vary according to whether the occlusion is complete, whether the ileocecal valve is competent (closed loop), and whether ischemia or intestinal necrosis is present. A patient may present with pronounced abdominal distension and discomfort and an inability to pass gas and feces, or may complain of constant pain, suggesting necrosis and peritonitis. Vomiting occurs in cecal volvulus; the clinical picture is that of a small-bowel obstruction. Fever, dehydration, hemodynamic changes, abdominal tenderness, and shock suggest ischemia or secondary perforation of the volvulus. Gangrene must be prevented because it increases the mortality rate by three to four times.

33.7.4 Diagnosis

On physical examination, abdominal findings are generally nonspecific. In addition to marked distension, intestinal meteorism with visible peristalsis may be observed, and bowel sounds with a metallic tone may be intensified. Peritoneal signs suggest colonic gangrene.

Plain abdominal radiographs are diagnostic or highly suggestive of volvulus (in 70–90 %), especially in sigmoid volvulus. On imaging, the sigmoid resembles a bent tube, with the apex pointing toward the left iliac fossa, or the cecum resembles a coffee bean. Cecal volvulus is usually associated with distended loops of small bowel. Diagnosis is confirmed using a water-soluble contrast enema, with the typical finding of a "bird-beak" appearance of the sigmoid at the point of torsion along the neck of the volvulus. The "twisted tape" sign strongly supports a recurrence of a sigmoid volvulus [22].

If volvulus of the sigmoid or left colon is suspected, flexible sigmoidoscopy or colonoscopy is diagnostic and usually therapeutic. These should not be performed if colonic perforation is suspected. The examination will show a twist of mucosal folds about 15–25 cm from the anal verge, indicating the disorder. Bloody fluid and ischemic mucosa suggest gangrene.

CT and magnetic resonance imaging can be additional diagnostic aids, especially with a three-dimensional reconstruction; they have an accuracy of about 100 % [23]. Both exams can reveal intestinal distension and the level of obstruction, and can demonstrate the mesenteric twist, visualized as a mass of soft tissue in the shape of a "whirl" (the "whirl" sign).

33.7.5 Treatment

33.7.5.1 Sigmoid Volvulus

The timing and nature of therapy depend on whether signs of gangrene or colonic perforation are present and whether endoscopic detorsion is effective. If signs of perforation are found, surgery is mandatory and urgent. The procedure consists of a segmental resection with stoma (the Hartmann procedure). When these serious complications are not present, the strategy is based on decompression and detorsion of the affected segment, followed in most cases by elective surgery. Endoscopic detorsion is successful in 80–90 % of cases. Rigid proctoscopy or flexible sigmoidoscopy may be used, but the latter procedure is preferred because it better visualizes the affected

area and can treat volvuli higher up in the bowel. Detorsion may succeed or fail. If it fails, surgery is indicated: resection of the sigmoid with primary anastomosis (with or without on-table lavage) or, less frequently, the Hartmann procedure [21].

The question arises of how to proceed after successful detorsion. If nothing more is done, the recurrence rate is over 50 %. Therefore surgery is recommended for most patients who suffer a colonic volvulus, usually within 2 days after the initial successful detorsion. Several surgical procedures have been described. Compared with resection, nonresection alternatives – simple detorsion, open or laparoscopic detorsion with colopexy or mesosigmoidoplasty, extraperitonealization of the colon, percutaneous endoscopic colostomy – result in lower morbidity/mortality but a higher recurrence rate. Thus, whenever the general status of the patient permits, a resection procedure should be chosen, mainly segmental resection with primary anastomosis (the gold standard), with a mean mortality of 8 %, a mean recurrence of 1.2 %, and a mean morbidity of 21.2 % [21]. In the case of associated megacolon, a subtotal colectomy with ileorectal anastomosis is preferred (Fig. 33.4).

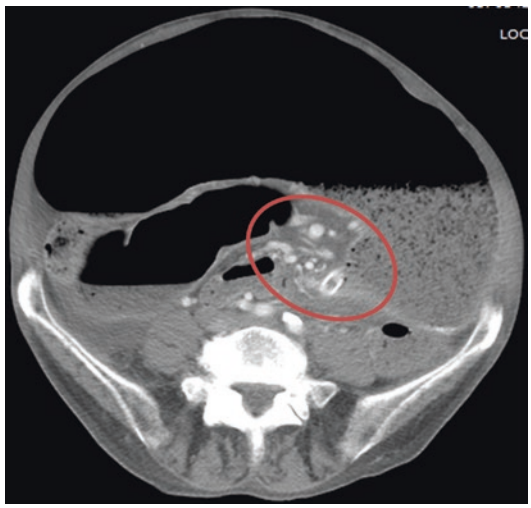


Fig. 33.4 Computed tomography scan of a sigmoid volvulus (notice the whirl sign of the twisted pedicle of the sigmoid)

33.7.5.2 Cecal Volvulus

Colonoscopic detorsion of a cecal volvulus may be attempted but is usually unsuccessful. A contrast enema for diagnostic purposes may occasionally be therapeutic. Since gangrenous changes are often seen during surgery (20–40 %), these procedures are contraindicated in daily practice. Surgery is frequently needed because of ischemia and should not be delayed. It involves resection of the colon with primary anastomosis (right hemicolectomy) [20]. Anastomosis should be avoided only in the case of fecal peritonitis, in which the option is resection with terminal ileostomy. In the absence of ischemia, resection procedures with primary anastomosis are preferred, given their obvious advantages over nonresectional methods – simple detorsion, detorsion with cecopexy, detorsion with cecostomy – with respect to their lower rates of recurrence and complications.

33.8 Other Conditions

Other conditions may cause LBO. They are described, along with their management, in dedicated chapters, including acute colonic pseudo-obstruction (O'Gilvie syndrome), diverticular disease (see Chap. 17), inflammatory bowel disease, radiation damage, fecal impaction and foreign bodies, endometriosis (see Chap. 20), and extrinsic expanding lesions (ovarian, bladder, or prostate cancers; noncolonic metastatic lesions).

Conclusion

Colorectal obstruction is much less frequent than small-bowel obstruction. Colorectal cancer is the main cause in Western countries. Colorectal obstruction is a serious condition that needs careful and prompt diagnostic and therapeutic measures to obviate harmful complications or even death (gangrene and perforation should be avoided). Recent technological innovations (on-table lavage, colonic stents) have changed the therapeutic strategy, with a marked benefit for patient outcomes. There is now a trend toward using single-stage procedures instead of a multi-

stage approach, the rationale being to reduce the morbidity inherent to the latter. Multistage procedures should, however, remain the preferable option for severely ill patients, those with associated conditions, or in the case of bowel gangrene or fecal peritonitis. The preferred approach should be selected on an individual basis and tailored to the particular situation. Understanding the various etiological hypotheses, as well as the clinical presentation and the use of appropriate tests, make selecting the best treatment option possible.

References

1. Cataldo PA. Large bowel obstruction. Sem Colon Rectal Surg. 2001;12:140–53.
2. Sawai RS. Management of colonic obstruction: a review. Clin Colon Rectal Surg. 2012;25:200–3.
3. Yeo HL, Lee SW. Colorectal emergencies: review and controversies in the management of large bowel obstruction. J Gastrointest Surg. 2013;17:2007–12.
4. Gash K, Chambers W, Ghosh A, et al. The role of laparoscopic surgery for the management of acute large bowel obstruction. Colorectal Dis. 2011;13:263–6.
5. Douglas JM, Stahl TJ. Obstructing cancer: overview and prognosis. Sem Colon Rectal Surg. 2001;12:154–7.
6. Frager D, Rovno HD, Baer JW, et al. Prospective evaluation of colonic obstruction with computed tomography. Abdom Imaging. 1998;23:141–6.
7. Frago RD, Ramirez E, Millan M, et al. Current management of acute malignant large bowel obstruction: a systematic review. Am J Surg. 2014;207:127–38.
8. Sagar J. Colorectal stents for the management of malignant colonic obstructions. Cochrane Database Syst Rev. 2011;11, CD007378.
9. van den Berg MW, Sloothaak DA, Dijkgraaf MGW, et al. Bridge-to-surgery versus emergency surgery for acute malignant colonic obstruction. Br J Surg. 2014;101:867–73.
10. Tan CJ, Dasari BVM, Gardiner K. Systematic review and meta-analysis of randomized clinical trials of self-expanding metallic stents as a bridge to surgery versus emergency surgery for malignant left-sided large bowel obstruction. Br J Surg. 2012;99:469–76.
11. Ye G-H, Cui Z, Chen L, et al. Colonic stenting vs emergency surgery for acute left-sided malignant colonic obstruction: a systematic review and meta-analysis. World J Gastroenterol. 2012;18:5608–15.
12. Cirochi R, Farinella E, Trastulli S, et al. Safety and efficacy of endoscopic colonic stenting as a bridge to surgery in the management of intestinal obstruction due to left colon and rectal cancer: a systematic review and meta-analysis. Surg Oncol. 2013;22:14–21.
13. Huang X, Lv B, Zhang S, et al. Preoperative colonic stents versus emergency surgery for acute left-sided malignant colonic obstruction: a meta-analysis. J Gastrointest Surg. 2014;18:584–91.
14. Ye G-H, Cui Z, Chen L, et al. Perforation in colorectal stenting: a meta-analysis and a search for risk factors:. Gastrointest Endosc. 2014;6:970–82.
15. Matsuda A, Miyashita M, Matsumoto S, et al. Comparison of long-term outcomes of colonic stent as "bridge to surgery" and emergency surgery for malignant large-bowel obstruction: a meta-analysis. Ann Surg Oncol. 2015;22:497–504.
16. Grundmann RT. Primary colon resection or Hartmann's procedure in malignant left-sided large bowel obstruction? The use of stents as a bridge to surgery. World J Gastroenterol. 2013;5:1–4.
17. Chereau N, Lefevre JH, Lefrancois M, et al. Management of malignant left colonic obstruction: is an initial temporary colostomy followed by surgical resection a better option? Colorectal Dis. 2013;15:e646–53.
18. SCOTIA Study Group. Single-stage treatment for malignant left-sided colonic obstruction: a prospective randomised clinical trial comparing subtotal colectomy with segmental resection following intraoperative irrigation. Br J Surg. 1995;82:1622–7.
19. Fuertes MJ, Navarro DC. Resection and primary anastomosis without diverting ileostomy for left colon emergencies: is it a safe procedure? World J Surg. 2012;36:1148–53.
20. Ballantyne G. Review of sigmoid volvulus: history and results of treatment. Dis Colon Rectum. 1982;25:494–501.
21. Raveentiran V, Madiba TE, Atamanalp SS, et al. Volvulus of the sigmoid colon. A review of 93 cases and current aspects of treatment. Colorectal Dis. 2010;12:e1–17.
22. Gopal K, Lim Y, Banerjee B. "Twisted tape sign": its significance in recurrent sigmoid volvulus. Review of sigmoid volvulus. Radiography. 2005;11:272–6.
23. Witherspoon P, Wright DM. Three-dimensional magnetic image guided percutaneous endoscopic sigmoidopexy for the treatment of recurrent sigmoid volvulus. Colorectal Dis. 2010;12:72–3.

Lower Gastrointestinal Bleeding: Diagnosis and Management

34

Eric Frampas and Paul-Antoine Lehur

34.1 Introduction

Gastrointestinal (GI) hemorrhages are divided according to the location of bleeding. Upper hemorrhages originate from the esophagus to the upper jejunum at the level of Treitz ligament, whereas lower hemorrhages include the small bowel, colon, and rectum. Modes of presentation vary from occult bleeds detected by a positive fecal occult blood test or iron-deficiency anemia test to massive bleeding associated with a life-threatening condition. Acute GI bleeding is a major cause of hospital admission, estimated in some US studies at 300,000 patients annually [1]. Although acute upper GI hemorrhage is more common, the annual incidence of lower GI bleeding ranges from 20.5 to 27 episodes per 100,000 persons. It accounts for approximately 30 % of all reported cases of GI bleeding. Its incidence increases with age and is more frequent in men than women [2]. Overall mortality varies from 8 % to 16 %, but can reach 40 % in the case of massive bleeding, especially in patients with associated comorbid conditions and advanced age [3].

E. Frampas
Central Department of Radiology and Medical Imaging, Nantes Cedex 1, France

P.-A. Lehur (✉)
Institut des Maladies de l'Appareil Digestif, University Hospital of Nantes – Hôtel-Dieu, 1, place Ricordeau, 44093 Nantes cedex 01, France
e-mail: paulantoine.lehur@chu-nantes.fr

Clinical presentation varies depending on the blood volume lost and the location of bleeding, and this may complicate the differentiation between upper and lower GI bleeding. It is generally accepted that 80 % of lower GI bleeding will resolve spontaneously [4]. Lower GI bleeding typically manifests as hematochezia or rectal bleeding. Bright red hematochezia tends to originate from the left side of the colon and anorectum. Dark-colored blood or blood mixed with stool may originate from the right colon and may be associated with melena in the case of small-intestine bleeding. Nevertheless, in the event of a massive lower GI bleed with hemodynamic instability, a source either proximal or distal to the ligament of Treitz should be considered and explored.

34.1.1 Causes of Lower GI Bleeding

Numerous etiologies have been reported for lower GI bleeding. Frequently encountered causes include diverticular disease, colonic vascular ectasia, inflammatory or ischemic colitis, colonic neoplasia, or bleeding after polypectomy.

34.2 Colonic Lesions

- Diverticular disease concerns nearly 65 % of the Western population by the age of 65 years. Hemorrhage occurs during the course of

© Springer-Verlag Berlin Heidelberg 2017

A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_34

diverticular disease in 20% of patients, but only 5% will suffer from severe hemorrhage, with spontaneous resolution in 70–80% of cases. Nevertheless, the cumulative risk of rebleeding is 25% after 4 years. Arterial hemorrhage is caused by erosion of the vasa recta at the dome or neck of the saclike diverticula. Because diverticular disease is so frequent, one may question the real implication of diverticula in lower GI bleeding: based on undoubted endoscopic criteria of bleeding such as active bleeding, an adherent clot, or a visible vessel, diverticula were found to be causative in 22% of cases of acute lower GI bleeding [5].

- Vascular Lesions
  - *Angiodysplasia*: This is a common source of GI bleeding. Asymptomatic colonic angiodysplasia is found in about 1% of patients undergoing colonoscopy (Fig. 34.1). Rare before age 60, the incidence increases with age, especially in the elderly [6]. Most are acquired vascular lesions that predominate in the right colon and correspond to abnormal thin-walled, tortuous arteriovenous vessels that develop in the superficial layers of the bowel wall. The pathophysiology remains unclear. Because most of angiodysplasias do not bleed spontaneously, factors favoring this condition, such as coagulopathy disorders, nonsteroidal anti-inflammatory drug use, antiplatelet or anticoagulant therapies, should be investigated [7]. An association with several diseases has been reported, including chronic renal failure, scleroderma, Crest syndrome, Turner syndrome, and portal hypertension. The association with aortic valve stenosis is still debated.
  - *Hemangiomas and vascular malformations* (Figs. 34.2, 34.3, and 34.4): GI hemangiomas are uncommon benign vascular tumors. They may occur as a single or multiple lesions along the intestinal tract; the small bowel is the most common site of occurrence, followed by the colon. Association with syndromes such as a rubber bleb nevus or Kippel-Trenaunay syndrome has to be investigated in cases of multiple lesions. Most are pedunculated, polypoid intraluminal masses, but they may also have an infiltrative growth pattern. Insidious or acute bleeding is the major complication [8].
- *Postradiation colitis*: This is a major complication of pelvic organ radiotherapy, especially following cervical or prostate cancer. Radiation induces endarteritis obliterans, fibrosis of the submucosal layer of the bowel, ischemic endarteritis, and neovascularization associated with the development of telangiectasis in 5–20% of cases. Four to 13% of

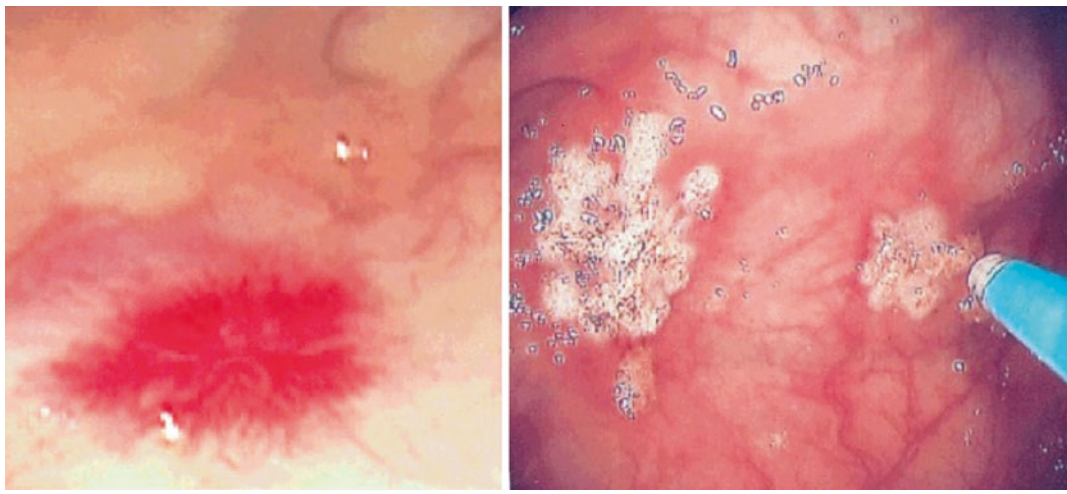


Fig. 34.1 Colonic telangiectasia. Endoscopic views before and after argon plasma therapy

patients report rectal bleeding following radiation therapy for prostatic carcinoma, most often several years after therapy.

- *Ischemic colitis*: This is a common cause of lower GI bleeding and typically affects the elderly. Risk factors include atherosclerosis, embolic disease, chronic renal failure, insufficient flow, or recent high-risk surgery [9]. The splenic flexure and rectosigmoid junction are typically affected. Stercoral colitis is a specific condition that typically affects old patients. Overdistension of the rectal lumen by severe fecal impaction leads to rectal ischemia, bleeding, and perforation [10].
- *Neoplasias*: Most neoplasias are responsible for occult or chronic lower GI bleeding. They account for 2–9 % of hematochezia [11]. Hemorrhage originates from tumor erosion and mucosal ulceration. In the case of high-stage carcinoma with local invasion, involvement and erosion of adjacent arteries may lead to acute lower GI bleeding.
- *Postpolypectomy bleeding*: This is the most frequent complication of colonoscopy and has been reported in 2–8 % of acute lower GI bleeding. Risk factors include the size and gross morphology of the polyp, the cutting mode of the electrosurgical current, inadvertent cutting before the current was applied, associated comorbidity, and the experience of the endoscopist [12].
- *Inflammatory bowel disease*: Acute bleeding is rare in inflammatory bowel disease, with an incidence of 0.9–6 %. Acute bleeding is more frequent in Crohn's disease because ulcers form deeper in the wall compared with ulcerative colitis with respectively 1.2 % and 0.1 % of hospitalization stay use eventually Hospitalization. Spontaneous cessation occurs in 50 % of cases, but rebleeding will occur in 35 % of cases.

34.3 Anorectal Lesions

- Rectal varices may occur in the setting of cirrhosis and portal hypertension, with a prevalence between 40 % and 77 %, but these are rarely responsible for acute lower GI bleeding (Fig. 34.5). In 2–9 % of patients, hemorrhoids are responsible for the bleeding [10].
- Dieulafoy lesion, a typical lesion of the upper stomach, may be discovered in the rectum. Bleeding is caused by a tiny erosion of an abnormally large submucosal end artery within a minute mucosal defect. Contrary to peptic ulcer, the absence of inflammation at the point of erosion and the small size of the mucosal defect make it difficult to locate in the absence of active bleeding [13].

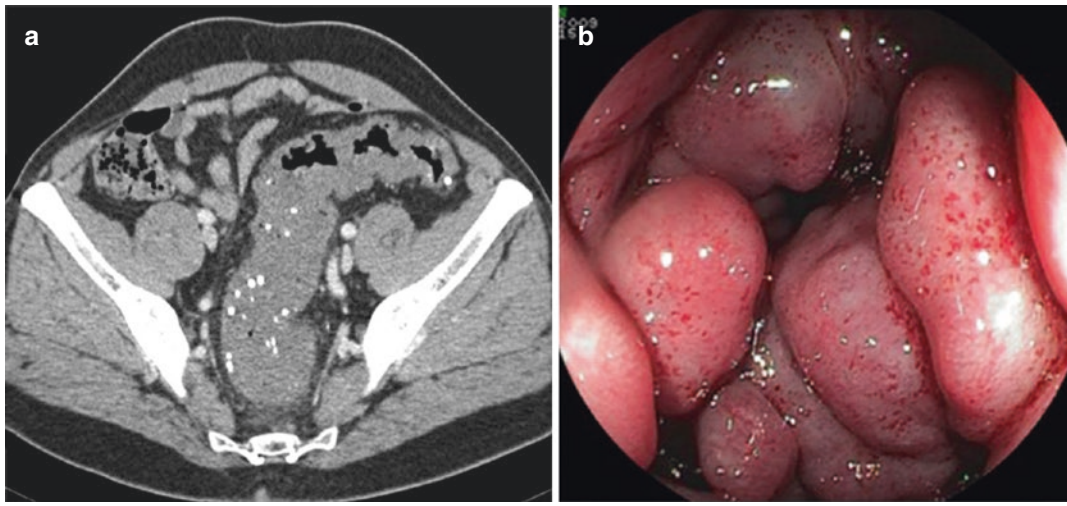


Fig. 34.2 Colonic angiomatosis. (**a**) Enhanced axial multidetector computed tomography showing rectosigmoid wall thickening with multiple clusters of phleboliths. (**b**) Endoscopic view

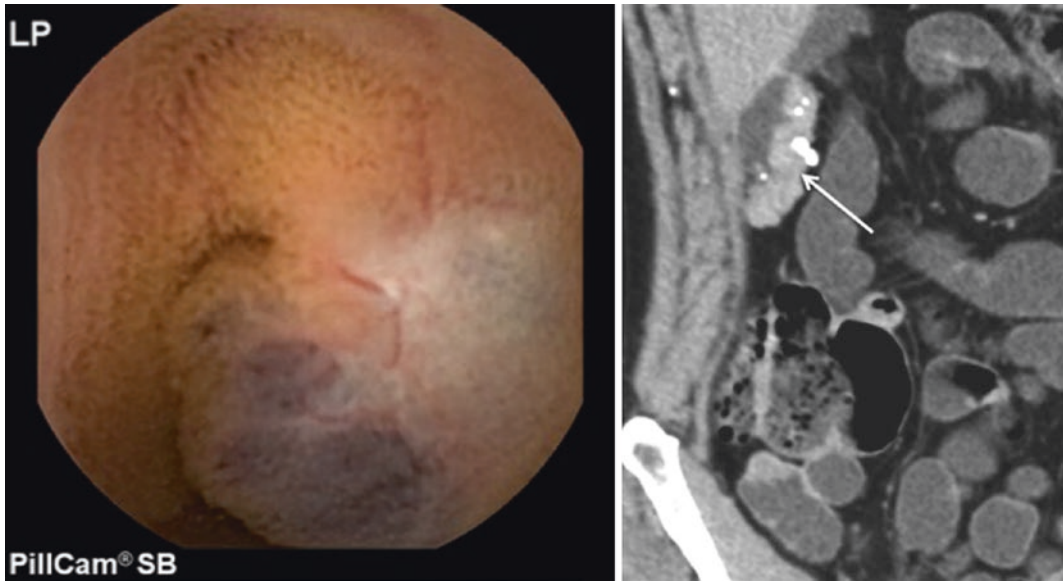


Fig. 34.3 Small-bowel hemangioma in a 40-year-old adult. Enhanced coronal multidetector computed tomography showing a lobulated mass with phleboliths (*arrow*)

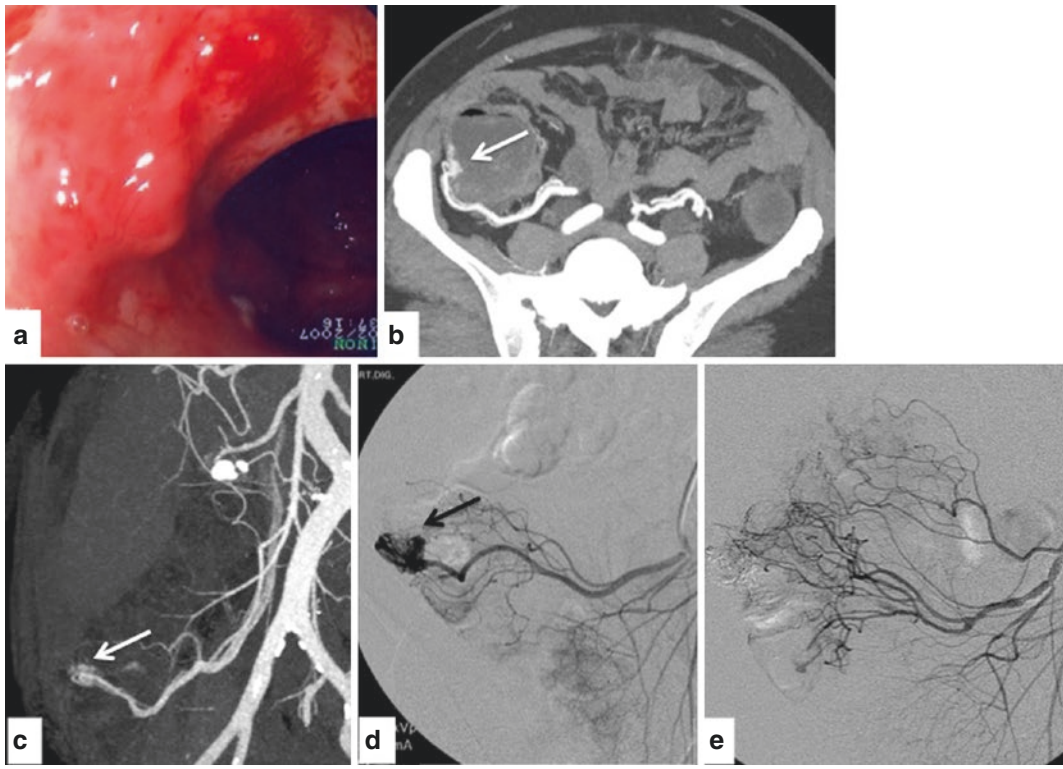


Fig. 34.4 Arteriovenous malformation of the right colon. (**a**) Endoscopic view. (**b**) Axial MIP enhanced axial MDCT view. Enhanced vascular wall lesion with arterial and venous abnormal vessels (*arrow*). (**c**) Coronal MIP vascular reconstruction. (**d**, **e**) Digital selective angiography before and after selective embolization

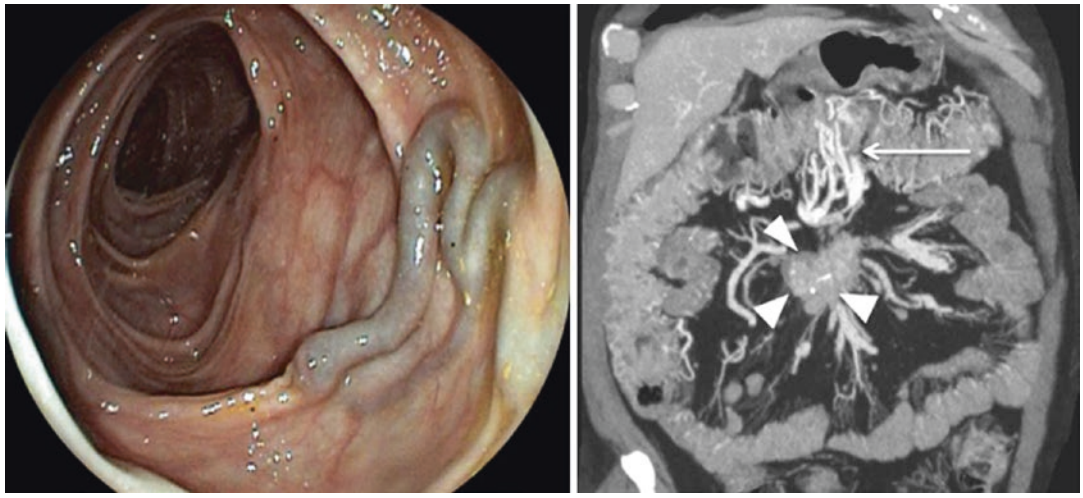


Fig. 34.5 Recurrent lower gastrointestinal bleeding in a 60-year-old adult. Colonic varices (*arrow*) caused by segmental venous mesenteric hypertension are complicating a small-bowel carcinoid tumor with a retractile mesenteric mass (*arrowheads*). Endoscopic view and enhanced coronal Maximum Intensity Projection (MIP) multidetector computed tomography view

34.4 Small-Bowel Lesions

A majority of lower GI bleeding arises from the colon and rectum. Nevertheless, 10–25 % of these bleeds may arise from the small bowel or proximal to the angle of Treitz.

- Angiodysplasia is the most common source of small-bowel bleeding, found in 30–60 % of reported cases, followed by tumors in 5–10 % of cases.
- In children, special attention should be devoted to Meckel diverticulum, which occurs in 2–3 % of the population. Lifetime risk of developing complications has been estimated at 4 % up to the age of 20 years, 2 % up to the age of 40 years, and 0 % in the elderly population. Hemorrhage is the most common complication, especially in the pediatric population. Ectopic gastric mucosa located inside the diverticulum produces gastric acid and may induce mucosal damage and bleeding.

34.4.1 Chronic versus Acute Bleeding

A wide range of underlying diseases may be the source of lower GI bleeding. Diagnosis and management differ depending on the type of bleeding (Tables 34.1 and 34.2).

- In the case of chronic or recurrent bleeding, determining the origin of the bleeding may be challenging. Diagnostic tools include endoscopy, radionuclide imaging, abdominal multidetector computed tomography, wireless capsule endoscopy, and double-balloon enteroscopy.
- Acute lower GI bleeding has been defined as a recent bleeding situation (within 3 days) and may result in instable vital signs, anemia, or the need for a blood transfusion. Although patients with lower GI bleeding classically present with less hemodynamic instability compared with patients with upper GI bleeding, anemia and hemodynamic instability are present in one-half of patients and cardiovascular collapse in 9 % [14]. Factors predicting a severe course include hemodynamic instability (heart rate ≥100 bpm, blood pressure <100 mmHg), syncope, initial hematocrit ≤35 %, active gross bleeding from the rectum, and more than two active associated comorbid conditions [15, 16].

In the presence of acute lower GI bleeding, clinical evaluation and resuscitation should be initiated before diagnostic evaluation [17]. This

Table 34.1 Assess the severity of a lower gastrointestinal bleeding

Massive bleeding per anum of red blood with or without clots + Haemodynamic compromise
Blood pressure ≤100 mmHg
± Pulse rate ≥100/min
± Hemoglobin <10 g/dL
± 6–8 units of blood required to stabilize the patient

Table 34.2 Some definitions

Chronic lower GI bleeding
Minor, melena, or hematochezia
Chronic anemia
Acute lower GI bleeding
Brisk, significant bleeding
Occurring in the past 3 days
Self limited; resolves spontaneously, allowing for investigations
Massive lower GI bleeding
Massive and continuous hemorrhage with the need for urgent resuscitation
Rule out an upper GI cause of bleeding (10–15 % of cases)
Occult/obscure lower GI bleeding
Cause not found, even with advanced investigations
5 % of cases
Could be massive and intermittent

take into account the patient's history, intake of antiplatelet or anticoagulant therapy, vascular disease, and the duration and frequency of previous bleedings. Physical examination should focus on the patient's vital signs. In the case of clinical evidence of acute bleeding or associated high comorbidity, patients should be monitored in an intensive care unit [18]. Management includes treatment of coagulopathy, volume replacement, and transfusions before the source of bleeding is investigated. In contrast to acute upper GI bleeding, only a few risk scores have been developed to accurately forecast the outcome of a patient with acute lower GI bleeding in terms of risk of recurrent bleeding, intensive management, and mortality. Useful tests include the Bleed classification system (based on ongoing bleeding, low systolic blood pressure, elevated prothrombin time, erratic mental status, and unstable comorbid disease), clinical risk factors, and an artificial neural network [19–21].

34.4.2 Investigations and Treatments

The goals of investigations for lower GI bleeding are (1) to identify the source of the bleed and (2) to allow its permanent treatment. Endoscopic and imaging techniques (nuclear scintigraphy, computed tomography angiography, and catheter angiography) are both of interest. Today they not only play a role in localizing and identifying the cause of bleeding but also are an important part of bleeding management; each of these approaches addresses the various types of bleeding. Because only specialist centers can offer the full range of these advanced procedures, patients who specifically require them must be identified. An algorithm addresses this selection process [22] (Fig. 34.6).

34.5 Endoscopy

34.5.1 Diagnostic Endoscopy

Endoscopy is considered as the investigation of choice. In acute lower GI bleeding, pan–upper GI endoscopy is mandatory to rule out a potential source of bleeding in the upper GI tract [23]. The use of a nasogastric tube and gastric lavage to exclude an upper GI source of bleeding is no longer recommended. Colonoscopy has been proposed as the first-line modality for diagnosis and therapy of lower GI bleeding. Because 80 % of hemorrhages will cease spontaneously, an elective colonoscopy is often indicated after standard bowel preparation. The accuracy of colonoscopy in identifying definitively the source of bleeding varies between 45 % and 90 % [24]. In the case of acute bleeding, the timing of colonoscopy is urgent. It may be hampered by incomplete preparation or poor observation of the colonic wall as a result of a massive hemorrhage. Urgent endoscopy has been defined as occurring within 12–48 h of admission. Earlier completion of colonoscopy has been associated with greater yield and shorter length of hospital stay [15].

Rapidly purging the colon through a nasogastric tube or by mouth has been recommended to facilitate mucosal observation and improve diagnostic yield. Although urgent colonoscopy can be performed without preparation, Jensen et al. [5] reported a significant reduction in sensitivity in cases of insufficient preparation and successful treatment in as few as 21 % of cases.

34.5.2 Therapeutic Endoscopy

Diagnostic colonoscopy can be associated with endoscopic hemostasis. Depending on the site and cause, several modalities are available, including thermal coagulation, injection of hemostatic agents, and mechanical devices. Thermal coagulation with bipolar electrocoagulation, argon plasma, and laser-mediated coagulation are the preferred methods for vascular lesions, especially angiodysplasia. Epinephrine injection and metal clips are recommended for diverticular disease or bleeding after polypectomy, with a limited risk of complication. The accuracy of hemostasis by endoscopic therapy in diverticular hemorrhage is 95 %, without morbidity, but recurrent bleeding is observed in more than 25 % of cases [25].

Rectal varices and hemorrhoids are best treated with rubber bands and a sclerosing injection.

34.5.3 Wireless Capsule Endoscopy

In the case of negative upper and lower GI endoscopies, the small bowel should be investigated. Wireless capsule endoscopy is a painless tool that allows a noninvasive evaluation of the

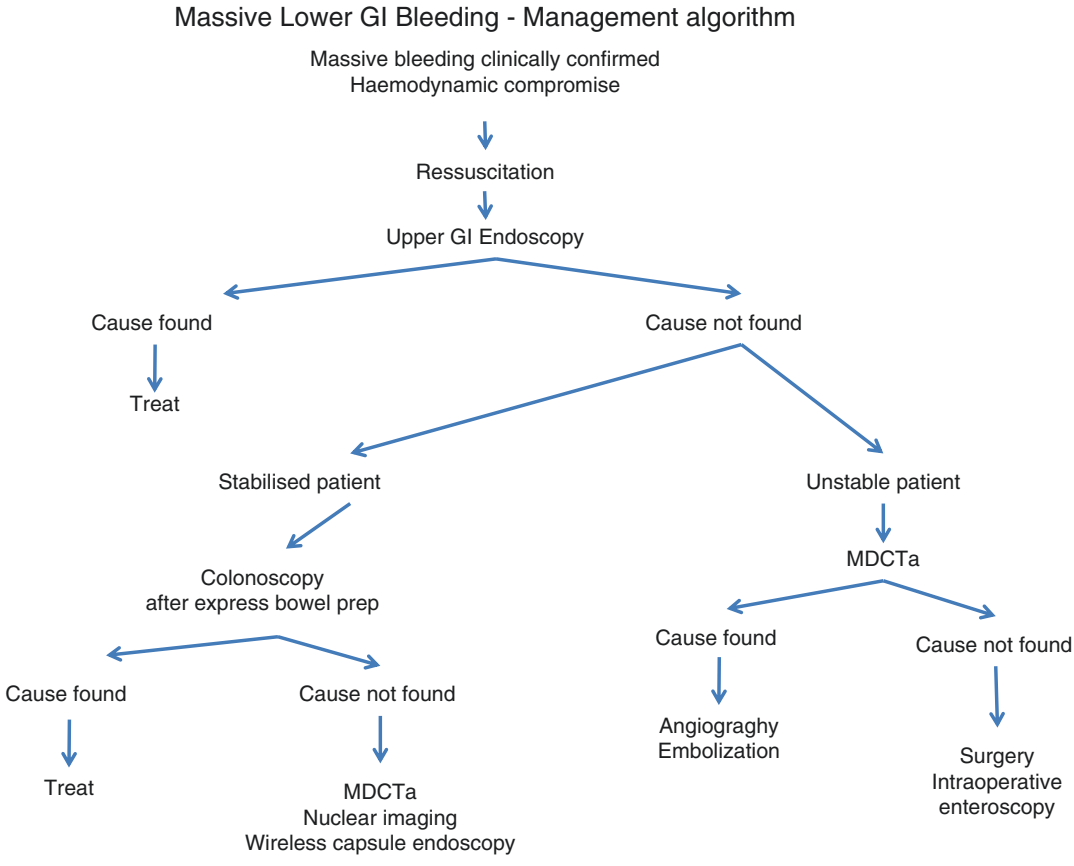


Fig. 34.6 Management algorithm for massive lower gastrointestinal bleeding

entire small bowel. A high diagnostic yield – more than 90 % – has been reported. Angiodysplasia is the most frequently observed lesion, found in up to 49 % of patients [26]. The best results were obtained in cases of ongoing obscure-overt bleeding (>90 %) and dropped to 12.9 % in cases of previous overt bleeding, in parallel with the duration of the interval since the bleeding episode began. Wireless capsule endoscopy seems to be superior to push-enteroscopy. The main contraindication is a bowel stricture. A 5 % rate of non-natural excretion has been reported.

34.6 Imaging

34.6.1 Nuclear Medicine

Radiolabeled technetium 99m – sulfur colloid – and labelled autologous red blood cell (RBC) scintigraphy has been used for more than 20 years as a method for localizing GI bleeding (Fig. 34.7). With a longer half-life, ^{99m}Tc RBCs allows intermittent bleeding to be detected and has become the standard of reference for the detection of active lower GI bleeding. Radionuclide scanning is a noninvasive method that can detect both arterial and venous bleeding

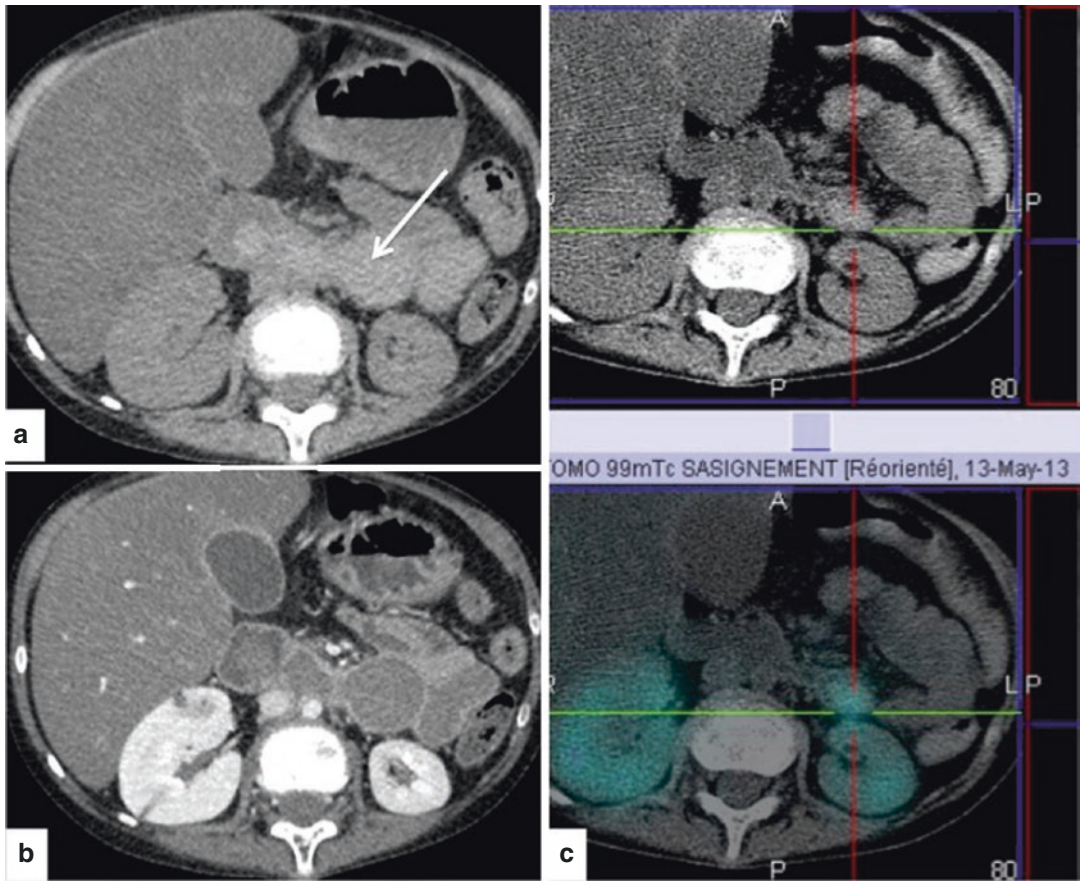


Fig. 34.7 A 10-year-old patient suffering from acute leukemia has recurrent, severe lower gastrointestinal (GI) bleeds. Upper and lower GI tract endoscopies failed to localize the site of bleeding. (**a**) Unenhanced multidetector computed tomography depicts a spontaneous hyperattenuating area (*arrow*) inside the jejunal lumen, corresponding to intraluminal clotted blood without an abnormality of the bowel wall after contrast medium injection. (**b**) Tc^{99m}-radiolabeled autologous red blood cell (RBC) scintigraphy identified the site in the proximal jejunum. (**c**) Small, superficial ulcers were discovered by enteroscopy

over a prolonged period of time without special preparation. The threshold rate of bleeding for scintigraphy is 0.1 mL/min in clinical studies. However, it is a time-consuming method with a relative imprecise anatomic location, as blood may spread proximally and distally from the site of the bleed on sequential static images. Accuracy drops from 95–100 % to 57–67 % when scans are positive within 2 h after the injection of RBCs compared with positive scans after more than 2 h. The accuracy of positive scans from pooling data was 41–97 %. In young adults and children, scintigraphic imaging based on ^{99m}Tc pertechnetate may be useful to detect a Meckel diverticulum because ^{99m}Tc pertechnetate is actively secreted by the mucous cells present within the heterotopic gastric mucosa. Diagnostic sensitivities range between 50 % and 86 % [27]. A lower sensitivity has been reported in the adult population.

34.6.2 Angiography and Multidetector Computed Tomography Angiography

Used for more than 40 years to investigate GI bleeding, angiography is often used when endoscopy fails to detect the site of bleeding. Rates of detection with angiography have been reported to be 58–86 %, depending on the bleeding rate (0.5–1.0 mL/min being considered necessary to demonstrate contrast extravasation), the number of blood transfusion units (>6), and blood pressure level [28]. Due to the invasiveness of angiography and the intermittent nature of GI bleeding, multidetector computed tomography angiography (MDCTa) has been developed to characterize location and cause of bleeding. It offers a number of advantages: lower invasiveness, wider availability, greater rapidity especially to evaluate unstable patients. High spatial and temporal resolution of MDCTa, multiphase acquisition with arterial and portal venous phase images are required to detect GI bleeding. A lower threshold of depicting active bleeding has been recently reported (0.35 mL/min) compared with angiography (0.96 mL/min) in vitro [29].

As for angiography, MDCTa should be performed while the patient is actively bleeding. No specific preparation, oral contrast, or colonic contrast material are needed. Active GI hemorrhage is defined as an active extravasation of contrast medium with a focal intraluminal area of high attenuation. Unenhanced phases provide information concerning spontaneous, hyperattenuating foci, including suture material, clips, foreign bodies, and hyperattenuating feces within diverticula, to avoid false-positive results.

As for conventional angiography, severe bleeding episodes with hemodynamic instability increase the probability of a positive result on MDCTa. Combining unenhanced with arterial and portal venous phases offers numerous advantages: comparison of different phases to depict, appreciate, and confirm the changing appearance of the focus of extravasated contrast medium; increase the blushes depicted on the portal venous phase as a result of delayed acquisition; and potential depiction of the cause of bleeding (diverticulosis, bowel tumor, vascular lesion) or associated pathologies (cirrhosis, portal hypertension) (Fig. 34.8).

Arterial GI bleeding appears as a focal area of high attenuation (>90 HU) during the arterial phase and increases during the portal venous phase. Spontaneous attenuations of clotted blood appear lower (mean, 54 HU), making the differentiation of active arterial extravasation from blood clots possible. In a meta-analysis of nine studies with 198 patients with acute GI bleeding, Wu et al. [30] reported a pooled sensitivity of 89 % (95 % confidence interval: 82–94 %) and a specificity of 85 % (95 % confidence interval: 74–92 %)30, similar to that reported with conventional angiography. By scanning the entire abdominal cavity, MDCTa allows the exploration of the entire bowel tract, notably the small bowel and extraluminal abnormalities. It is also informative regarding vascular anatomy and feeding and draining vessels. Moreover, it may be performed before interventional invasive angiography, enabling the radiologist to directly perform time-saving superselective angiograms and therapy. Copland et al. [31] proposed the

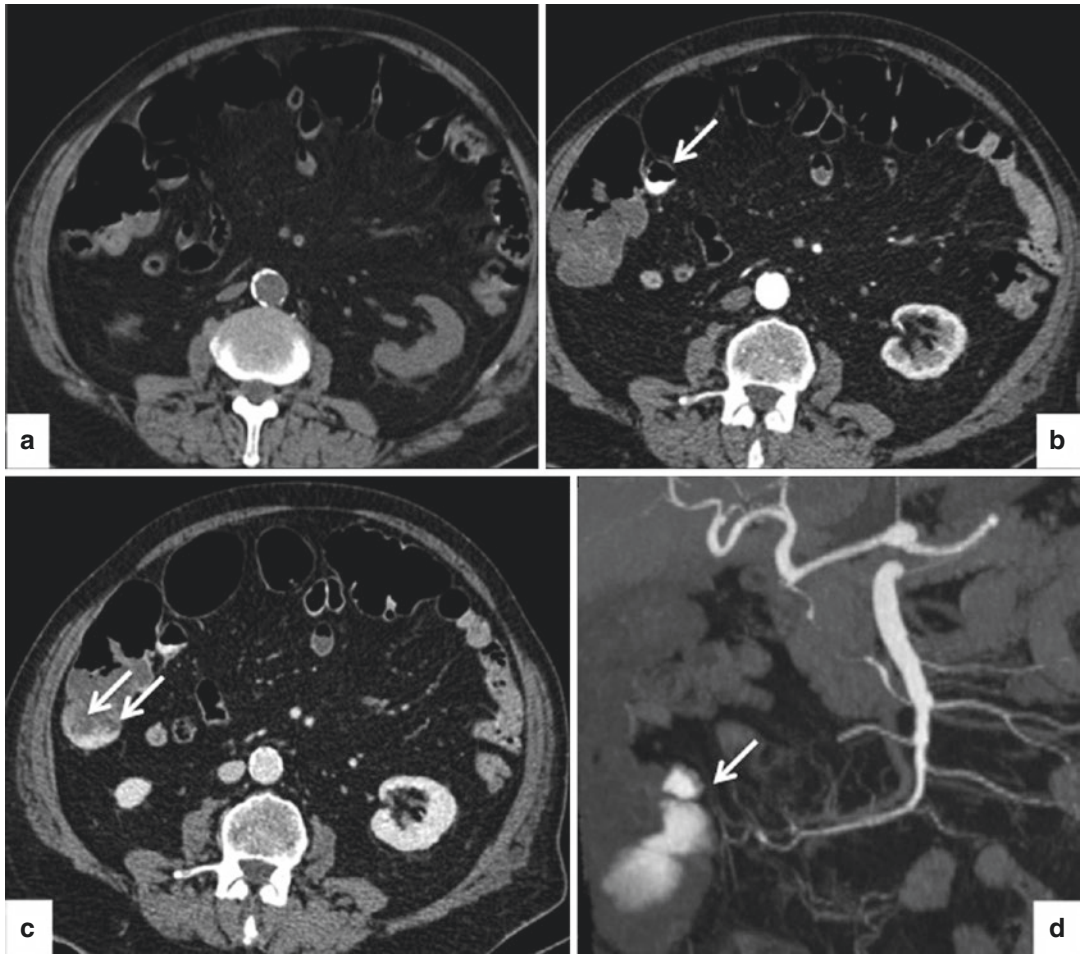


Fig. 34.8 Multidetector computed tomography angiography aspects of acute lower gastrointestinal bleeding originating from a right colonic diverticula. (**a**) Unenhanced view (absence of hyperattenuating foci). (**b**) Arterial phase with extravasated contrast medium inside the diverticula (*arrow*). (**c**) Portal phase with an increase in the blush within the colonic lumen (*double arrow*). (**d**) Corresponding coronal MIP view

incorporation of MDCTa early in the management of acute GI bleeding in conjunction with resuscitation. A positive result leads to more accurate endoscopic, angiographic, or surgical management of patients, depending on the location and cause. In the case of a negative result, colonoscopy could be performed after bowel preparation [31].

34.6.3 Therapeutic Angiography

Transcatheter arterial therapies are effective to interrupt blood flow. Vasopressin is a constrictor agent that directly acts on arterioles and capillaries. The intra-arterial infusion dose has to be adapted according to the bleeding rate, followed by a continued infusion for another 6–12 h. Bleeding ceases in 80 % of cases. Side effects of arterial constriction include myocardial ischemia, cerebral and renal arterial constriction, and bowel ischemia. Vascular embolization has recently been developed with several embolization materials (polyvinyl alcohol particles, gelatin sponges) and coils alone or in combination. In the case of nonselective embolizations of proximal branches, colonic ischemia was reported in up to 20 % [17]. Therefore

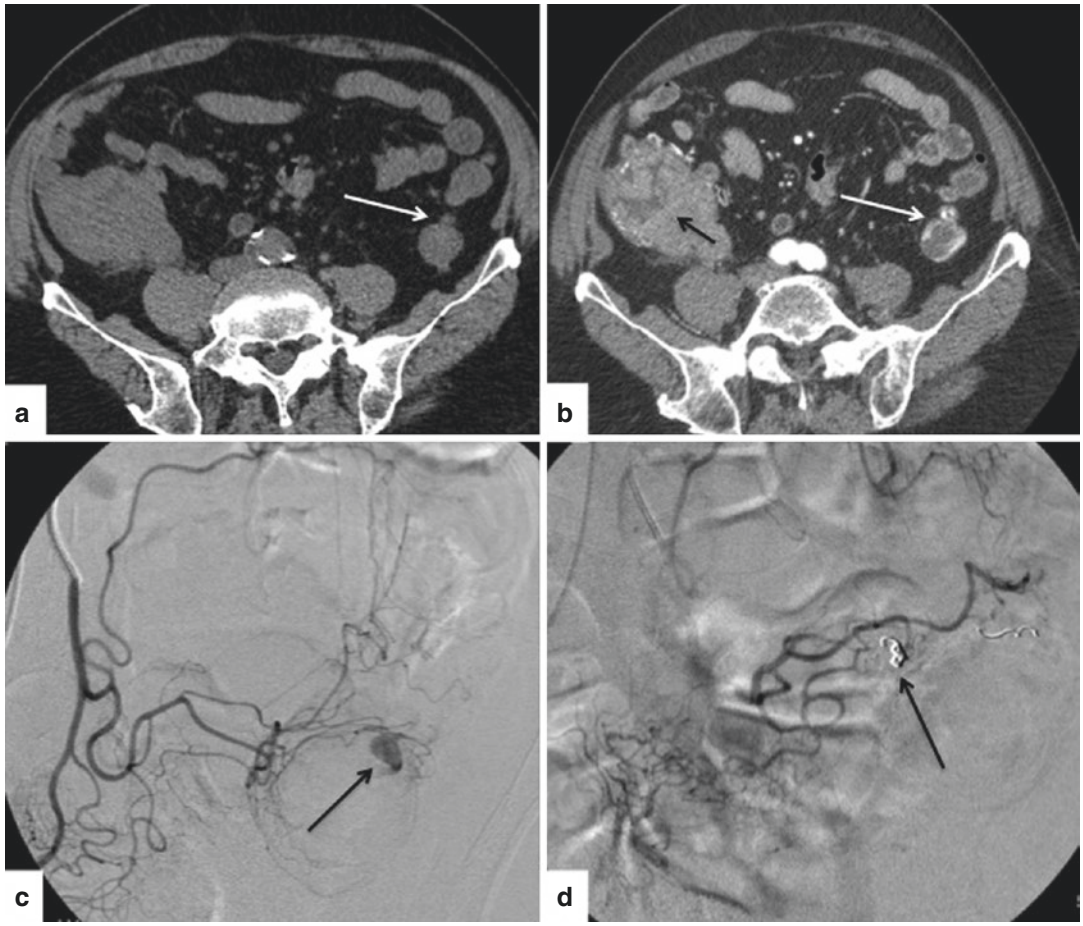


Fig. 34.9 An 80-year-old patient with acute lower gastrointestinal bleeding. (**a**, **b**) Unenhanced and arterial enhanced axial multidetector computed tomography angiography shows bleeding originating from a left colonic diverticula (*white arrow*). There is an associated finding of a right colonic adenocarcinoma (*black arrow*). (**c**, **d**) Digital selective angiography of the inferior mesenteric artery depicting contrast medium extravasation (*black arrow*). Successful embolization with microcoils (*white arrow*)

hyperselective embolization is now recommended. The development of microcatheters allows the catheterization of small branches of the visceral arterial tree proximal to the bleeding site. Microcoils offer the advantages of good radiopacity and the possibility of more precise deployment compared with Gelfoam pledgets and particulate agents. Hyperselective embolization allows high performance yields with successful control of bleeding in 80–90 % of patients and rebleeding rates of 14 %, without major complications [32]. Arterial embolization is now considered a first-line therapy for patients with massive GI bleeds [17] (Figs. 34.9, 34.10, 34.11, and 34.12).

34.7 Operative Strategy

Surgery is required in up to 18–25 % of patients with acute lower GI bleeding who require blood transfusion. Surgery should be considered under two circumstances [18]:

- In patients with ongoing bleeding and failure of interventional treatment

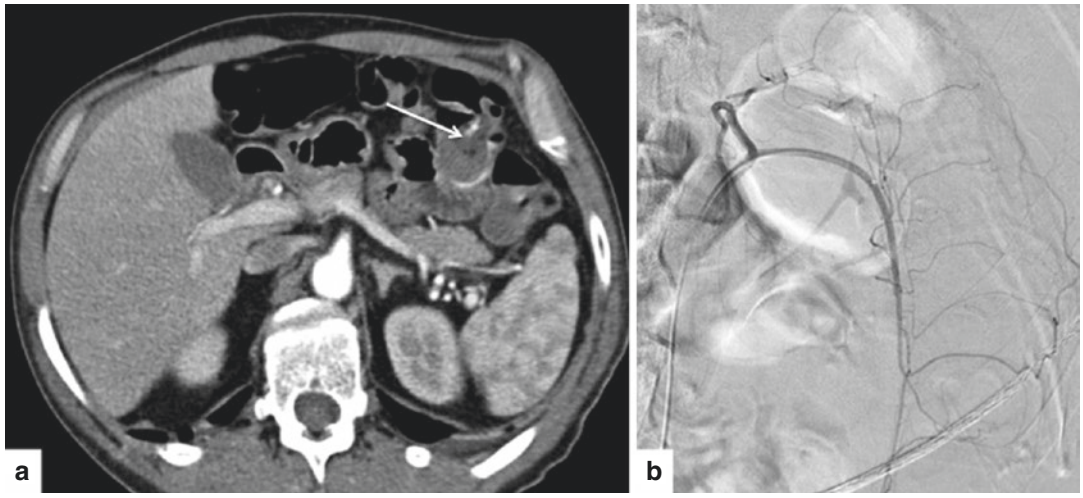


Fig. 34.10 Arterial bleeding complicating an endoscopic per-colonoscopic polypectomy. Axial Multidetector computed tomography angiography depicted a focal area of extravasated contrast medium (**a**, *arrow*). No blush was found during therapeutic angiography (**b**). No embolization was performed. Bleeding spontaneously resolved

- In patients who suffer from recurrent severe bleeding [18]

Locating the bleeding site before surgery is critical because segmental colectomy can be performed, contrary to subtotal colectomy, which has a higher mortality rate (20 %) but less risk of recurrent bleeding. Surgery is usually recommended after a second episode of bleeding from diverticular disease because the risk of a third one exceeds 50 % [33].

When preoperative imaging or endoscopic modalities fail to detect the source of bleeding, intraoperative enteroscopy should be planned and associated with laparotomy as a last option with a high diagnostic yield (80–92 %) [34].

Surgery is associated with significant mortality (10–25 %) and morbidity. Recurrent bleeding is not uncommon in segmental resections, leading some to recommend subtotal colectomy with or without anastomosis, depending on the patient's intraoperative condition. Identified factors predicting death are a delay in the decision to operate, the transfused blood required (ten units seem to be critical), and comorbidities.

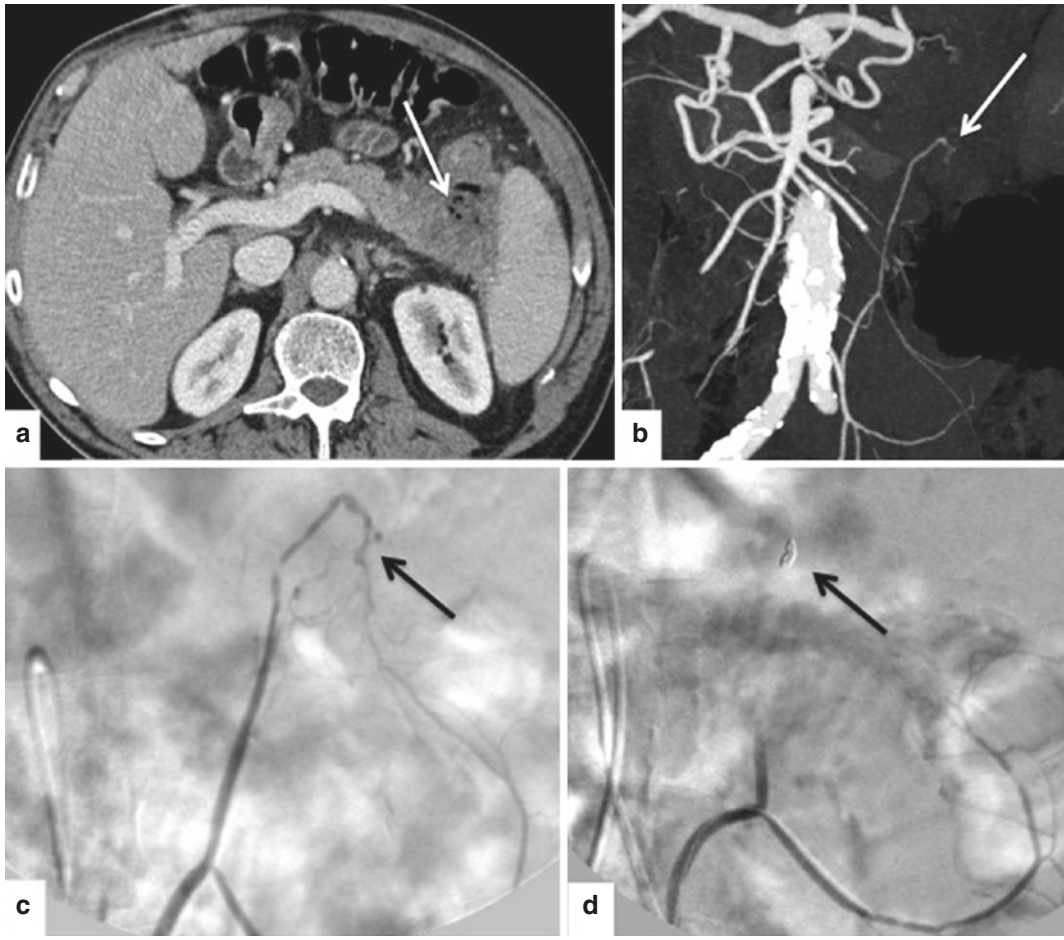


Fig. 34.11 Acute lower gastrointestinal bleeding from the left colonic wall involved with a pancreatic carcinoma. (**a**) Axial enhanced axial view from multidetector computed tomography (MDCT) shows a pancreatic carcinoma invading the colon and spleen (*arrow*). (**b**) Coronal MIP reconstruction of MDCT angiography with abnormal acute arterial disruption of a branch of the inferior mesenteric artery (*white arrow*). (**c**) Corresponding selective angiography. (**d**) Successful selective embolization with a microcoil (*arrow*)

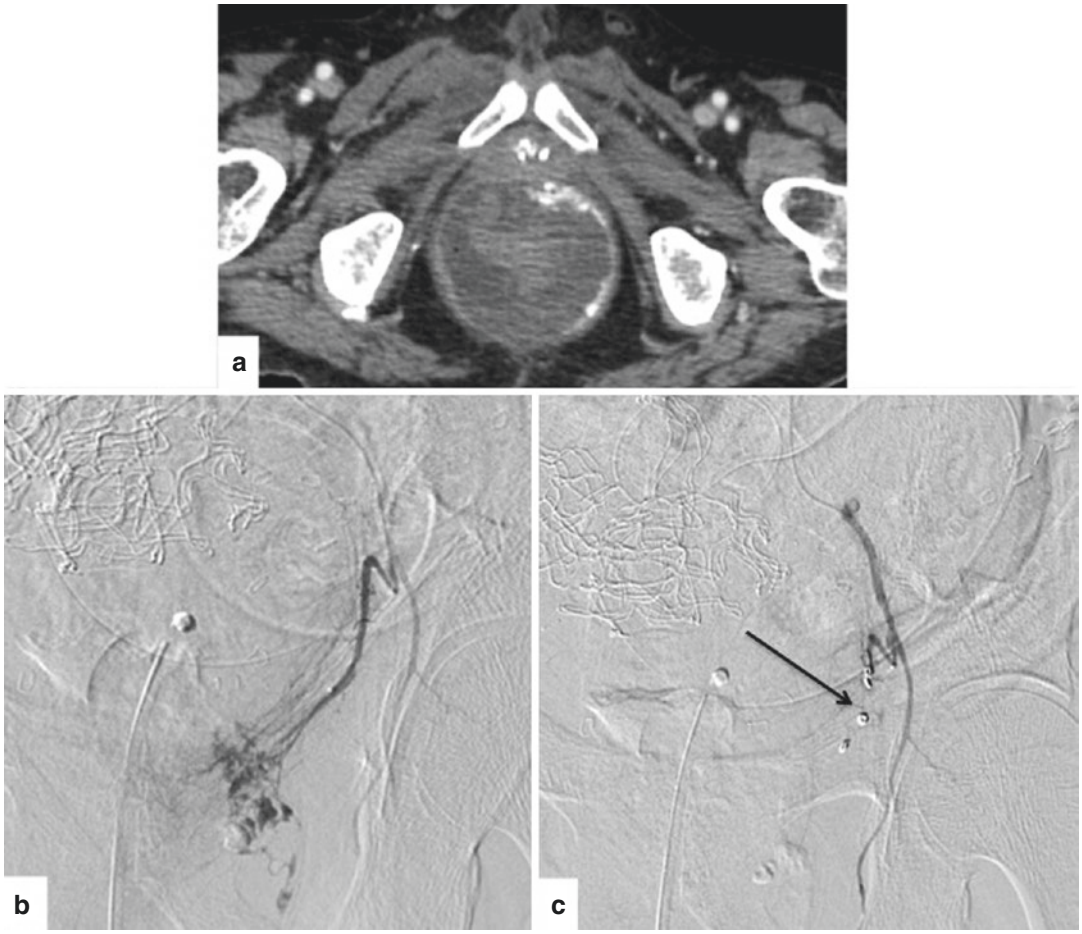


Fig. 34.12 Acute rectal bleeding following subtotal colectomy for ulcerative colitis. (**a**) Axial view of multidetector computed tomography angiography with acute extravasation of contrast medium. (**b**) Selective angiography of the inferior rectal artery demonstrated distal extravasation. (**c**) Successful selective embolization with microcoils

Conclusion

Although most lower GI bleeds resolve spontaneously, acute and massive bleeding still results in significant morbidity and mortality. Optimal management requires a multidisciplinary approach for diagnosis and treatment. Nonsurgical therapeutic options include conservative medical management, endoscopic procedures, and transcatheter embolization. Colonoscopy remains a diagnostic and therapeutic tool of choice in the management of patients with lower GI bleeding. Imaging modalities including MDCTa and transcatheter arterial embolization have strengthened the emergency management of acute GI bleeding. MDCTa has emerged as an accurate imaging modality that can detect the source of bleeding, and it is now incorporated in the diagnostic algorithm for active hemorrhage. It has become the first step in therapeutic angiography, allowing faster localization and embolization. Superselective catherization and embolization is a safe and highly successful procedure. Surgery, a high-risk option, should be limited during the acute phase of uncontrolled bleeding.

References

1. Manning-Dimmitt LL, Dimmitt SG, Wilson GR. Diagnosis of gastrointestinal bleeding in adults. Am Fam Physician. 2005;71:1339–46.

2. Farrell JJ, Friedman LS. Review article: the management of lower gastrointestinal bleeding. Aliment Pharmacol Ther. 2005;21:1281–98.
3. Edelman DA, Sugawa C. Lower gastrointestinal bleeding: a review. Surg Endosc. 2007;21(4):514–20.
4. Zuccaro G. Management of the adult patient with acute lower gastrointestinal bleeding. Am J Gastroenterol. 1998;93(8):1202–8.
5. Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med. 2000;342:78–82.
6. Regula J, Wronska E, Pachlewski J. Vascular lesions of the gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2008;22(2):313–28.
7. Kwan V, Bourke MJ, Williams SJ, Gillespie PE, Murray MA, Kaffes AJ, et al. Argon plasma coagulation in the management of symptomatic gastrointestinal vascular lesions: experience in 100 consecutive patients with long-term follow-up. Am J Gastroenterol. 2006;101:58–63.
8. Levy AD, Abbott RM, Rohrmann Jr CA, Frazier AA, Kende A. Gastrointestinal hemangiomas: imaging findings with pathologic correlation in pediatric and adult patients. AJR Am J Roentgenol. 2001;177:1073–81.
9. Chavalitdhamrong D, Jensen DM, Kovacs TO, Jutabha R, Dulai G, Ohning G, et al. Ischemic colitis as a cause of severe hematochezia: risk factors and outcomes compared with other colon diagnoses. Gastrointest Endosc. 2011;74(4):852–7.
10. Daram SR, Lahr C, Tang SJ. Anorectal bleeding: etiology, evaluation, and management (with videos). Gastrointest Endosc. 2012;76(2):406–17.
11. Barnert J. Acute and chronic lower gastrointestinal bleeding. In: Messmann H, editor. Atlas of colonoscopy. Stuttgart: Thieme; 2006. p. 118–42.
12. Kim HS, Kim TI, Kim WH, Kim YH, Kim HJ, Yang SK, et al. Risk factors for immediate postpolypectomy bleeding of the colon: a multicenter study. Am J Gastroenterol. 2006;101(6):1333–41.
13. Abdulian JD, Santoro MJ, Chen YK, Collen MJ. Dieulafoy-like lesion of the rectum presenting with exsanguinating hemorrhage. Am J Gastroenterol. 1993;88(11):1939–41.
14. Bramley PN, Masson JW, McKnight G, Herd K, Fraser A, Park K, et al. The role of an open-access bleeding unit in the management of colonic haemorrhage. A 2-year prospective study. Scand J Gastroenterol. 1996;31(8):764–9.
15. Strate LL, Syngal S. Timing of colonoscopy: impact on length of hospital stay in patients with acute lower intestinal bleeding. Am J Gastroenterol. 2003;98(2):317–22.
16. Velayos FS, Williamson A, Sousa KH, Lung E, Bostrom A, Weber EJ, et al. Early predictors of severe lower gastrointestinal bleeding and adverse outcomes: a prospective study. Clin Gastroenterol Hepatol. 2004;2(6):485–90.
17. Barkun AN, Bardou M, Kuipers EJ, Sung J, Hunt RH, Martel M, Sinclair P. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152:101–3.
18. Marion Y, Lebreton G, Le Pennec V, Hourna E, Viennot S, Alves A. The management of lower gastrointestinal bleeding. J Visc Surg. 2014;151:191–201.
19. Kollef MH, O'Brien JD, Zuckerman GR, Shannon W. BLEED: a classification tool to predict outcomes in patients with acute upper and lower gastrointestinal hemorrhage. Crit Care Med. 1997;25:1125–32.
20. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med. 2003;163:838–43.
21. Das A, Ben-Menachem T, Cooper GS, Chak A, Sivak Jr MV, Gonet JA, et al. Prediction of outcome in acute lower gastrointestinal haemorrhage based on an artificial neural network: internal and external validation of a predictive model. Lancet. 2003;362:1261–6.
22. Eisen GM, Dominitz JA, Faigel DO, Goldstein JL, Kalloo AN, Petersen BT, et al. ASGE standards of practice committee. An annoted algorithmic approach to acute lower gastrointestinal bleeding. Gastrointest Endoscop. 2001;53(7):859–63. revised Gastrointest Endosc 2005; 62(5):656–60.
23. Lee EW, Laberge JM. Differential diagnosis of gastrointestinal bleeding. Tech Vasc Interv Radiol. 2004;7(3):112–22.
24. Strate LL. Lower GI, bleeding: epidemiology and diagnosis. Gastroenterol Clin North Am. 2005;34:643–64.
25. Rustagi T, McCarty TR. Endoscopic management of diverticular bleeding. Gastroenterol Res Pract. 2014;2014:353508.
26. Apostolopoulos P, Liatsos C, Gralnek IM, Kalantzis C, Giannakoulopoulou E, Alexandrakis G, et al. Evaluation of capsule endoscopy in active, mild-to-moderate, overt, obscure GI bleeding. Gastrointest Endosc. 2007;66:1174–81.
27. Howarth DM. The role of Nuclear Medicine in the detection of acute gastrointestinal bleeding. Sem Nucl Med. 2006;36:133–46.
28. Abbas SM, Bissett IP, Holden A, Woodfield JC, Parry BR, Duncan D. Clinical variables associated with positive angiographic localization of lower gastrointestinal bleeding. ANZ J Surg. 2005;75:953–7.
29. Roy-Choudhury SH, Karandikar S. Multidetector CT of acute gastrointestinal bleeding. Radiology. 2008;246(1):336.
30. Wu LM, Xu JR, Yin Y, Qu XH. Usefulness of CT angiography in diagnosing acute gastrointestinal bleeding: a meta-analysis. World J Gastroenterol. 2010;16(31):3957–63.
31. Copland A, Munroe CA, Friedland S, Triadafilopoulos G. Integrating urgent multidetector CT scanning in the diagnostic algorithm of active lower GI bleeding. Gastrointest Endosc. 2010;72(2):402–5.
32. DeBarros J, Rosas L, Cohen J, Vignati P, Sardella W, Hallisey M. The changing paradigm for the treatment of colonic hemorrhage: superselective angiographic embolization. Dis Colon Rectum. 2002;45:802–8.
33. Wolff BG, Devine RM. Surgical management of diverticulitis. Am Surg. 2000;66:153–6.
34. Dulai GS, Jensen DM. Severe gastrointestinal bleeding of obscure origin. Gastrointest Endosc Clin N Am. 2004;14:101–13.

Chronic Pelvic and Perineal Pain

35

Guillaume Meurette and Jean-Jacques Labat

35.1 Definition

Chronic pain is a well-described situation, but the pathophysiology remains a matter of discussion in the literature. In fact, this debilitating situation affects a heterogeneous group of patients, and pain occurs in various situations. Moreover, patients often experience negative and repeated investigations that severely affect their relationship with physicians. The underlying cause of pain varies, and adapted management usually requires a multidisciplinary approach that should include coloproctological, urogynecological, and neurophysiological assessment along with input from a specialist in pain management. This multidisciplinary team approach is the key for global management of patients suffering from chronic perineal pain.

35.2 Introduction

Chronic pelvic and perineal pain can be defined as ongoing pain or severe discomfort located in the pelvic and/or perineal area that leads to psychological and social consequences during a period longer than 6 months. For the purposes of this chapter, pain from primary or recurrent malignant disease is not included.

35.3 Clinical Examination

The first step in a chronic pelvic pain assessment must be a complete medical history. The clinical history of the pain is of paramount importance. Any event possibly related to the pain must be considered and carefully noted in the medical chart. If related to a surgical operation, the time between the surgery and the onset of the pain should be determined. Successive medications must be listed and may affect the clinical perception of the pain's intensity.

It is also important to characterize the distribution (topography) of the pain (Fig. 35.1). Three anatomic distributions of pain can be identified:

- Pudendal nerve area
- Iliohypogastric area
- Inferior cluneal nerve area

Third, the nature of the pain must be identified and carefully investigated:

- *Inflammatory pain*: The pain is usually worse at night, causing sleep loss. No position eases the pain. Anti-inflammatory drugs can usually be effective in controlling the pain.

G. Meurette, MD, PhD (✉) • J.-J. Labat, MD, PhD
Institut fédératif de pelvi-périnéologie,
Nantes, France
e-mail: Guillaume.meurette@chu-nantes.fr

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_35

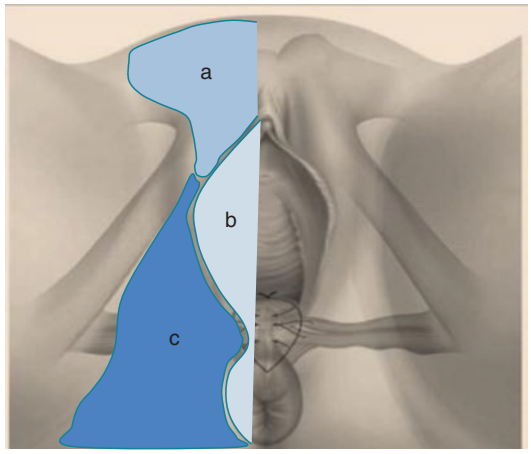


Fig. 35.1 Topography of perineal nerve distribution: (**a**) iliohypogastric area; (**b**) pudendal nerve area; (**c**) inferior cluneal nerve area

- *Mechanical pain*: The physical position usually influences the pain (sitting or standing position) and the decubitus position alleviates the symptoms.

Fourth, associated symptoms (urinary dysfunction, obstructed defecation, vaginal dryness, fecal and urinary incontinence) are sometimes helpful to correlate the pain to a global syndrome such as myofascial syndrome or complex chronic pelvic pain syndrome. Skin lesions and scars must be carefully investigated. Local infection is a common condition and may influence the pain.

Finally, the history of medications and treatments offered to the patient must be investigated.

The physical examination and subsequent investigations should exclude anatomic scars and abnormalities that could be related to malignant and inflammatory pelvic disease. Moreover, the complete physical examination should give careful attention to any congenital disorder (dysmorphia) or anorectal malformation.

35.4 Investigations

Investigations can include imaging, endoscopic, and functional investigations. Imaging is useful to exclude benign or malignant tumors. Vascular and inflammatory diseases can also be investigated and are helpful to confirm some diagnoses. Both computed tomography and magnetic resonance imaging are required standard imaging examinations. A particular focus on the lumbosacral spine is mandatory to identify anatomic abnormalities of the spine or compression of the cauda equine or lumbar and sacral roots. Particular attention must be paid to the presacral space, looking for possible tumors or bone metastasis.

Endoscopic investigations are useful to evaluate any mucosal abnormality. Colonoscopy, hysteroscopy, and cystoscopy should be performed based on associated symptoms and the topography of the pain.

Neurophysiological studies can be helpful in identifying nerve dysfunction. Pudendal nerve terminal motor latency, external anal sphincter electromyography, and the bulbospongiosus or clitoridoanal reflexes allow assessment of both the motor and sensory functions of the perineal and pelvic areas. Despite the value of these investigations, electromyography is invasive, and interpretation of the results may be difficult and related to the clinical features.

35.5 Classification

Several pain classifications are available in the literature (Table 35.1). The most common is based on the clinical characteristics of the pain.

35.5.1 Pain Influenced by the Sitting Position

35.5.1.1 Pudendal Nerve Entrapment

Pudendal nerve entrapment is the most frequent and best described cause of chronic pelvic pain. The topography of the pain is typically medial or unilateral and localized between the penis and the anus (in men) or the clitoris and the anus (in women). In men, the pain usually does not involve the scrotum or the testicles. The onset of pain occurs after a physical effort made while in a sitting position, such as cycling; this is typical

Table 35.1 Classification of nonorganic chronic pelvic and perineal pain

Pain influenced by the sitting position	Pain not influenced by the sitting position
Pudendal nerve entrapment	Sacral nerve irritation
Piriformis muscle syndrome	Abdominogenital pain
Coccygodynia	Vulvodynia
Obturator internis muscle syndrome	Urethral syndrome
Inferior cluneal (perineal) nerve syndrome	Paroxystic algias (proctalgia fugax)
Levator ani syndrome	Myofascial syndrome

of the pudendal nerve entrapment. Nevertheless, in several cases pain can occur with no particular triggering event. Pain is described as a burning or strangling feeling, either superficially or deep inside the perineum in the ipsilateral nerve area. It can be associated with signs of hypersensitivity upon touching the skin. A trigger zone can be found during the rectal digital examination portion of the physical exam, at the level of the ischial spine or sometimes while pressing the levator ani muscle.

A diagnosis is based on clinical findings, associated with improvement of the symptoms after pudendal nerve infiltration around the entrapment area at the ischial spine (Nantes criteria; Table 35.2). A diagnosis is also supported by the finding of prolonged pudendal nerve motor latency on electrophysiological studies.

35.5.1.2 Piriformis Syndrome

The posterior cutaneous nerve of the thigh can be entrapped into the subpiriformis canal. This entrapment may lead to chronic perineal pain that is often associated with perineal radiation into the cluneal (perineal) and/or pudendal nerve territories.

35.5.1.3 Coccygodynia

In the case of coccygodynia, the pain is usually located at the midline around and anterior to the coccyx. A coccyx trauma most likely occurred in the patient's medical history. Pressing the coccyx increases the pain, whereas standing and walking alleviate the symptoms. Clinical examination

Table 35.2 Nantes criteria for pudendal nerve entrapment

1. Pain in the territory of the pudendal nerve, from the anus to the penis or clitoris
2. Pain is predominantly experienced while sitting
3. The pain does not wake the patient at night
4. Pain with no objective sensory impairment
5. Symptoms are relieved after a pudendal nerve block

associated with dynamic radiography may show hypermotility of the coccyx and the sacrococcygeal space. Relief of symptoms after local anesthetic drugs infiltrate the sacrococcygeal space reinforces the hypothesized diagnosis of coccygodynia. Pelvic floor exercices, massage and analgesic infiltration. Coccygectomy is rarely necessary.

35.5.1.4 Obturator Internis Syndrome

The gluteal part of the obturator internis muscle is in close contact with the pudendal and obturator muscles. Muscle hypertonicity may result in nerve irritation. The pain is typically located in the perineal area and radiates into the sciatic nerve area. Clinical examination can confirm the diagnosis: it shows a significant increase in pain when pressing on the inside of the ischial tuberosity.

35.5.1.5 Inferior Cluneal (Perineal) Nerve Syndrome

The inferior cluneal (perineal) nerve has several connections with the posterior cutaneous nerve of the thigh. A lesion of this superficial nerve can lead to severe chronic pain in the posterior part of the thigh and under the buttock toward the lateral perineal area. The pain usually does not involve the vulva (in women) nor the anus.

35.5.1.6 Levator Ani Syndrome

This syndrome of chronic pelvic pain results in complaints of anorectal pain while sitting. This is typically associated with several anorectal symptoms such as tenesmus and mucous discharge. Defecation disorder is also associated with the pain.

35.5.2 Pain Not Influenced by a Sitting Position

35.5.2.1 Sacral Nerve Irritation

Sacral radiculopathy is usually associated with compression or irritation of the nerves of the sacral plexus. Loss of perineal sensation and difficulties with either defecation or micturition are serious clinical findings that should prompt urgent investigations (particularly magnetic resonance imaging of the lumbosacral spine) to identify the nerve compression.

35.5.2.2 Abdominogenital Pain and Myofascial Syndrome

Entrapment or compression of the ilioinguinal or iliohypogastric nerves can cause chronic pain that is often associated with dysesthesia or anesthesia at the inguinal and scrotal or labial cutaneous distribution of the nerve. The usual cause is a surgical injury during inguinal hernia repair. Local anesthesia administered along the surgical scar can confirm the diagnosis.

35.5.2.3 Vestibulodynia (Vulvar Vestibulitis)

A burning sensation localized at the vestibule represents the typical description of this pain. Tight clothes may be uncomfortable. Dyspareunia and vulvar hyperesthesia occur, usually in younger women. Vestibulodynia has profound effects on sexual function and emotional consequences.

35.5.2.4 Urethral Syndrome

In urethral syndrome, pain occurs during micturition or ejaculation. Those signs may be related to interstitial cystitis or chronic prostatitis.

35.5.2.5 Proctalgia Fugax

The diagnosis of proctalgia fugax is based on symptoms only, but they are well characterized. Pain is located at the anal canal and does not radiate. The pain usually begins suddenly and is severe, lasting for a few minutes, then abruptly stops. The whole period of pain is usually 15 min. A spasm into the internal anal sphincter or levator ani is often used to explain the syndrome. There is no specific treatment, although many patients find that bearing down or straining during an attempt to defecate increases the pain level. This condition is rarely associated with obstructed defecation.

35.6 Treatment

Treatment of chronic pelvic and perineal pain remains challenging because of the heterogeneity of the population concerned, because of the number of various causes, and in part because of the psychological consequences when medications and strategies fail (Fig. 35.2).

The main objective is to manage both physical symptoms and the psychological state of the patient. Quality of life and social impairment must also be considered. All these parameters often require the assistance of specialists in pain management and sometimes psychiatric support.

Conservative management must be proposed as a first step to avoid any invasive procedure that could emphasize nociception and impair the patient's situation. Medications (pain killers) can be tested in each area of pain: inflammation/nociception and neurological dimensions. Pelvic floor retraining, massage and analgesic infiltration (Fig. 35.3) targeting the area of pain should be proposed. Surgical procedures can be proposed in particular cases of clearly identified cases, such as pudendal nerve entrapment after a positive neurological block test.

The major goals of management differ:

- Provide explanations to and reassure the patient regarding the severity of the pain.
- Try to avoid focusing on the etiology itself; rather, emphasize the symptomatic efficacy of the treatment, irrespective of the cause.
- Initiate general drugs associated with targeted conservative management (infiltrations).
- Avoid any aggressive or traumatic procedure as a first line treatment.

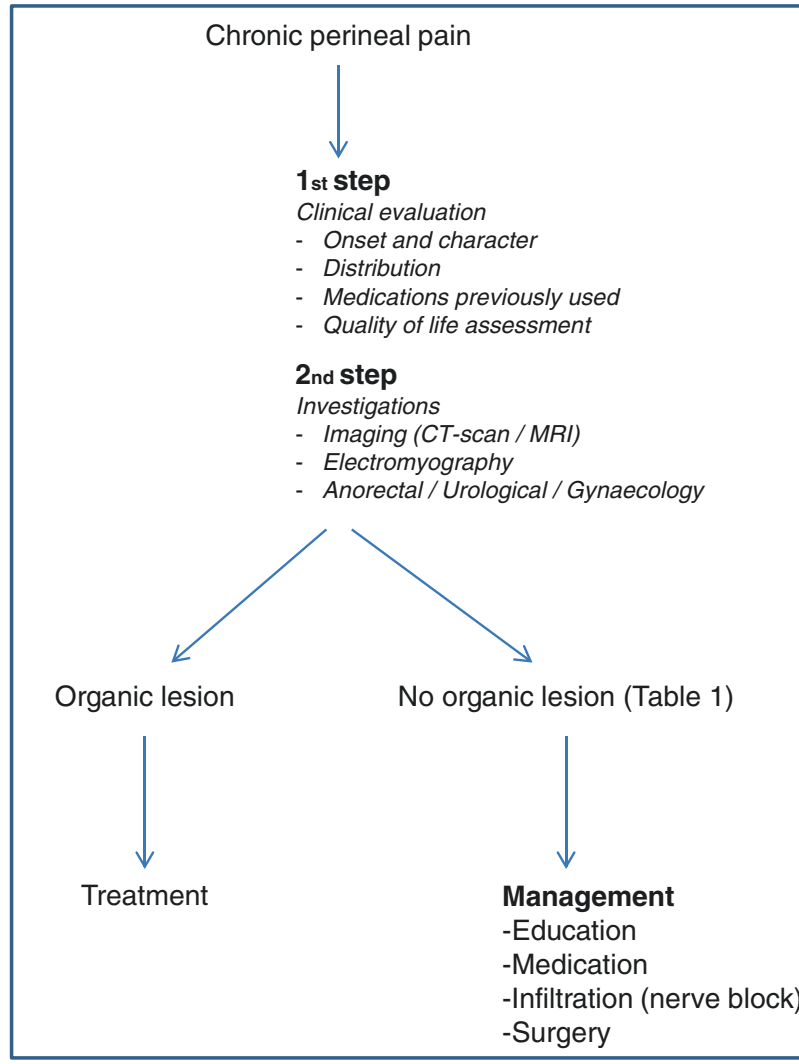


Fig. 35.2 Algorithm for the management of chronic pelvic and perineal pain

35.7 Particular Situation: Postoperative Pain

Postoperative pain is defined as a pain occurring after a surgical procedure and

- Lasting at least 2 months long
- Without any organic cause identified (e.g., carcinoma)
- Without preexisting lesions and occurring before a surgical procedure

Mechanisms of postoperative pain may involve a nerve trauma (section or lesion during a procedure). Symptoms occur early after a procedure (usually immediately). A nerve lesion can also be associated with compression (retractor lesion). In that case, symptoms are less typical and the relation to the procedure is more doubtful. Improvement during the months after surgery can be expected in that specific case. Finally, a nerve lesion can be associated with iatrogenic chronic muscular hypertony as a result of prosthesis insertion. Symptoms can occur after several months or years and are not always typical of a single nerve area, but rather are associated with radiations according to the muscular distribution. A physical examination

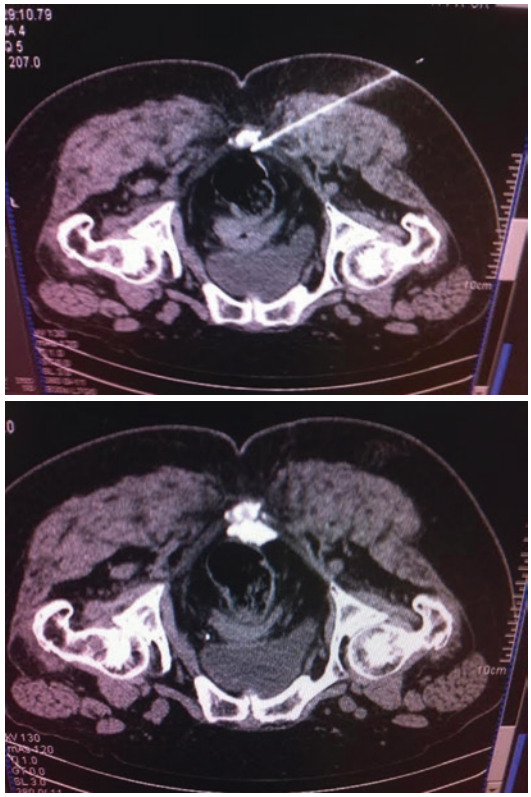


Fig. 35.3 Computed tomographic images of locoregional infiltration: example of an impar node block

should describe the exact topography of the pain and its relation to scars; this can confirm the hypothetical relation between a nerve trauma and a surgical procedure. Imaging and electrophysiological exams may also be helpful to describe the nerves involved and to exclude any organic (tumor) lesion underlying the pain. Infiltration, with the patient showing positive improvements, is the best evidence to confirm a nerve lesion. The surgical approach must be considered with caution because of the risk of de novo lesions induced by the second surgery.

Conclusion

Despite recent advances in perineal imaging and investigations, chronic perineal pain remains a poorly described condition. A better description of the characteristics and history of the pain would be helpful to offer patients an adapted therapeutic approach. Several options for conservative management must be proposed as first-line treatment (pharmaceuticals, infiltrations). Surgery is sometimes mandatory for selected cases after conservative management fails.

References

1. Goodson J. Pudendal neuritis from biking (letter). N Engl J Med. 1981;304:365.
2. Mamlouk MD, vanSonnenberg E, Dehkharghani S. CT-guided nerve block for pudendal neuralgia: diagnostic and therapeutic implications. AJR Am J Roentgenol. 2014;203(1):196–200.
3. Robert R, Prat-Praddal D, Labat JJ, et al. Anatomic basis of chronic pain: role of the pudendal nerve. Surg Radiol Anat. 1998;20:93–8.
4. Robert R, Labat JJ, Bensignor M, et al. Decompression and transposition of the pudendal nerve in pudendal neuralgia: a randomised controlled trial and long terms results. Eur Urol. 2005;47:403–8.
5. Pereira A, Pérez-Medina T, Rodríguez-Tapia A, Rutherford S, Millan I, Iglesias E, Ortiz-Quintana L. Chronic perineal pain: analyses of prognostic factors in pudendal neuralgia. Clin J Pain. 2014;30(7):577–82.
6. Misirlioglu TO, Akgun K, Palamar D, Erden MG, Erbilir T. Piriformis syndrome: comparison of the effectiveness of local anesthetic and corticosteroid injections: a double-blinded, randomized controlled study. Pain Physician. 2015;18(2):163–71.
7. Wald A. Anorectal and pelvic pain inwomen. J Clin Gastroenterol. 2001; 33:293–88. Chiarioni G, Asteria C, Whitehead WE. Chronic proctalgia and chronic pelvic pain syndromes: new etiologic insights and treatment options. World J Gastroenterol. 2011;17(40):4447–55
8. Andromanakos NP, Kouraklis G, Alkiviadis K. Chronic perineal pain: current pathophysiological aspects, diagnostic approaches and treatment. Eur J Gastroenterol Hepatol. 2011;23(1):2–7.

Perioperative Management

36

Martin Hübner and Dieter Hahnloser

Abbreviations

CI	Confidence interval
CRP	C-reactive protein
ERAS	Enhanced recovery after surgery
IL	Interleukin
RCT	Randomized controlled trial
SSI	Surgical site infection

36.1 Pathophysiology of the Surgical Stress Response

- Surgical trauma is followed by a metabolic stress response that is related to impaired recovery, postoperative morbidity, and to prolonged hospital stay (Fig. 36.1). In the initial phase, postsurgical stress response has to be understood as a physiological reaction to increased oxygen demands and energy expenditure in association with posttraumatic hyperinflammation. The metabolic stress response involves complex endocrine and immunological pathways. It is characterized by a complex interplay of endocrine and immunological pathways that are not yet fully understood. The common final path is characterized by electrolyte and fluid shifts, distribution of cytokines, important hormone changes (cortisol, insulin, thyroid hormones), and altered metabolism. Fatty acids and proteins are mobilized from body stores as an energy source and substrates to supply vital organs, enforce the immune system, and help wound healing [4, 13, 21, 53].
- The metabolic stress response varies widely. It seems to be commensurate with the extent and the type of the surgical procedure (Fig. 36.1). Surgical surrogate parameters such as operation time and blood loss have an important impact, and surgical stress is reduced by a minimally invasive approach. On the other hand, patient-related factors are important; risk factors are a diagnosis of cancer, concomitant malnutrition, and frailty with multiple comorbidities [6, 13, 21, 27]. A prolonged or excessive stress response inevitably leads to hypercatabolism and its feared sequelae – namely, hyperglycemia, immunosuppression, and depletion of muscle protein stores with consecutive hypoproteinemia. Clinical consequences are, among others, fatigue, pulmonary complications, wound healing problems, and ileus. Aiming for the prevention or early treatment of a pathological stress response is therefore mandatory [4, 21, 31, 53].

M. Hübner, MD • D. Hahnloser, MD CHUV (✉)
University Hospital Lausanne, Department of Visceral Surgery, Rue du Bugnon 46, CH-1011 Lausanne, Switzerland
e-mail: martin.hubner@chuv.ch; dieter.hahnloser@chuv.ch

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_36

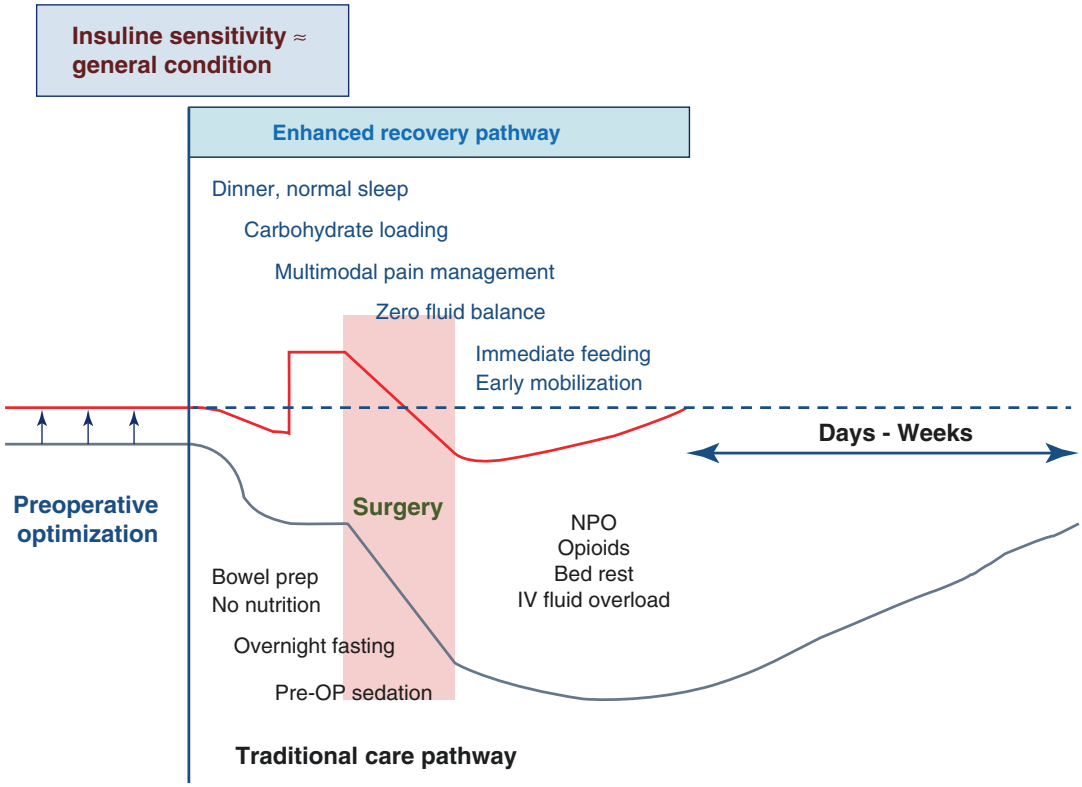


Fig. 36.1 Surgical stress response depends on perioperative care

- Several perioperative measures have been shown to dampen the excessive stress response, to restore homeostasis, and thus to positively influence clinical outcomes [22, 28]. These various interventions are addressed and discussed in the following paragraphs of this book chapter.

  Obviously, reliable prediction of surgical stress response could help to guide the use of potential preventive or therapeutic interventions. The ideal marker or tool should be easy to use, available early, and inexpensive. To be meaningful, the marker needs to show a strong correlation with the extent of surgical trauma and with clinical outcome.

Insulin resistance has been proposed as a promising surrogate parameter for the extent of the postsurgical stress response [46, 47]. However, insulin resistance, as well as interleukin (IL)-6 and IL-10, have never found their way into routine clinical used because of sophisticated analysis techniques and cost issues. C-reactive protein (CRP) is used in clinical practice to document postoperative inflammation and to detect postoperative complications [1, 22, 40]. CRP peaks typically around postoperative day 2 or 3, which is too late to initiate measures to modulate the postoperative stress response.

Because no reliable predictor has yet been identified, *combined measures should be applied to prevent a pathological stress response with deleterious consequences*.

36.2 Postoperative Morbidity: Incidence, Risk Factors, Consequences

Despite evolving surgical techniques and increasing specialization, the occurrence of surgical complications seems to be unchanged. There is no doubt that surgical progress has been, to a

certain extent, counteracted by extended indications and increasingly frail patients. On the other hand, the underlying pathophysiology of the postsurgical metabolic stress response was neglected for a long time by the surgical community. As a consequence, preventive measures are not yet widely implemented [7, 29]. Outcomes after colorectal surgery vary widely, and comparisons between studies are clearly hampered by serious methodological shortcomings such as different definitions, incomplete reporting, and heterogenous cohorts [15, 41, 52].

Three major randomized studies comparing open with laparoscopic procedures (the CLASSIC, COLOR, and COST trials) reported overall complication rates between 20 % and 33 % and median postoperative hospital stays from 5 to 11 days [11, 18, 48]. Outcomes were similar for open versus minimally invasive surgeries but slightly worse for rectal resections when compared with colectomies. Of note, none of the study protocols included enhanced recovery elements. The mortality rate was 1–2 % in the COST and COLOR studies and 4–5 % in the CLASSIC trial. However, true morbidity and mortality rates in the "real world" outside randomized trials are probably much higher and tend to increase considerably with longer follow-up: a recent nationwide study in England revealed 90 day mortality rates after colorectal surgery of 11.3 % [7]. Complications are clearly related to longer hospital stay and increased level of care needed after discharge. Last, complications are associated with higher in-hospital mortality and to a delay in adjuvant treatment that leads to worse oncological outcomes [43, 44].

Multiple risk factors for postoperative complications were recently identified (Table 36.1). These include patient-related parameters such as age, male sex, higher ASA class, and obesity. A number of factors relate to the procedure and the surgeon (blood loss, operating time, experience). Most of these risk factors cannot be changed, but some of them are modifiable and thus offer opportunities for therapeutic interventions [29].

Table 36.1 Pathological stress response: risk factors, prevention, and treatment

Risk factor	Prevention	Treatment
Procedure		
Type of surgery	–	–
Surgical approach	Minimally invasive surgery	–
Operation time	Consider preemptive conversion	–
Blood loss	Handle tissue gently	–
Patient		
Malnutrition	Nutritional screening and support No fasting Immunonutrition	Early food intake
Comorbidities	–	–
Cancer	–	–
Smoking	Smoking cessation counseling	Physiotherapy
Reduced performance	Prehabilitation	Early mobilization
Perioperative care		
Fasting	No fasting	Early food intake
Fluid overload	Zero fluid balance	Early oral intake Early discontinuation of intravenous fluids
Ileus	Minimally invasive surgery Stringent fluid administration	Early mobilization Opioid-sparing pain strategy
Pain	Preoperative information Multimodal pathway	Physiotherapy
Immobilization	Prehabilitation Omission of drains, nasogastric tubes Early removal of Foley catheters	Early mobilization

Recent improvements in perioperative care have targeted these modifiable risk factors and aim to modify a pathologically increased stress response. The resulting interventions and clinical pathways have been proven effective and are therefore outlined in the following sections (Table 36.1).

36.3 Optimizing Perioperative Management

36.3.1 Preparation: Smoking Cessation, Prehabilitation

- The importance of initiation of protective measures *before* the offending hit (e.g., surgery) is largely acknowledged. Smoking is a modifiable risk factor that is particularly prone to pulmonary and wound-healing complications. An extensive recent Cochrane review summarized the findings from 13 randomized controlled trials (RCTs) including 2,010 patients [45]. Using dedicated preoperative smoking cessation counseling with or without concomittant pharmacotherapy, postoperative complications could be reduced from 46 % to 19 %. This corresponds to a relative risk reduction of 58 % (confidence interval [95 % CI] 35–78) and only four patients as the number needed to treat. This is largely due to a relative risk reduction of 69 % (38–84) for wound complications. Intensive and brief behavioral interventions both induced smoking cessation. It is important, however, to notice that only intensive preoperative behavioral interventions reduced surgical complications and achieved sustained behavioral change.
- The preoperative physical status of the individual patient has an obvious impact on his or her tolerance of major surgery, multimodal treatment, and their consequences. Assessment and correction of reduced general condition require additional resources and have been neglected so far. This is true in particular for preoperative physiotherapy (called *prehabilitation*).

A recent publication suggested a simple walking test (the Timed Up and Go test) as a reliable detection tool that is easy to perform and has a high predictive value for postoperative morbidity and mortality [37]. The next logical step is to strive to improve a patient's reduced physical condition. Initial works in different fields of surgery have been promising, especially with regard to reducing cardiopulmonary morbidity [25, 35]. There is no established standard, however, and adopted protocols differ widely. Furthermore, reported outcome measures were poorly standardized and heterogeneous [36].

The McGill group from Montréal recently reported that pre- and postoperative physical ability of patients undergoing colorectal surgery could be improved by two different exercise programs. However, the adherence to physical exercise programs was low, and a clear link between enhanced physical status and improved clinical outcomes has not yet been established [8]. Nonetheless, the rationale behind and the available data should encourage the pursuit of this approach.

36.3.2 Nutritional Screening and Perioperative Nutrition

- Malnutrition is probably the most prevalent modifiable risk factor for adverse outcomes and infectious complications in particular. This condition affects up to 40 % of patients undergoing major surgery. It has been convincingly shown that malnourished patients have at least twice the risk of developing overall and major complications sorensen clin nutr 2008 (EuroOOPS).

  The European and American guidelines (ESPEN, ASPEN) therefore recommend routine nutritional screening for every patient *before* undergoing major surgery. Several screening tools have been proposed and validated in large prospective cohorts: the nutritional risk score (2002), The Malnutrition Universal Screening Tool, and the subjective global assessment. Preoperative weight loss remains one of the most reliable criteria to guide nutritional interventions; serum albumin

and prealbumin can also be used as screening parameters and to monitor the efficacy of nutritional support [9, 51].

- Pre- or perioperative nutrition is recommended for all patients who are (1) scheduled for major surgery and (2) malnourished or at nutritional risk according to the screening tool used. Most patients can be conditioned with oral nutritional supplements for 5–7 days before surgery, whereas severely malnourished patients might require enteral or even parenteral nutrition for at least 2 weeks; in these patients, surgery needs to be postponed.

  Immunonutrition has been suggested as a specific nutritional formula not only to improve nutritional status but also primarily to modulate the immune response. The active ingredients arginine, glutamine, n-3-fatty acids, and ribonucleic acid help to enhance cellular and humoral immune function and to modulate an excessive immune response in the postoperative phase. Several systematic reviews have evaluated its clinical effects. In 21 RCTs (2,730 patients), overall and infectious complications were halved in patients receiving perioperative immunonutrition. This translated into reduced hospital stays (>2 days) and costs. Mortality was not different between the groups. Consistent outcomes were found for the subset of colorectal patients and when including only high-quality studies. Nevertheless, a significant heterogeneity between the studies does not permit immunonutrition to be uncritically recommended to all patients [10, 51].

36.3.3 Bowel Preparation: Sense or Nonsense?

- Mechanical bowel preparation is another long-standing dogma in colorectal surgery that has been challenged only recently. The obvious rationale was to avoid intestinal spillage and intraoperative contamination, and hence to reduce surgical site infection rates. Furthermore, an empty colon tends to be easier to handle. The downsides of mechanical bowel preparation seem obvious as well: major fluid shifts, electrolyte losses, and bowel wall alterations with impaired barrier function. Furthermore, the risk of intestinal spillage seems to be increased even in prepped patients with liquid colonic content.

  A Cochrane collaboration summarized the available evidence on preoperative bowel preparation on postoperative outcomes in four systematic reviews since 2003. The latest update is based on 18 RCTs including 5,805 subjects [17]. No statistical difference was observed for anastomotic leak rate or wound infections after colon and rectal resections, respectively. The authors and subsequent guidelines suggested that bowel preparation should be omitted before colon surgery but may be selectively used for low rectal resections [17, 20, 33].
- This cautious specification for rectal surgery is the result of GRECCAR III, a French multicenter study. Bretagnol and colleagues [5] reported significantly more overall and infectious complications as well as a trend toward a higher leak rate in patients undergoing rectal resections without mechanical bowel preparation. However, these results have not yet been confirmed by other randomized studies and contrast with the results of the Cochrane review. It is worth mentioning, however, that bowel preparation is still widely practiced despite the convincing evidence against its use.
- In summary, bowel preparation should not be used for right or transverse colectomies, whereas retrograde enemas are accepted before left-sided resections. A full anterograde bowel preparation should be reserved for specific situations such as intraoperative colonoscopy to locate a tumor and the creation of a neovagina, and should be further studied in the case of low anterior resections of the rectum.

36.3.4 Steroids: From Foe to Friend?

- Steroids have been demonized for decades and are still feared by many surgeons for their negative impact on immune defense and

wound healing. Indeed, chronic steroid use seems to increase infectious complications, especially after rectal resections. The effect on wound healing seems to be time- and dose-dependent. Even high-dose corticosteroids have not been associated with adverse outcomes if administered for <10 days before surgery. Other studies reported more wound complications only for patients on high-dose corticosteroids for at least 30 days. The threshold dosage in most studies is around 20 mg/day of prednisone [34, 39].

- Single-dose preoperative administration of corticosteroids was suggested many years ago to dampen an excessive postsurgical stress response and thus to positivley influence surgical outcomes. While wound problems remained unaffected, a decrease in pulmonary complications was observed. Dexamethasone has been studied extensively with regard to its effect on postoperative nausea and vomiting, and the literature was recently summarized by a systematic review of 60 RCTs including 6,696 participants. By a single dose of 4–5 mg dexamthasone, incidence of postoperative nausea and vomiting was largely reduced, achieving an odds ratio of 0.31 (95% CI 0.23–0.41) and a number needed to treat of only 3.7 (95% CI 3.0–4.7). No further clinical benefit was observed when comparing 4–5 mg of dexamethasone with higher doses (8–10 mg) [12].
- Low-dose steroids are successfully used as an adjunct pain treatment in multimodal pathways. According to a systematic review of 45 RCTs (5,796 patients), patients receiving dexamthasone at a dose between 1.25 and 20 mg benefitted from a lower postoperative pain score, reduced opioid consumption, less rescue analgesia, and a shorter stay in the recovery room when compared with the control group. No negative effect on wound healing was noted, and blood glucose levels increased only moderately. The clinical benefits were not related to the dose of dexamethasone [50]. Therefore, most modern perioperative care pathways suggest preoperative administration of dexamthasone at a dose of 4–8 mg.

36.3.5 Avoidance of Surgical Site Infections

- Wound infections are a deplorable but, at the same time, an inevitable risk after colorectal surgery. Honest reporting and clinical follow-up situate surgical site infection (SSI) rates after colorectal surgery around 20% after open resections and around 10% after laparoscopic resections. Much "lower" SSI rates are reported from US centers, where a chart-based review is performed for surveillance of SSIs. This is an important methodological difference when comparing SSI between centers, especially as a quality parameter. The better a patient's follow-up, the higher are the SSI rates!

  Risk factors for SSIs are many and are mainly related to the patient or to the procedure [24]. Many of these factors, such as correction of malnutrition, smoking cessation, and proper hair removal, are potentially modifiable and have been addressed in recent recommendations. The guidelines of the UK National Institute for Clinical Excellence provide an exhaustive overview and mostly clear recommendations [30]. Surgeons' adherence to these evidence-based guidelines remains modest at best and varies largely across the different items. "Easy" measures such as properly timed antibiotic prophylaxis, prevention of hypothermia, and adequate skin disinfection have been widely adopted. On the contrary, smoking cessation counseling, screening and treatment of malnutrition, and a "no-drain" policy seem to pose problems. It must be mentioned that at least half of the recommendations are not really based on a solid scientific evidence [14].
- Furthermore, rigid application of "prevention bundles" have not necessarily improved outcomes. The surgeon and his or her surgical procedure have probably the highest impact on the risk for SSI. This has statistically been shown in a prospective multicenter study, but it remains extremely difficult to describe or measure a surgeon's performance [3, 24, 42]. Discipline in the operating room and high

adherence to standard antiseptic measures are probably the two key elements for low SSI rates.

36.4 Minimal Invasive Surgery

- Many prospective randomized trials including benign diseases and oncologic patients (COST, CLASSIC, and COLOR trials) demonstrated clear short-term patient-related benefits for a minimally invasive approach compared with open surgery. Patients operated on laparoscopically had less pain; faster recovery of bowel movement, allowing earlier oral intake; less postoperative ileus; and earlier first bowel movement, resulting in earlier discharge and return to regular physical activity.

  Patients converted to open surgery lose all these patient-related benefits, with a similar length of stay and morbidity as patients undergoing primary open surgery.

  Of note, if conversion was performed preemptively and not reactively as the result of an intraoperative adverse event or complication, the benefits of a minimally invasive approach can be preserved.
- In the Laparoscopic and/or Fast Track Multimodal Management versus Standard Care (LAFA) trial, patients with adenoma or colon cancer were randomized to laparoscopic or open resection within a fast-track or standard perioperative program [49]. Patients treated laparoscopically with fast-track perioperative care had an accelerated recovery and were discharged fastest without significant differences in morbidity. The LAFA trial also demonstrated that the accelerated recovery is correlated more to the type of surgery (laparoscopy) and less to aftercare. Regression analysis showed that laparoscopy was the only independent predictive factor to reduce hospital stay and morbidity. Other significant factors determining early recovery were enforced advancement of oral intake, early mobilization, and female sex. This faster recovery is also true in older (>65 years) patients undergoing laparoscopic resection for colon cancer. In addition, after a median follow-up of 3.4 years, patients undergoing laparoscopic resection in the LAFA trial had fewer incisional hernias and fewer adhesional small-bowel obstructions [2].
- Patients undergoing laparoscopic resections showed higher human leukocyte antigen-DR on monocytes, a marker for preserved immune competence, until 3 days after surgery compared with open resections. Inflammatory values such as CRP and IL-6 were highest after open surgery. These differences in immune competence and inflammatory response seem to be correlated to the type of surgery and not aftercare. Thus a minimally invasive approach is preferable [27].

36.5 Multimodal Pathways: Enhanced Recovery After Surgery

Adverse postoperative outcomes are closely related to the magnitude of the postsurgical metabolic stress response. The previous chapters outlined different individual measures to optimize perioperative care in order to improve postoperative outcomes. Most of these items have a positive influence on the metabolic stress response. It is therefore a logical consequence to bundle these preventive and beneficial measures in *clinical pathways* to optimally target surgical stress response and hence to improve postoperative recovery (Fig. 36.1).

36.5.1 History and Development

- The first reports of fast-track surgery were published almost two decades ago by Kehlet and coworkers. By applying dedicated pathways, patients were able to recover quickly, leading to hospital stays of only 2–3 days after colon resections, whereas the usual average was about 10 days. These clinical results have been reproduced [16].

  O. Ljungquist is credited with the further development of fast-track surgery to enhanced

recovery after surgery (ERAS) pathways. The main focus was on improving, not accelerating, the recovery process. Based on pathophysiological considerations and a thorough review of the literature, ERAS guidelines have been established and actualized for several types of surgeries.

36.5.2 Definition and Protocols

- ERAS is a multimodal pathway aiming to reduce the postsurgical stress response and thus to enhance the recovery process. The current protocols combine over 20 individual items, most of which have an evidence-based positive impact on the metabolic stress response and/or clinical outcomes [20, 33] (Fig. 36.2). Key factors of those pathways are stringent fluid management (zero fluid balance), early mobilization and food intake, and modern multimodal opioid-sparing pain strategies. Epidurals remain the backbone of analgesia regimens for open procedures; however, for laparoscopic procedures, other options such as intravenous lidocaine, transversus abdominis plane blocks, or spinal injections have proven to be easier to handle and equivalent, if not superior, in terms of pain relief and recovery [23, 26, 32]. An important part of enhanced recovery protocols is the omission of unnecessary or even deleterious measures such as bowel preparation, prophylactic nasogastric tubes, surgical drains, and Foley catheters for >24 h.
- Several measures act together to achieve the main goals of pain control, homeostasis, prevention of ileus, and patient comfort. Hence the protocol is no arbitrary accumulation of items but a conclusive master plan. It has been shown that clinical outcomes relate directly to the adherence with the protocol [19]. A systematic implementation process can help to increase

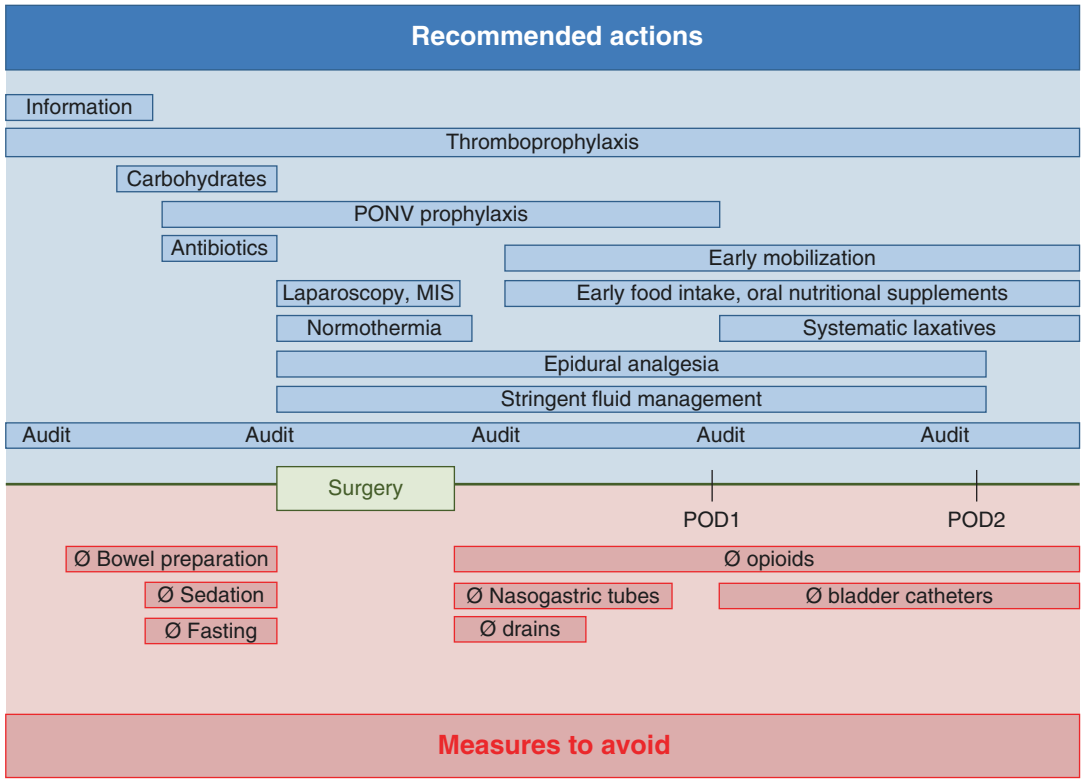


Fig. 36.2 The multimodal enhanced recovery pathway

application of the pathway and to improve outcomes. Prospective audit of the compliance with the intended pathway and of the clinical results is extremely helpful to improve the results and to identify and correct problems.

36.5.3 Clinical Results

The initial fast-track protocols focused mainly on reducing the duration of hospital stay, and a median length of stay of 3 days could be achieved after colectomy without increasing readmission rates. The Zurich multicenter study was the first randomized trial that also showed a largely reduced complication rate by applying an enhanced recovery pathway [32]. The current evidence encompasses 16 RCTs and 2,376 patients. By applying an ERAS protocol, overall complications were significantly reduced, with a calculated odds ratio of 0.60 (95 % CI 0.46–0.76) [16]. It is important to mention that this effect was the result of a reduction of nonsurgical complication, whereas surgical morbidity, including anastomotic leak and wound infections, remained unchanged. Hospital stay was shortened by 2.3 days (95 % CI 1.47–3.09), whereas readmissions and mortality were similar between the comparative groups.

In addition to the proven clinical benefits, ERAS pathways have been proven to be cost-effective [38] (despite initial high costs for implementation) and should be considered the standard of care, at least for colorectal surgery.

36.5.4 Challenges and Perspective

It takes time to overcome traditional care, to fight old dogmas, and to transfer scientific evidence into daily routine. Furthermore, enhanced recovery protocols vary considerably. Comprehensive ERAS recommendations provide easy-to-follow, evidence-based guidance [20, 33]. However, Dutch and Swiss experiences showed that "a protocol was not enough to implement an enhanced recovery program." A structured implementation program has been proven to be effective in fostering successful implementation with good sustainable results. These encouraging results can motivate centers that have not yet adopted a modern perioperative care pathway.

- All evidence-based recommendations have to be considered as temporary and subject to change according to new, evolving evidence. This is particularly true for enhanced recovery guidelines, which should be challenged and updated regularly. Continuous clinical research and auditing of the protocol and clinical outcomes well help to develop optimal perioperative care further.

Multiple factors contribute to the surgical stress response. These include risk factors related to the procedure, to the patient, or to perioperative care. Many risk factors can be corrected preoperatively (prevention) or be addressed by perioperative multimodal pathways.

Insulin resistance is a reliable surrogate parameter for a patient's general status. Many patients undergoing major surgery arrive at the hospital already in a poor condition. Surgical trauma and many factors of traditional care pathways contribute to the further deterioration of the physical condition, leading to a long and tedious recuperation.

Optimization of a patient should start during the outpatient period (e.g., nutritional screening and support, smoking cessation, prehabilitation). Then the patient should be included in a comprehensive multimodal pathway to improve surgical stress response and thereby enhance recovery and improve outcomes. A shorter hospital stay is a welcome side effect.

Evidence-based measures are bundled together to improve the surgical stress response and to reduce consequent complications. The pathway contains a multitude of beneficial actions; on the other hand, several detrimental or unnecessary measures should be omitted.

Suggested Reading

1. Adamina M, Steffen T, Tarantino I, Beutner U, Schmied BM, Warschkow R. Meta-analysis of the predictive value of C-reactive protein for infectious complications in abdominal surgery. Br J Surg. 2015;102(6):590–8.

2. Bartels SA, Vlug MS, Hollmann MW, Dijkgraaf MG, Ubbink DT, Cense HA, et al. Small bowel obstruction, incisional hernia and survival after laparoscopic and open colonic resection (LAFA study). Br J Surg. 2014;101(9):1153–9.
3. Beldi G, Bisch-Knaden S, Banz V, Muhlemann K, Candinas D. Impact of intraoperative behavior on surgical site infections. Am J Surg. 2009;198(2):157–62.
4. Blackburn GL. Metabolic considerations in management of surgical patients. Surg Clin North Am. 2011;91(3):467–80.
5. Bretagnol F, Panis Y, Rullier E, Rouanet P, Berdah S, Dousset B, et al. Rectal cancer surgery with or without bowel preparation: the French GRECCAR III multicenter single-blinded randomized trial. Ann Surg. 2010;252(5):863–8.
6. Buunen M, Gholghesaei M, Veldkamp R, Meijer DW, Bonjer HJ, Bouvy ND. Stress response to laparoscopic surgery: a review. Surg Endosc. 2004;18(7):1022–8.
7. Byrne BE, Mamidanna R, Vincent CA, Faiz O. Population-based cohort study comparing 30- and 90-day institutional mortality rates after colorectal surgery. Br J Surg. 2013;100(13):1810–7.
8. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. Br J Surg. 2010;97(8):1187–97.
9. Cerantola Y, Grass F, Cristaudi A, Demartines N, Schafer M, Hubner M. Perioperative nutrition in abdominal surgery: recommendations and reality. Gastroenterol Res Pract. 2011;2011:739347.
10. Cerantola Y, Hubner M, Grass F, Demartines N, Schafer M. Immunonutrition in gastrointestinal surgery. Br J Surg. 2011;98(1):37–48.
11. Clinical Outcomes of Surgical Therapy Study G. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med. 2004;350(20):2050–9.
12. De Oliveira Jr GS, Castro-Alves LJ, Ahmad S, Kendall MC, McCarthy RJ. Dexamethasone to prevent postoperative nausea and vomiting: an updated meta-analysis of randomized controlled trials. Anesth Analg. 2013;116(1):58–74.
13. Desborough JP. The stress response to trauma and surgery. Br J Anaesth. 2000;85(1):109–17.
14. Diana M, Hubner M, Eisenring MC, Zanetti G, Troillet N, Demartines N. Measures to prevent surgical site infections: what surgeons (should) do. World J Surg. 2011;35(2):280–8.
15. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205–13.
16. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World J Surg. 2014;38(6):1531–41.
17. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev. 2011;9, CD001544.
18. Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005;365(9472):1718–26.
19. Gustafsson UO, Hausel J, Thorell A, Ljungqvist O, Soop M, Nygren J, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. Arch Surg. 2011;146(5):571–7.
20. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS((R))) Society recommendations. World J Surg. 2013;37(2):259–84.
21. Haga Y, Beppu T, Doi K, Nozawa F, Mugita N, Ikei S, et al. Systemic inflammatory response syndrome and organ dysfunction following gastrointestinal surgery. Crit Care Med. 1997;25(12):1994–2000.
22. Hall R. Identification of inflammatory mediators and their modulation by strategies for the management of the systemic inflammatory response during cardiac surgery. J Cardiothorac Vasc Anesth. 2013;27(5):983–1033.
23. Hubner M, Blanc C, Roulin D, Winiker M, Gander S, Demartines N. Randomized clinical trial on epidural versus patient-controlled analgesia for laparoscopic colorectal surgery within an enhanced recovery pathway. Ann Surg. 2015;261(4):648–53.
24. Hubner M, Diana M, Zanetti G, Eisenring MC, Demartines N, Troillet N. Surgical site infections in colon surgery: the patient, the procedure, the hospital, and the surgeon. Arch Surg. 2011;146(11):1240–5.
25. Hulzebos EH, Smit Y, Helders PP, van Meeteren NL. Preoperative physical therapy for elective cardiac surgery patients. Cochrane Database Syst Rev. 2012;11, CD010118.
26. Joshi GP, Bonnet F, Kehlet H, collaboration P. Evidence-based postoperative pain management after laparoscopic colorectal surgery. Colorectal Dis: Off J Assoc Coloproctol G B Irel. 2013;15(2):146–55.
27. Karanika S, Karantanos T, Theodoropoulos GE. Immune response after laparoscopic colectomy for cancer: a review. Gastroenterol Rep. 2013;1(2):85–94.
28. Kehlet H. Manipulation of the metabolic response in clinical practice. World J Surg. 2000;24(6):690–5.
29. Kirchhoff P, Clavien PA, Hahnloser D. Complications in colorectal surgery: risk factors and preventive strategies. Patient Saf Surg. 2010;4(1):5.
30. Leaper D, Burman-Roy S, Palanca A, Cullen K, Worster D, Gautam-Aitken E, et al. Prevention and treatment of surgical site infection: summary of NICE guidance. BMJ. 2008;337:a1924.
31. Lin E, Calvano SE, Lowry SF. Inflammatory cytokines and cell response in surgery. Surgery. 2000;127(2):117–26.

32. Muller S, Zalunardo MP, Hubner M, Clavien PA, Demartines N, Zurich Fast Track Study G. A fast-track program reduces complications and length of hospital stay after open colonic surgery. Gastroenterology. 2009;136(3):842–7.
33. Nygren J, Thacker J, Carli F, Fearon KC, Norderval S, Lobo DN, et al. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS(R)) Society recommendations. Clin Nutr. 2012;31(6):801–16.
34. Orci LA, Toso C, Mentha G, Morel P, Majno PE. Systematic review and meta-analysis of the effect of perioperative steroids on ischaemia-reperfusion injury and surgical stress response in patients undergoing liver resection. Br J Surg. 2013;100(5):600–9.
35. Pehlivan E, Turna A, Gurses A, Gurses HN. The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. Ann Thorac Cardiovasc Surg: Off J Assoc Thorac Cardiovasc Surg Asia. 2011;17(5):461–8.
36. Pouwels S, Stokmans RA, Willigendael EM, Nienhuijs SW, Rosman C, van Ramshorst B, et al. Preoperative exercise therapy for elective major abdominal surgery: a systematic review. Int J Surg. 2014;12(2):134–40.
37. Robinson TN, Wu DS, Sauaia A, Dunn CL, Stevens-Lapsley JE, Moss M, et al. Slower walking speed forecasts increased postoperative morbidity and 1-year mortality across surgical specialties. Ann Surg. 2013;258(4):582–8; discussion 8–90.
38. Roulin D, Donadini A, Gander S, Griesser AC, Blanc C, Hubner M, et al. Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. Br J Surg. 2013;100(8):1108–14.
39. Sauerland S, Nagelschmidt M, Mallmann P, Neugebauer EA. Risks and benefits of preoperative high dose methylprednisolone in surgical patients: a systematic review. Drug Saf: Int J Med Toxicol Drug Exp. 2000;23(5):449–61.
40. Singh PP, Zeng IS, Srinivasa S, Lemanu DP, Connolly AB, Hill AG. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg. 2014;101(4):339–46.
41. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg. 2013;258(1):1–7.
42. Stulberg JJ, Delaney CP, Neuhauser DV, Aron DC, Fu P, Koroukian SM. Adherence to surgical care improvement project measures and the association with postoperative infections. JAMA. 2010;303(24):2479–85.
43. Tevis SE, Kennedy GD. Postoperative complications and implications on patient-centered outcomes. J Surg Res. 2013;181(1):106–13.
44. Tevis SE, Kohlnhofer BM, Stringfield S, Foley EF, Harms BA, Heise CP, et al. Postoperative complications in patients with rectal cancer are associated with delays in chemotherapy that lead to worse disease-free and overall survival. Dis Colon Rectum. 2013;56(12):1339–48.
45. Thomsen T, Villebro N, Moller AM. Interventions for preoperative smoking cessation. Cochrane Database Syst Rev. 2014;3, CD002294.
46. Thorell A, Efendic S, Gutniak M, Haggmark T, Ljungqvist O. Development of postoperative insulin resistance is associated with the magnitude of operation. Eur J Surg Acta Chir. 1993;159(11–12):593–9.
47. Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. Curr Opin Clin Nutr Metab Care. 1999;2(1):69–78.
48. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol. 2005;6(7):477–84.
49. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, et al. Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). Ann Surg. 2011;254(6):868–75.
50. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110(2):191–200.
51. Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN guidelines on enteral nutrition: surgery including organ transplantation. Clin Nutr. 2006;25(2):224–44.
52. Whistance RN, Forsythe RO, McNair AG, Brookes ST, Avery KN, Pullyblank AM, et al. A systematic review of outcome reporting in colorectal cancer surgery. Colorectal Dis: Off J Assoc Coloproctol G B Irel. 2013;15(10):e548–60.
53. Wilmore DW. Metabolic response to severe surgical illness: overview. World J Surg. 2000;24(6):705–11.

Intestinal Failure

37

Mattias Soop and Gordon Carlson

Abbreviations

HPN Home parenteral nutrition
IF Intestinal failure

37.1 Definitions

37.1.1 Intestinal Failure

The concept of intestinal failure (IF) was introduced in 1981 [1]. IF is currently defined as a reduction of gut function below the minimum necessary for the absorption of macronutrients, water, or electrolytes, such that parenteral supplementation is required [2]. This definition encompasses not only states where absolute intestinal length has been reduced (short bowel syndrome) but also conditions in which functional intestinal length has been reduced, such as proximal enterocutaneous fistulation, as well as conditions where the bowel is anatomically intact but intestinal function is severely impaired, such as in motility disorders or radiation enteritis.

M. Soop, MD, PhD (✉) • G. Carlson, BSc, MD, FRCS
Irving National Intestinal Failure Unit, Salford Royal NHS Foundation Trust, Stott Lane,
M6 8HD Manchester, UK
e-mail: mattias.soop@manchester.ac.uk; gordon.carlson@srft.nhs.uk

37.1.2 Intestinal Dysfunction

Some patients with impaired gut function may remain nutritionally independent by significantly increasing their oral intake (compensatory hyperphagia). This state is usually referred to as intestinal dysfunction rather than IF [3].

37.2 Classification

IF can range from a brief and self-limiting to a chronic and irreversible condition. IF can be broadly classified into three commonly occurring subtypes characterized by increasing duration and clinical severity [4] (Table 37.1). Patients with type 1 and type 2 IF (known as acute and acute severe IF, respectively) are usually cared for in a hospital, typically on a surgical ward or in a critical care environment. Patients with type 3 IF (known as chronic IF) are usually managed in an outpatient setting, receiving home parenteral nutrition (HPN) under the care of medical gastroenterologists. Gastroenterological surgeons frequently encounter patients with type 1 IF, for example, following abdominal surgery, when digestive function may be slow to return, or in the setting of intestinal obstruction. Such patients usually require little more than safe parenteral nutrition until IF resolves (by definition, within 28 days). By contrast, patients with type 2 IF are usually critically ill, at least at the onset of their

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_37

Table 37.1 Three common types of intestinal failure

	Duration	Reversible	Examples
Type 1	<28 days	Yes Often spontaneous resolution	Postoperative ileus, mechanical small-bowel obstruction
Type 2	≥28 days	Yes Often requires complex interventions and reconstructive surgery	Enterocutaneous fistula Crohn's disease with abdominal sepsis
Type 3	Chronic	Rarely Small-bowel transplantation, small bowel lengthening, or glucagon-like peptide 2 agonist therapy can be considered in selected cases	Massive small-bowel resection Radiation enteritis

illness, as a result of severe abdominal sepsis and intestinal fistulation. Type 2 IF is relatively uncommon and management in the United Kingdom and increasingly in Europe is being confined to specialized centers as multidisciplinary teams are needed to provide cost-efficient care and obtain the best outcomes.

37.3 Epidemiology of Intestinal Failure

Postoperative paralytic ileus and small bowel obstruction are by far the most common causes of type 1 IF. The incidence of type 1 IF greatly depends on how ileus is defined, since the duration of postoperative gastrointestinal dysmotility varies greatly. For example, patients typically cannot eat for about 3 days after elective open colorectal surgery performed with traditional perioperative care, whereas patients undergoing laparoscopic surgery within an enhanced-recovery protocol usually tolerate solid food after 1 day [5]. Many definitions of ileus have been put forward, but regardless of which is used, it is clear that a substantial proportion of patients require parenteral fluids, and often parenteral nutrition, for periods lasting from days to weeks in both acute and elective surgical care. The incidence of type 1 IF is therefore substantial.

The incidence of type 2 IF is probably far less common than type 1 IF, although there are relatively few good epidemiological data. In the United Kingdom, the prevalence of type 2 IF, estimated from the number of patients receiving in-hospital parenteral nutrition lasting 28 days or more, indicates a point prevalence of 9 in 1 million population [6]. This is an indirect estimate based on actual total parenteral nutrition prescriptions and may underestimate the number of cases. Thus the true prevalence of type 2 IF remains unknown, but it is probably somewhat higher than usually reported.

The prevalence of type 3 IF can similarly be estimated from the number of patients who receive HPN. This is known to vary greatly between and within countries, indicating important regional variations in both the availability of and indications for HPN. In the United Kingdom, where HPN is not frequently prescribed as part of palliative care, the number of patients receiving HPN in 2011 was 624, yielding an estimated prevalence of type 3 IF of ten per million population [7].

37.4 Etiology and Prevention of IF

37.4.1 Type 1 IF

The most common preventable cause of type 1 IF is postoperative ileus. Several perioperative interventions and techniques have been shown to attenuate this common condition, including avoidance of fluid overloading, minimising opioid administration, using mid-thoracic epidural analgesia, and administration of peripheral opioid antagonists. The combination of such interventions in enhanced-recovery protocols has been shown to preserve normal gastrointestinal function after major colorectal surgery [8] (see Chap. 36).

37.4.2 Type 2 IF

In at least one-third of patients with IF, the underlying cause is a major complication of abdominal surgery [9] (Table 37.2). The second most common underlying cause is Crohn's disease, followed by mesenteric ischaemia.

Type 2 IF can result from any abdominal surgical procedure. Laparoscopic division of adhesions, laparoscopic hernioplasty, and bariatric surgery are increasingly important causes of type 2 IF. The characteristic sequence of events that leads to type 2 IF is an unrecognized or inadequately treated enteric injury or an anastomotic or suture line dehiscence resulting in abdominal sepsis, for which further surgery may have been performed, leading to a high output stoma or intestinal fistula.

Emergency surgery for sepsis or trauma may occasionally necessitate leaving the abdomen open in an attempt to control sepsis and prevent intra-abdominal compartment syndrome. Leaving the abdomen open in the setting of trauma seems to be associated with relatively low (<5 %) rates of intestinal fistulation and type 2 IF, whereas in patients with sepsis the rates of intestinal fistulation and type 2 IF may exceed 10 %; some studies have suggested rates in excess of 20 %. Use of negative-pressure devices to manage the open abdomen in this setting is highly controversial, with some studies reporting a significant increase in fistulation and mortality [10, 11]. However, the largest prospective study reported to date failed to identify an increase in the rate of fistulation or type 2 IF in patients with an open abdomen (caused by sepsis in 70 %), treated with negative-pressure wound therapy [12].

Table 37.2 Underlying causes of intestinal failure in patients admitted to Salford Royal Hospital Intestinal Failure Unit (institutional audit data from 2002–2005; $n = 134$)

Underlying cause	Frequency (%)
Postoperative complications	32
Crohn's disease	21
Mesenteric ischemia	13
Dysmotility disorder	14
Malignancy	8
Radiation	2
Celiac disease	2
Others	8

Avoiding type 2 IF depends not only on the careful selection of patients and meticulous surgical technique avoid complications but also prompt recognition and expert senior management of complications when they arise. Anticipating and avoiding bowel injury in reoperative surgery [13] and avoiding construction of an anastomosis in unfavorable circumstances [6] may enable type 2 IF to be avoided completely in many such cases.

In patients with mesenteric ischemia, revascularization is occasionally possible in cases of early arterial embolic ischemia. It may be appropriate to retain bowel that is not clearly necrotic, which can be reexamined at a planned second-look laparotomy 24–72 h later. Anastomosis should only be considered if the bowel is clearly viable and the patient hemodynamically stable. In the event that the bowel is viable but the patient unstable, a double-barreled stoma is preferable, and bowel continuity can be restored later, without the need for a full laparotomy.

Crohn's disease is the second most common underlying cause of type 2 IF, as indicated earlier. Patients with complications of surgery for Crohn's disease represent one of the largest groups with type 2 IF. This association between Crohn's disease and IF must be recognized so that unnecessary surgical risks and bowel resection can be avoided. Bowel-sparing techniques such as balloon dilatation of strictures and stricturoplasty, in association with biologic therapy, may be important to conserve the bowel.

The vast majority of type 3 IF in Crohn's disease results from poor management of type 2 IF. In other words, progression from severe acute to chronic IF in Crohn's disease is mainly the result of complications of surgery rather than bowel loss resulting from multiple, uncomplicated bowel resections [14]. The risks of complications from surgery for Crohn's disease can be reduced by meticulous technique and careful selection of cases for primary anastomosis [15] (see Chap. 15).

37.4.3 Type 3 Intestinal Failure

Patients with type 3 IF represent the end stage of processes that lead to irreversible functional or anatomic loss of small intestine, beyond the amount required to maintain life without parenteral nutrition. The majority of patients with type 3 IF have short bowel syndrome, most commonly as a consequence of the conditions that lead to type 2 IF. A smaller proportion of patients develop type 3 IF as a result of conditions that neither arise from, nor usually require, surgical treatment, including scleroderma and motility disorders. Their etiology is beyond the scope of this chapter.

37.5 Management

37.5.1 Management of Type 1 IF

The management of type 1 IF is usually relatively simple, and the expertise and facilities required should be available in every center in which patients with abdominal surgery are treated. The vast majority of patients with type 1 IF require little more than safe and effective parenteral fluid therapy – and often parenteral nutrition – until the underlying condition resolves. Whether resolution requires active intervention (e.g., the management of some cases of mechanical intestinal obstruction) or conservative treatment (e.g., the management of an ileus resulting from severe acute appendicitis) is irrelevant. In all cases, the focus must be on providing complication-free and effective nutritional and fluid therapy. The role of dedicated nutrition support teams and avoidance of catheter-related sepsis are important to ensure the best outcomes [6].

37.5.2 Management of Type 2 IF

The presentation of type 2 IF is complex and often life-threatening. Patients are usually systemically unwell from multiple disease processes, including sepsis, malnutrition, electrolyte disturbances, underlying disease activity, and concurrent complications. In addition, there is often an open abdominal wound and/or enterocutaneous fistulation (Fig. 37.1). A structured approach is therefore essential for a successful outcome. The goals in managing type 2 IF are multiple: to prevent mortality; to restore as much intestinal function as possible, thus avoiding progression to chronic (type 3) IF; to establish HPN when indicated; and to close fistulas, stomas, and open abdominal wounds when possible.

A multidisciplinary team comprising nurses (with specialized nutrition and stoma care experience), dieticians, pharmacists, intensivists, physicians, clinical psychologists, and surgeons is needed to manage such patients effectively. Recognizing this, many centers in the United Kingdom and elsewhere have begun to centralize the care of such patients in dedicated intestinal failure units.

To address the multiple clinical challenges that type 2 IF presents in the order in which they cause mortality and morbidity, the so-called SNAP (sepsis, nutrition, anatomy, procedure) approach was proposed and has evolved over time [16]. This mnemonic outlines a rational approach to management in an appropriate order of clinical priorities for the majority of patients with type 2 IF.

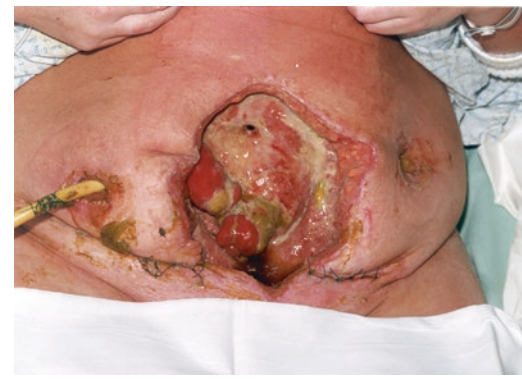


Fig. 37.1 Severe abdominal sepsis associated with fistulation in the open abdomen

37.6 Sepsis and Skin Care

A majority of patients with type 2 IF have active intra-abdominal infection at presentation. Sepsis, as conventionally defined (i.e., by the presence of signs such as fever, tachycardia, tachypnea, and leukocytosis), is frequently absent in patients with type 2 IF, possibly because infection is long-standing and walled off. More than half of patients with active abdominal infection in type 2 IF have no overt clinical signs of sepsis. Infection in this group more often presents with subtle signs such as persistent hypoalbuminemia, hyponatremia, high levels of inflammatory markers, deranged liver function (notably unexplained jaundice), and failure to gain weight (or even cachexia) despite appropriate nutritional support.

Whether overt or subtle, diagnosis and treatment of infection are nevertheless the first priority, for two main reasons. First, sepsis locks intermediary metabolism in a state of catabolism. Thus, until sepsis has resolved, there is resistance to the normally anabolic effects of insulin on carbohydrate and protein metabolism, and little progress is possible, even though nutritional needs can be met or even exceeded [17].

Second, severe sepsis can develop quickly in this population, often following surgical intervention. Sepsis remains the most common direct cause of death in IF; some 70 % of deaths in an intestinal failure unit are a direct result of sepsis [9]. Therefore, as soon as possible after presentation, blood and line cultures, wound swabs, urine cultures, chest films, and computed tomography (CT) of the abdomen and pelvis with oral and intravenous contrast should be obtained. These tests may need to be repeated in patients who fail to thrive and complemented as required by echocardiography, magnetic resonance cholangiopancreatography, labelled leucocyte scintigraphy, and occasionally positron emission tomography/CT to identify occult septic foci.

Radiologically guided percutaneous drainage of abdominal and pelvic abscesses is the treatment of choice, unless the anatomic position of collection renders this impossible or anastomotic continuity is completely lost (in which case drainage without a defunctioning stoma is unlikely to provide adequate source control). Drainage should be supported (but not replaced) by antibiotic therapy, guided by expert microbiological advice, and adjusted following microbiological analysis of samples sent at the time of drainage.

Emergency laparotomy in type 2 IF should be undertaken only in systemically unwell patients in whom abdominal infection cannot be treated adequately by other means. At laparotomy, collections should be thoroughly washed out and cavities controlled with large-bore drains. Importantly, any suspicion of a visceral leak "feeding" the septic cavity warrants diversion of intestinal contents by resection and exteriorization of the bowel ends or the formation of a proximal diverting loop stoma. Severe, poorly controlled abdominal or pelvic sepsis, especially when there are multiple small-bowel loops fixed within the inflammatory process, may necessitate leaving the abdomen open. This improves control of abdominal sepsis, but at the cost of more complex wound management, more demanding abdominal wall reconstruction during later definitive surgery, and an increased risk of enteroatmospheric fistulation [12].

From the patient's point of view, the presence of an intestinal fistula, particularly poorly controlled drainage of fistula effluent onto the abdominal wall, is one of the most harrowing features of type 2 IF (Fig. 37.1). The involvement of expert enterostomal therapy in wound management should be considered early to protect the skin from leakage of enteric content. Given the complexity of intestinal fistulas in this setting, an individualized solution is likely to be required for each patient and may need to be revised as the size and shape of the wound changes with time (Fig. 37.2). Uncontrollable fistula leakage is an infrequent but important indication for a proximal defunctioning stoma.

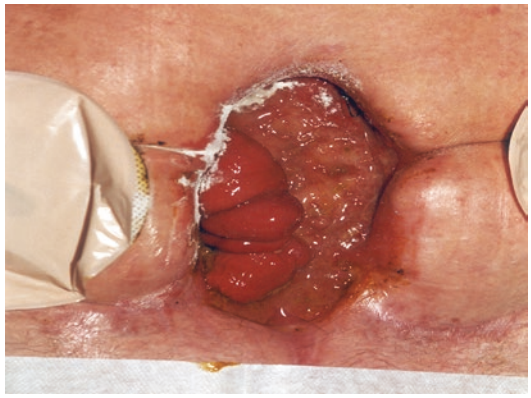


Fig. 37.2 Same patient as in Fig. 37.1 after 3 months of meticulous wound care, showing the beginning of bowel prolapse and a shrinking defect filled with granulation tissue

37.7 Nutrition and Medical Therapy

With the exception of complex research tools, there is no precise measure of nutritional status in severe illnesses such as type 2 IF. Weight and anthropometric measurements are often misleading because of the water retention and fluid shifts associated with acute illness. Hypoalbuminemia reflects systemic inflammation and is not a valid marker of nutritional status [18]. Other carrier proteins such as prealbumin and transferrin are similarly affected by acute disease states. In practical terms, a detailed history of recent nutritional intake and an estimate of weight loss are the most important pieces of information in the assessment of nutritional status in this population.

Nutritionists, dieticians, and pharmacists are essential members of the multidisciplinary team caring for patients with type 2 IF. Maintenance requirements of calories, protein, and micronutrients are estimated. Refeeding syndrome is an important concern for many patients and needs to be prevented using standard precautions [19]. Patients with type 2 IF are usually allowed fluids and food ad libitum, unless doing so would impede the resolution of abdominal sepsis, delay spontaneous fistula closure, or complicate wound management or fluid balance. Remaining fluid, electrolyte, and nutritional needs are met by parenteral nutrition.

In patients with an enterocutaneous fistula, the chance of spontaneous closure is assessed using established criteria (Table 37.3). Although the efficacy of bowel rest in this setting is only supported by observational data, it is often used and has been suggested to decrease the time to, and increase the probability of, spontaneous closure in cases where spontaneous closure is deemed likely [20]. In this group of patients, parenteral nutrition is therefore started and the patient given nothing by mouth or allowed only sips of water for comfort. Fistulas that close spontaneously invariably do so within the first 7 weeks [20, 21]; therefore, if a fistula fails to close within 7 weeks, oral or enteral nutrition is restarted at this point. Somatostatin analogues, frequently used for postoperative pancreatic fistulas, have been suggested as adjuncts in the management of enterocutaneous fistulas. The literature is unclear regarding the efficacy of somatostatin analogues; meta-analyses have included patients with pancreatic fistulas and patients with enterocutaneous fistulas [22]. An ongoing Cochrane review assesses the role of somatostatin analogues specifically in patients with enterocutaneous fistulas [23].

Patients with at least 80 cm of healthy, defunctioned, nonobstructed, and accessible (through an enterocutaneous or a mucous fistula) small intestine can successfully receive a significant amount of nutrition or fluids through distal enteral feeding or fistuloclysis. Such feeding can be used to condition the distal bowel before restoring continuity and may reduce or eliminate the need for parenteral fluids or nutrition in suitable patients [24].

Many patients with type 2 IF require a prolonged period of parenteral nutrition until definitive reconstructive surgery can be performed. This allows body composition and nutritional status to be restored while the patient recovers physically and psychologically from a period of critical illness. When possible, our preference is to discharge patients on parenteral nutrition to their own homes until reconstructive surgery is appropriate (see Sec. 37.9.1).

37.8 Investigation of Anatomy and Function

Cross-sectional imaging is often obtained to diagnose sepsis during initial assessment. CT of the abdomen and pelvis with both intravenous and oral contrast is ideal; it both enhances abscess

Table 37.3 Likelihood that a postoperative enterocutaneous fistula will close spontaneously can be estimated from the presence of favorable and unfavorable factors

Factor	Favorable	Unfavorable
Fistula	Long, narrow track	Short, wide track
	Intestinal continuity	Mucosal separation
	No obstruction	Diseased bowel
		Downstream obstruction
	Closed abdomen	Abdominal defect
Organ	Gastric	Duodenal
	Colon	Jejunoileal
Sepsis	Absent	Present
Aetiology	Inflammatory bowel disease	Other benign disease
		Malignancy
Age	<50 years	>50 years
Origin	Same hospital	Transfer
Fistula output	<500 mL/day	>500 mL/day
Malnutrition	Absent	Present
Duration	<7 weeks	>7 weeks

walls and gives an indication of the amount of bowel in and out of continuity. An early fistulogram may also be appropriate to determine whether there are factors that may allow or prevent spontaneous closure (Table 37.3). Other forms of radiological assessment are seldom of value until reconstructive surgery is planned and are therefore usually postponed, with the focus being clearly on treating infection and providing wound and stoma care and complication-free nutritional support.

Before reconstructive surgery, water-soluble contrast studies may be of value to precisely map the anatomy. The distal bowel should never be assumed to be healthy before any restoration of bowel continuity because clinically significant strictures caused by adhesions or nonidentified disease can be missed, leading to postoperative obstruction and anastomotic dehiscence. Radiological assessment includes, but is not limited to, small-bowel follow-through studies, fistulograms, and loopograms, the latter of which are undertaken to assess defunctioned intestinal segments. Retrograde studies via an ileostomy may also be helpful. Finally, the colon, if present and even if assumed to be healthy, must always be assessed, typically using a water-soluble, single-contrast water contrast enema. Occasionally, clinically silent fistulation to other structures may suggest the need for other imaging, including of the urinary and biliary tracts.

The size of any abdominal wall defect should be assessed using cross-sectional imaging shortly before performing reconstructive surgery so that an appropriate strategy can be developed for the reconstruction of any associated abdominal wall defect [25].

37.9 Surgical Procedures

37.9.1 Preoperative Planning

Definitive surgery for type 2 IF often has two principal and separate goals, both of which can be challenging. The first goal is to restore gastrointestinal continuity to the degree that the patient's anatomy allows, with the ultimate aim of restoring nutritional autonomy. The second goal, in the frequent case of an open abdomen or hernia, is to reconstruct the patient's abdominal wall. The timing of such surgery is critical. Although surgeons who rarely manage intestinal failure may feel the need to intervene early, experience has shown that attempting to restore intestinal continuity too early leads to an increased rate of complications, including anastomotic dehiscence and refistulation [20]. This is likely to be the result of both local factors, such as ongoing inflammation, and systemic pathophysiology, such as a catabolism and immunosuppression.

In practice, most patients with type 2 IF require 6–12 months of rehabilitation before definitive surgery. Local signs that wound healing

has been completed in the abdomen and that the peritoneal cavity has become less hostile (or reestablished, in the case of an open abdomen) include a soft abdominal wall and, specifically, prolapse of stomas or fistulas upon coughing. Systemic assessment includes, in addition to a routine physical examination and nutritional assessment, a preoperative cardiopulmonary exercise tolerance test and serum albumin determination as a marker of occult inflammation. Considerable planning should be undertaken with respect to the strategy for reconstructing both the gastrointestinal tract and abdominal wall, so that the proposed treatment plan can be discussed in detail with the patient first. Reconstructive surgery is frequently high risk, complex, and undertaken in stages, and there may be a variety of surgical options. It is essential that, as part of the process of informed consent, the patient and his or her family understand what treatment is being proposed and the associated risks and benefits.

Surgery is usually undertaken in the Lloyd-Davies position. Ureteric catheters are beneficial to help identify the ureters, which are frequently displaced and scarred from previous surgery. Ample time in the operating room should be allowed. Because of the length (often on the order of 10–12 h) and complexity of surgery, definitive reconstructive surgery for type 2 IF is best performed by teams with two senior gastrointestinal surgeons and colleagues from relevant specialties such as urology, plastic surgery, and occasionally vascular surgery [25].

37.9.2 Restoration of Gastrointestinal Continuity

For patients with available distal discontinuous bowel, restoration of continuity may obviate or reduce the need for long-term parenteral nutrition and its associated complications. In each case these potential benefits must be weighed against the risks of anastomotic dehiscence. This risk is reduced by delaying surgery as described until local and systemic factors are optimized, including weaning from steroid therapy and treatment with biologics and immunomodulators, where appropriate. Enterocutaneous and other intestinal fistulas should be formally resected, rather than simply repaired, which almost inevitably fails [25].

After careful reentry into the abdomen, the full length of the small bowel is mobilized and freed of adhesions to reduce the risk of postoperative obstruction. Avoidance of serosal tears and enterotomies is essential. For dense adhesiolysis, such as in the dissection of fragile, defunctioned small intestine off the abdominal wall, we prefer meticulous knife dissection to diathermy or scissors (Fig. 37.3). The anastomotic technique must be meticulous. The choice of anastomotic technique is probably less important, although stapled side-to-side anastomosis may facilitate the restoration of continuity where there is a significant size discrepancy between two bowel ends. It does, however, result in a modest loss of available functional surface area, which, when multiple anastomoses are created in a relatively short bowel, may become critical. Anastomoses should never be left in old abscess cavities, as this increases the likelihood of refistulation. The omentum may be used to fill old cavities and sutured into position to prevent the small intestine from falling into the sites of old abscesses. Multiple anastomoses should be defunctioned with a proximal loop or double-barreled (split) stoma, and this can be subsequently closed when downstream imaging has confirmed satisfactory healing.

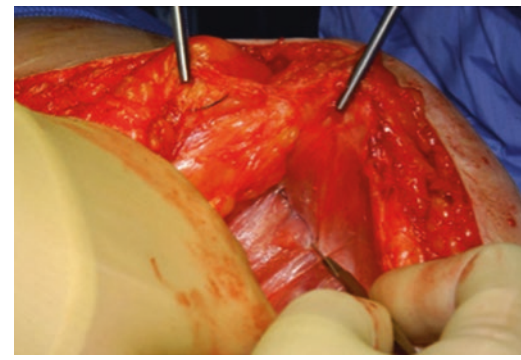


Fig. 37.3 Sharp knife dissection of dense abdominal adhesions

37.9.3 Abdominal Wall Reconstruction

The scope of this chapter does not allow a comprehensive review of abdominal wall reconstruction; however, a few points specific to IF surgery are warranted. Reconstruction of an associated abdominal wall defect has a crucial impact on the outcome of reconstructive surgery. Failure of abdominal wall reconstruction is associated with an unacceptable risk of refistulation, and the optimal strategy for abdominal wall reconstruction should therefore be considered at the outset [25, 26].

Implantation of nonbiological foreign material should be avoided whenever possible, as abdominal wall defects are almost always heavily contaminated. In moderately large fascial defects, closure can often be achieved using component separation techniques [27], perhaps reinforced by inserting porcine dermal collagen implants. The use of implants alone has been associated with very poor results in this setting [26], whereas recent refinements in technique, such as the posterior separation of components, have reduced some of the complications associated with anterior abdominal wall release [28].

In very large abdominal wall defects, free pedicled musculocutaneous flaps are indicated and excellent outcomes have been reported, provided the necessary plastic surgery expertise is available [29].

37.10 Management of Type 3 IF

Surgery currently has a limited role in the management of patients with type 3 IF. The vast majority of adult patients with type 3 IF seem to have an acceptable quality of life on HPN. Intestinal transplantation is reserved for otherwise healthy individuals who develop complications of HPN, such as IF-associated liver disease, requiring liver transplantation, or loss of venous access, usually as a consequence of repeated episodes of catheter-related sepsis or thrombosis. In such cases, intestinal transplantation may be appropriate.

Alternative strategies for increasing the length of functional small intestine in patients with short bowel syndrome, including intestinal lengthening procedures, have been evaluated in children and may be successful in restoring nutritional autonomy [30]. Experience with similar techniques in adults is, however, considerably more limited and the outcomes currently unclear [31]. In select patients with a marginal amount of small bowel, growth factor therapy with a glucagon-like peptide 2 analogue has been shown to reduce dependence on HPN.

References

1. Fleming CR, Remington M. Intestinal failure. In: Hill GL, editor. Nutrition and the surgical patient. Edinburgh: Churchill Livingstone; 1981. p. 219–35.
2. Pironi L, Arends J, Baxter J, Bozzetti F, Peláez RB, Cuerda C, et al. Clinical nutrition. Amsterdam: Elsevier Ltd; 2014. p. 1–10.
3. Jeppesen PB, Mortensen PB. Intestinal failure defined by measurements of intestinal energy and wet weight absorption. Gut. 2000;46(5):701–6.
4. Shaffer DJ. Intestinal failure. Clinical nutrition. Elsevier Sci Ltd. 2002;21(Supplement 1):144–5.
5. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, et al. Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). Ann Surg. 2011;254(6):868–75.
6. Carlson GL, Gardinger K, McKee R, MacFie J, Vaizey CJ. The surgical management of patients with acute intestinal failure. London: Association of Surgeons of Great Britain and Ireland; 2010. p. 40.
7. Smith T, Micklewright A, Hirst A, Stratton RJ, Baxter J. BANS: annual BANS report, 2011 [Internet]. Smith T, editor. BAPEN; 2011 Nov pp. 1–50. Available from: http://www.bapen.org.uk.
8. Basse L, Madsen JL, Kehlet H. Normal gastrointestinal transit after colonic resection using epidural analgesia, enforced oral nutrition and laxative. Br J Surg. 2001;88(11):1498–500.
9. Lal S, Teubner A, Shaffer JL. Review article: intestinal failure. Aliment Pharmacol Ther. 2006;24(1):19–31.
10. Trevelyan SL, Carlson GL. Is TNP in the open abdomen safe and effective? J Wound Care. 2009;18(1):24–5.
11. Rao M, Burke D, Finan PJ, Sagar PM. The use of vacuum-assisted closure of abdominal wounds: a word of caution. Colorectal Dis. 2007;9(3):266–8.
12. Carlson GL, Patrick H, Amin AI, McPherson G, MacLennan G, Afolabi E, et al. Management of the open abdomen. Ann Surg. 2013;257(6):1154–9.

13. Van Der Krabben AA, Dijkstra FR, Nieuwenhuijzen M, Reijnen MM, Schaapveld M, van Goor H. Morbidity and mortality of inadvertent enterotomy during adhesiotomy. Br J Surg. 2000;87(4):467–71.
14. Agwunobi AO, Carlson GL, Anderson ID, Irving MH, Scott NA. Mechanisms of intestinal failure in Crohn's disease. Dis Colon Rectum. 2001;44(12):1834–7.
15. Tzivanakis A, Singh JC, Guy RJ, Travis SPL, Mortensen NJ, George BD. Influence of risk factors on the safety of ileocolic anastomosis in Crohn's disease surgery. Dis Colon Rectum. 2012;55(5):558–62.
16. Williams NM, Scott NA, Irving MH. Successful management of external duodenal fistula in a specialized unit. Am J Surg. 1997;173(3):240–1.
17. Streat S, Beddoe A, Hill G. Aggressive nutritional support does not prevent protein loss despite fat gain in septic intensive care patients. J Trauma. 1987;27(3):262–6.
18. Smith G, Robinson PH, Fleck A. Serum albumin distribution in early treated anorexia nervosa. Nutrition. 1996;12(10):677–84.
19. NICE Clinical Guidelines No. 32 [Internet] [cited 2014 Nov 19]. Available from: http://guidance.nice.org.uk.
20. Visschers R, Olde Damink S, Winkens B, Soeters P, van Gemert W. Treatment strategies in 135 consecutive patients with enterocutaneous fistulas. World J Surg U S. 2008;32(3):445–53.
21. Reber HA, Roberts C, Way LW, Dunphy JE. Management of external gastrointestinal fistulas. Ann Surg. 1978;188(4):460–7.
22. Rahbour G, Siddiqui MR, Ullah MR, Gabe SM, Warusavitarne J, Vaizey CJ. A meta-analysis of outcomes following use of somatostatin and its analogues for the management of enterocutaneous fistulas. Ann Surg. 2012;256(6):946–5.
23. Stevens P, Burden S, Delicata R, Carlson GL, Lal S. Somatostatin analogues for treatment of enterocutaneous fistula (protocol). Cochrane Database Syst Rev. 2013:CD010489.
24. Teubner A, Morrison K, Ravishankar HR, Anderson ID, Scott NA, Carlson GL. Fistuloclysis can successfully replace parenteral feeding in the nutritional support of patients with enterocutaneous fistula. Br J Surg. 2004;91(5):625–31.
25. Slade DA, Carlson GL. Takedown of enterocutaneous fistula and complex abdominal wall reconstruction. Surg Clin N Am Elsevier Inc. 2013;93(5):1163–83.
26. Connolly P, Teubner A, Lees N, Anderson I, Scott N, Carlson G. Outcome of reconstructive surgery for intestinal fistula in the open abdomen. Ann Surg. 2008;247(3):440–4.
27. de Vries Reilingh TS, Bodegom ME, van Goor H, Hartman EHM, van der Wilt GJ, Bleichrodt RP. Autologous tissue repair of large abdominal wall defects. Br J Surg. 2007;94(7):791–803.
28. Novitsky YW, Elliott HL, Orenstein SB, Rosen MJ. Transversus abdominis muscle release: a novel approach to posterior component separation during complex abdominal wall reconstruction. Am J Surg Elsevier Inc. 2012;204(5):709–16.
29. Lambe G, Russell C, West C, Kalaiselvan R, Slade DAJ, Anderson ID, et al. Autologous reconstruction of massive enteroatmospheric fistulation with a pedicled subtotal lateral thigh flap. Br J Surg. 2012;99(7):964–72.
30. King B, Carlson G, Khalil BA, Morabito A. Intestinal bowel lengthening in children with short bowel syndrome: systematic review of the Bianchi and STEP procedures. World J Surg. 2012;37(3):694–704.
31. Yannam GR, Sudan DL, Grant W, Botha J, Langnas A, Thompson JS. Intestinal lengthening in adult patients with short bowel syndrome. J Gastrointest Surg. 2010;14(12):1931–6.

Abdominal Wall Reconstruction

38

Neil J. Smart and Ian R. Daniels

38.1 Introduction

In their desire to access the colon and rectum, surgeons may be guilty of overlooking one of the most important structures necessary for the well-being of their patient – the anterior abdominal wall. This complex structure, bounded superiorly by the costal margin and xiphoid process; inferiorly by the symphysis pubis, superior pubic ramus, inguinal ligament, and iliac crest; and laterally by the midaxillary line, comprises skin, subcutaneous adipose tissue, superficial and deep fascia, muscles, extraperitoneal fascia, and peritoneum. The four pairs of muscles that comprise the anterior abdominal wall are the rectus abdominis, the external and internal obliques, and the transversus abdominis. It is beyond the scope of this chapter to provide a comprehensive overview of all the pertinent anatomy, and readers are directed to the many excellent anatomy texts available, both in print and online. Suffice it to say, a detailed understanding of anatomy is necessary not only to understand the reconstructive techniques available for hernia repair but also to avoid making many of the common operative mistakes that lead to complications, which may haunt both patient and surgeon alike.

The anterior abdominal wall serves many functions, the least of which is to act as a barrier to contain the intestines. Roles in respiration (expiration in particular), locomotion, micturition, defecation, and parturition are all equally as important. However, these functions may have been overlooked by the surgical community in the past in favour of the concept of the abdomen as a "*passive container for the gut,*" most frequently reported in studies as "*the incisional hernia rate*" or "*recurrence rate*". Disability and impaired quality of life caused by abdominal wall herniae should not be underestimated, but while quality of life outcomes have been reported, functional outcomes are conspicuous because of their near total absence from the literature [1]. What follows in this chapter is a discussion derived from a scientific evidence base that reports rates of recurrence almost always, complications frequently inconsistently, quality of life occasionally, and functional outcomes almost never.

38.2 Definition and Classification

The nomenclature and classification of abdominal wall herniae and the surgical approaches to repair encompass a diverse range of anatomic defects, patients, and situations. Standardization of the terminology relating to both classification

N.J. Smart, MBBS(Hons) PhD FRCSEd(Gen Surg)
I.R. Daniels, BSc, MB BCh, FRCS (✉)
Exeter Surgical Health Service Research Unit (HeSRU), Royal Devon & Exeter Hospital, Barrack Road, Exeter, Devon, UK, EX2 5DW
e-mail: i.daniels@nhs.net

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2_38

and surgical techniques allows comparison of outcomes and, ultimately, optimal patient selection and tailored therapies. While colorectal surgeons are very familiar with this approach from a cancer perspective, the process is, by comparison, in its infancy as it relates to abdominal wall herniae, which makes interpretation of the literature challenging.

Over the past 15 years, attempts to classify abdominal wall herniae have been made; for example, Chevrel and Rath [2] focused on location, size, and recurrence. Subsequent modifications were proposed that incorporated reducibility, symptoms, and the abdominal wall-defect ratio [3, 4]. The first expert consensus classification under the auspices of the European Hernia Society provided a standardized definition of incisional hernia: "*Any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging*" [3]. This definition has gained popularity, and its use persists in the most recent European Hernia Society classification of primary and incisional abdominal wall herniae [5]. Unfortunately, none of these classifications have been widely adopted in everyday clinical practice or in the reporting of studies. The main limitations are that they are cumbersome to use, focus on the hernia rather than the whole patient, and fail to define what represents "*simple*" and what is "*complex*." There is no account of domain loss, concurrent bowel disease (e.g. Crohn's disease, cancer, stoma, enterocutaneous fistula), infection, comorbidities, mode of assessment (clinical vs. radiological vs. intraoperative), or situation (emergency vs. elective). The differentiation between what is one surgeon's "*incisional hernia repair*" and another's "*complex abdominal wall reconstruction*" remains vague (Fig. 38.1).

Recent attempts have been made to create more holistic classifications of abdominal wall herniae. The Ventral Hernia Working Group (VHWG) developed a classification that uses an intuitive blend of patient and hernia characteristics to provide four categories [6] (Fig. 38.1). Simple and easy to use, it has gained popularity in reports of large case series, particularly those originating from North America. This simplicity, although appealing, may be a significant limitation, with marked intragroup variability. Only one study has assessed prospectively the validity of the classification system, and it recommended modifications [7]. Slater et al. [8] attempted to define "*complex abdominal wall hernia*" on the basis of 22 patient- and hernia-related variables and also proposed three categories of patient severity. Although comprehensive, its use is complex and widespread adoption has not yet occurred.

38.3 Epidemiology

Incisional hernia after laparotomy is common and may affect up to 20% of unselected patients and up to 50% of high-risk patients [9]. The rate of incisional hernia development reported in the literature varies widely, in part because of the differences in the duration of follow-up and also because of the techniques used to detect herniae [10–12]. The longer the duration of follow-up, the higher the incisional hernia rate; long-term follow-up of randomized studies suggests that the rate of incisional hernia increased from 12.6% at 1 year to 22.4% after 3 years [13]. Axial computed tomography has a sensitivity for hernia detection far higher than clinical examination, particularly in obese patients and in those who have had previous hernia repairs [14, 15]. Increased use of cross-sectional imaging as part of colorectal cancer follow-up programs

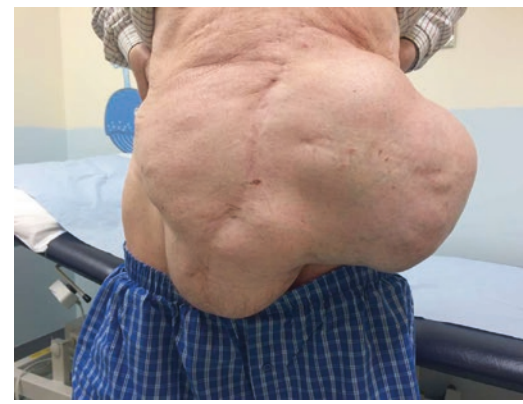


Fig. 38.1 Nomenclature regarding abdominal wall defects remains vague. Is this patient due to have an incisional hernia repair or a complex abdominal wall reconstruction?

will inevitably lead to a higher rate of hernia detection compared with clinical examination, but it does not necessarily inform which of the herniae found incidentally will ultimately require surgical intervention. This represents the rate of incisional hernia following laparotomy and the variation relates to time from surgery [16]. Nevertheless, laparotomy remains a common procedure, with an estimated 4–5 million being performed annually in the United States, resulting in an estimated 500,000 incisional herniae, of which between 15% and 47% may be classified as "*large*" and in need of abdominal wall reconstruction [17].

38.4 Etiology

Traditional wisdom held that incisional herniae resulted from technical failure during the surgical closure of the abdominal wall. The situation is far more complicated, however, with a myriad of factors pertaining to the patient, the surgeon, and the postoperative course all playing a role – namely, to have an adverse effect on wound healing. The quality of the data underpinning this wider appreciation of hernia development has largely been derived from retrospective series, and the relative importance of each factor has been incompletely characterized.

38.4.1 Patient Factors

Factors that predispose a patient to incisional hernia formation may be broadly categorized as congenital or acquired. Both, however, are related in that the underlying pathology relates to connective tissue abnormalities resulting from altered synthesis, maturation, or degradation of collagen [18]. This manifests as a decreased Type I : Type III collagen ratio and altered matrix metalloproteinase activity. Congenital syndromes such as Marfan, Loeys-Dietz, and Ehlers-Danlos are well recognized, but in these cases it has become increasingly accepted that herniae may be a reflection of a wider systemic disease process that has been termed *herniosis* [19, 20]. This represents an as-yet poorly defined nonspecific connective tissue disorder that may encompass conditions as diverse as abdominal wall herniae, aortic aneurysms, diverticulosis, and pelvic organ prolapse [21].

The relationship between herniosis, genetics, and epigenetic factors is not clearly understood. Mutations in certain genes have been implicated in the development of some abdominal wall herniae [22, 23], but this does not explain the formation of a hernia in the majority of those afflicted by the condition [24]. It is more likely that differential gene expression (i.e. epigenetics) plays a part and may be related to collagen synthesis, deposition, maturation, and turnover regulated by matrix metalloproteinases and their endogenous inhibitors (tissue inhibitors of metalloproteinases) [18, 25]. As a systemic disease, the changes in collagen are noted in both the skin and abdominal wall fascia [25, 26].

Numerous acquired factors have been postulated as predisposing to incisional hernia; these are summarized in Table 38.1. The deleterious effects of smoking [27] and obesity [28] on hernia formation have been known for some time and are likely to be mediated via epigenetic influences on several aspects of collagen metabolism. From a specifically colorectal perspective, the influence of neoadjuvant therapies such as radiotherapy and/or chemotherapy on rates of hernia formation has not been studied, although their detrimental effect on tissue healing is generally well known. Whether the innate or acquired aspects of abnormal collagen metabolism are more important in the development of incisional herniae is unclear, but a deeper understanding of the molecular, genetic,

Table 38.1 Acquired factors postulated to predispose patients to incisional hernia development

Age
Malnutrition/micronutrient deficiency
Obesity
Diabetes
Wound infection
Smoking
Steroids/immunosuppression
High intra-abdominal pressure (chronic obstructive pulmonary disease, benign prostatic hyperplasia, ascites)

and epigenetic bases of the disease is likely to offer new avenues for therapeutic interventions.

38.4.2 Surgeon Factors

Midline incisions remain the most common source of incisional hernia, in part because of the popularity of this method of surgical access to the abdominal cavity. Transverse incisions have been advocated by some surgeons because of a claimed lower incisional hernia rate. This was supported by a recent update of a Cochrane systematic review (odds ratio 0.49; 95 % confidence interval 0.26–1.72), although the methodological and clinical diversity, and the potential for bias in the studies included in the meta-analysis, invoked caution from the authors [29]. This is understandable given that incisions away from the midline, such as those used for a temporary stoma, remain a common site of incisional herniae [30].

The type of suture material used and the technique used to close the wound have been subject to increased scrutiny. A systematic review and meta-analysis of randomized controlled trials (RCTs) suggests that slowly absorbable sutures result in lower incisional hernia rates than the use of rapidly absorbable or nonabsorbable suture material, and that continuous suturing techniques are superior to interrupted [9]. The basis of abdominal closure as described by Jenkins [31] regarding the size of the pieces of tissue has been promulgated for decades as 1 cm "*bites*" 1 cm apart, but his has been challenged by both animal models and human evidence from RCTs [32, 33]. Multicenter RCTs are ongoing, and the adoption of the "*small bite*" technique is not yet widespread [34].

38.4.3 Postoperative Factors

Postoperative wound infection carries a significant risk of hernia development and is probably the single most important factor, although all complications that increase intra-abdominal pressure may also have deleterious effects on wound healing and rate of incisional hernia occurrence [35].

38.5 Preoperative Planning

> Many very skilful operators are not good surgeons.
> William J. Mayo, cofounder of the Mayo Clinic, Rochester, MN.

The traditional aphorisms that abound in surgery regarding the appropriate investigation, planning, and selection of patients are pertinent to abdominal wall reconstruction. Performing the wrong operation on the wrong patient at the wrong time is a recipe for disaster for both the surgeon and patient. Every effort should be made to avoid getting into trouble in the first instance, and meticulous planning combined with multidisciplinary teamwork is essential. Optimizing the patient to minimize risk and maximize success should be the team's endeavour before embarking on operative intervention.

38.5.1 Deciding Whom to Operate on

Not all patients who have an incisional hernia require surgery. Some undoubtedly present as an emergency with symptoms of strangulation or obstruction, but more common is the elective patient who has symptoms either of pain or relating to impairment of abdominal wall function and a subjective diminished quality of life. The patient must therefore be counseled in depth before embarking on an operation that carries not insignificant risk in many circumstances. This may necessitate a staged approach over time as all investigations are completed and (peri-)operative risk is accurately assessed. Asymptomatic patients may come to less harm if left alone, but if their hernia enlarges and causes problems, reassessment is advisable.

38.5.2 Computed Tomography

Cross-sectional imaging with computed tomography allows accurate assessment of the hernia defect, the quality of abdominal wall tissue, the contents of the hernia sac itself, and of the rest of the abdominal cavity. For patients who have had previous colorectal or other intra-abdominal cancer surgery, exclusion of recurrent or metachronous

malignancy is mandatory (Fig. 38.2). Computed tomography allows the surgical approach to be planned preoperatively and may be used to calculate the risk of development of postoperative abdominal compartment syndrome [36] (Fig. 38.3).

38.5.3 Smoking Cessation

Smoking is associated with a significant increase in the risk of hernia recurrence following surgery and predisposes patients to postoperative wound complications (Fig. 38.4). In addition, smoking cessation during the perioperative period reduces surgical site infections [27]. The evidence for the benefits of smoking cessation before a wide variety of surgeries is now well established, and insistence on smoking cessation should be considered every bit as essential as the correction of other medical comorbidities such as hypertension, diabetes, and cardiac disease [37]. Perioperative smoking cessation programs are effective in an elective setting, and patients should be referred as necessary.

38.5.4 Obesity Management and Dietitian Assessment

Obesity is well recognized as a risk factor for the development of incisional hernia, and it is also associated with an increased risk of recurrence and postoperative complications [28, 38, 39]. Conclusive evidence that preoperative weight

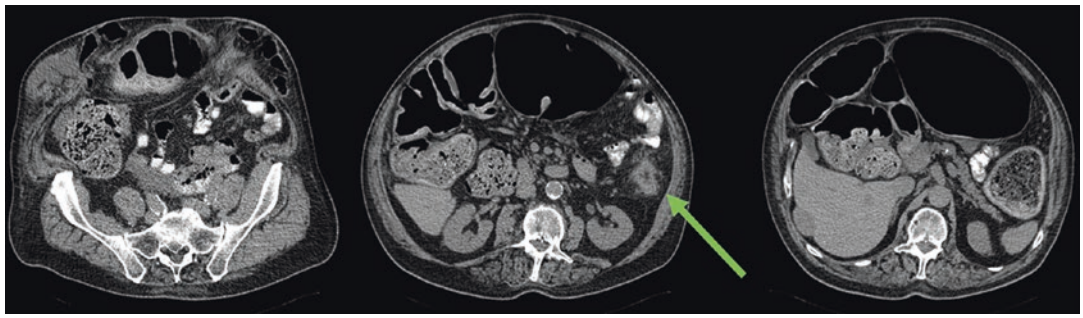


Fig. 38.2 Cross-sectional imaging with computed tomography not only demonstrates the complex nature of the abdominal wall defect but also shows any pathology, such as a metachronous colonic carcinoma (*arrow*)

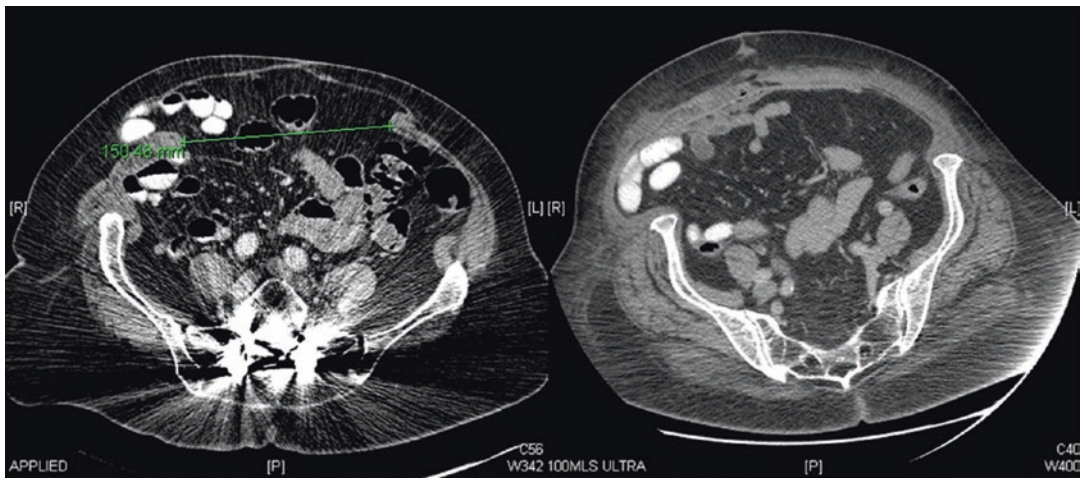


Fig. 38.3 Computed tomography allows for the defect to be assessed in detail, operative techniques to be planned, and the risk of abdominal compartment syndrome to be assessed once the abdomen has been reconstructed

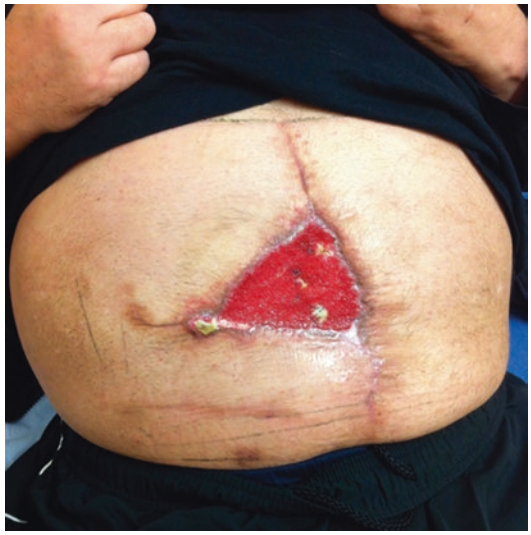


Fig. 38.4 Smoking predisposes patients to wound complications such as flap necrosis due to microvascular insufficiency

loss makes a positive difference is lacking because few studies have been performed, and those that have lack statistical power [40]. The degree of weight loss required to effect a clinically significant reduction in either recurrence rates or postoperative complications is simply unknown. The complication rate and risk of hernia recurrence increase sharply with a body mass index >35 kg/m^2. Therefore, in the elective setting, postponing surgery and referring the patient to an obesity management service seems prudent. If the patient loses weight, they should be encouraged to carry on. The optimal timing of surgery is probably when the patient's BMI is <30 kg/m^2 or when their weight stops decreasing.

Despite the prevalence of obesity among those with large incisional herniae, micronutrient imbalance is common, with tissue concentrations of copper and zinc being depleted [41, 42]. These trace elements have a well-described role in wound healing, and it is highly conceivable that their diminished concentrations have a negative effect on hernia recurrence rates. Correcting levels in either the tissue or plasma by supplementation alone may not be sufficient without addressing the complex interplay with inflammatory processes that initiated the imbalance. Although studies of micronutrient supplementation have been performed in conditions of superficial wound healing, burns, and pressure sores, there is an absence of data to support their use in patients with hernia.

38.5.5 Cardiopulmonary Exercise Testing

Cardiopulmonary exercise testing has recently come to the fore as the method of choice for assessing the cardiorespiratory fitness of any patient due to undergo high-risk surgery as well as high-risk patients (usually elderly [i.e. >70 years old]) due to undergo any surgery. The level of an anaerobic threshold "*cut off*" between those deemed fit and unfit varies in the literature between 10 and 11 mL/kg/min, but it seems to correlate with outcome across a range of abdominal operations, although data specific to abdominal wall reconstruction are absent. This correlation may be useful when counseling patients regarding complex surgery and when planning postoperative care pathways, such as elective admission to critical care units [43]. The data may also be used as a baseline to monitor improvements in fitness with graduated exercise or "*prehabilitation*" programs.

38.5.6 Elderly Patients

Elderly patients warrant special consideration because of the relatively high prevalence of medical comorbidities. Perioperative care of older people having surgery services have been developed over the past decade or so, predominantly in orthopedic surgery, with considerable benefit and are now extending across many other areas of surgical practice [44]. This positive development is to be welcomed; its benefits include better preoperative optimization, fewer postoperative medical complications, and better discharge planning for those with complex social care needs.

38.5.7 Anaemia

Anaemia is a common among the general population but particularly in the preoperative population, and patients with concomitant gastrointestinal diseases have a high prevalence [45]. Several cohort studies of a wide range of surgical procedures consistently demonstrated that patients with preoperative anemia have poorer postoperative outcomes than nonanemic patients to the extent that many now regard anemia as a contraindication to elective surgery [45]. Transfusion of packed red blood cells has long been considered the default option for correction of anemia, but it is increasingly recognized that it may be associated with adverse postoperative outcomes [46]. Consequently, a multimodal approach to patient blood management is now advocated, and guidance exists on strategies for preoperative correction [45].

38.6 Operative Strategies

No single operative strategy is sufficient for every hernia, patient, or situation, and consequently those surgeons who perform abdominal wall hernia repair require a large armamentarium of techniques. The key principles of any hernia repair have been defined as closure of the defect without excess tension and excision or obliteration of the sac, which can be achieved by several approaches. The first dichotomy relates to an open or laparoscopic approach. Open surgery remains the method of choice for large hernia defects, patients who require concomitant bowel surgery, and patients in whom laparoscopy is not feasible because of intra-abdominal adhesions. Debate remains regarding what may be classed as a "*large defect*" with most advocating open surgery for hernia defects larger than 10 cm in diameter. While hernia defects with a diameter less than 5 cm may be most amenable to the laparoscopic approach, the optimal approach for defects with diameters between 5 and 10 cm remains a source of controversy.

38.6.1 Open Approaches

Open repair of complex abdominal wall defects has the potential to be one of the most technically challenging procedures in the field of abdominal surgery. It may be associated with a significant physical insult to the patent, and meticulous preoperative planning is essential, not least in terms of pain relief that the patient will require in the postoperative setting. Patients with large defects usually benefit from epidural analgesia, which offers superior analgesia compared with alternative strategies and results in fewer postoperative complications [47].

38.6.1.1 Primary Suture Repair

The challenge of obtaining good long-term results with fascial apposition using sutures alone has been recognized for some time. Although some surgeons have advocated specific suture techniques designed to allow progressive tensioning via what is essentially a pulley mechanism [48], high-quality long-term data demonstrating effectiveness are lacking. Simple suture repair alone often fails because the edges of the repair are under tension following closure. The superiority of mesh repair compared with suture repair is now well established [49], and suture repair is no longer advocated in the setting of planned, clean surgery. The role of suture repair is now confined to the contaminated and or infected setting, which often occurs in emergency surgery, where the operating surgeon feels the placement of mesh (of whatever type) is contraindicated, largely because suture repair has a significantly lower rate of infective complications. A definitive repair with mesh can be performed at a future date as a planned procedure should a hernia develop again.

38.6.1.2 Components Separation

A technical advance on simple suture repair is the separation of the components of the abdominal wall to allow medial displacement of the myofascial edge, thus reducing tension to physiological levels and consequently facilitating the repair. Although various descriptions of lateral relaxing incisions have appeared in the literature for

nearly 100 years [50], their use in abdominal wall reconstruction was popularized by Ramirez et al [51] in 1990. In anterior component separation, the rectus abdominis, internal oblique, and transversus abdominis are separated from the external oblique by an incision of the external oblique aponeurosis just lateral to the linea semilunaris. This may allow the unilateral medial fascia to be advanced a maximum of 10 cm. Despite the ability to close large defects, evidence to support the superiority of anterior component separation over primary suture repair is lacking, and high recurrence rates have been reported [52]. Consequently, many now describe its use in conjunction with reinforcing mesh repairs. The anterior component separation technique is also associated with significant tissue trauma, which may result in lipocutaneous flap necrosis, seroma, and wound infection. Minimally invasive variants of the anterior component separation technique have been described that seek to minimize such tissue trauma [53].

An alternative strategy to facilitate closure of large defects is posterior component separation, which releases the rectus abdominis and external and internal oblique muscles from the transversus abdominis. During a laparotomy, the retrorectus plane is developed laterally until the perforating neurovascular bundles are reached, just medial to the linea semilunaris. The posterior rectus sheath is incised to afford access to the plane between the internal oblique and transversus abdominis. The insertion of the transversus abdominis muscle into the posterior sheath can be divided and the muscle separated from the underlying transversalis fascia and peritoneum. This technique avoids the large lipocutaneous flaps of the anterior component separation technique and associated wound morbidity, but still allows a similar degree of myofascial medialization [54]. Evidence of its effectiveness is limited to case series where it is usually combined with a retromuscular mesh repair.

38.6.1.3 Mesh Repair

Mesh repairs of herniae have been used for over 100 years, but only with the advent of modern synthetic materials and the pioneering work of the American surgeon Francis Usher in the 1950s did any significant advance in outcome occur. Meshes work via two main mechanisms. Initially, they have their own tensile strength that imparts additional support to the repair. They subsequently induce (or support) tissue ingrowth and collagen deposition to form a scar that adds strength. Mesh may be placed in numerous positions within the abdominal wall.

In the onlay technique, the mesh sits superficial to the anterior rectus sheath and usually overlies the apposed fascial edges, with an overlap of 5–8 cm. The inlay technique essentially utilises the mesh as a bridge across the fascial edges of the hernia defect. This was a popular technique during the 1990s and borrowed the concept of "*tension-free*" repair from inguinal hernia surgery and applied it to abdominal wall hernias, although the biomechanics of the two areas are different. The mesh may overlap, either superficially or deep, beyond the margins of the defect to facilitate fixation.

"*Sublay*" is a term that results in some confusion because it has been used to refer to both the retromuscular and intraperitoneal positions. In retromuscular placement, the plane between the rectus abdominis muscle and the posterior rectus sheath is developed by incising the posterior rectus sheath approximately 0.5 cm from its medial edge. Dissection may be the initiated just above the level of the umbilicus and progressed laterally using diathermy until the linea semilunaris is reached. The perforating neurovascular bundles that enter the rectus sheath just medial to the linea semilunaris are preserved. Once both sides are mobilized, the posterior sheath is closed. If the posterior sheath is incomplete and cannot be approximated, either the hernia sac may be used to provide coverage of the abdominal contents, the falciform ligament, or bladder, or the omentum can be carefully placed over the bowel to prevent adhesions forming to the mesh. The mesh lies posterior to the rectus abdominis muscle but superficial to the posterior rectus sheath cranial to the arcuate line (Fig. 38.5). The mesh lies in the preperitoneal plane, caudal to the arcuate line. The anterior sheath is then reapproximated in the midline.

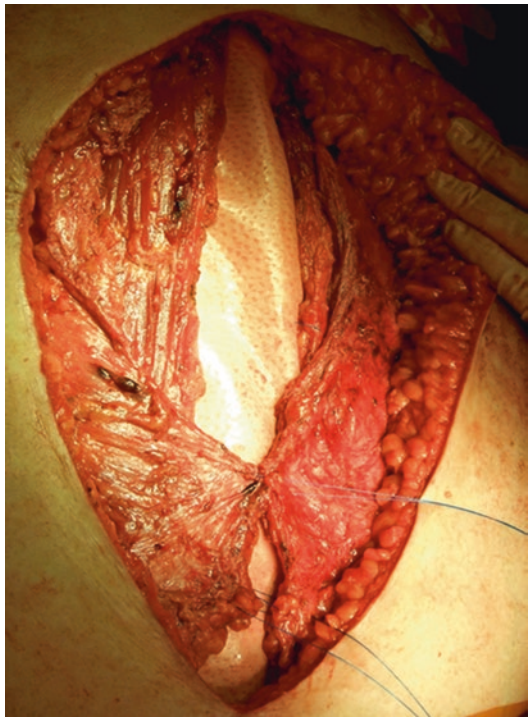


Fig. 38.5 Retrorectus placement of a biologic mesh during an open repair

In the intraperitoneal placement technique, the mesh lies inside the abdominal cavity and is fixed to the abdominal wall. In open surgery, the midline defect is usually closed, whereas in the laparoscopic variant, the defect is not necessarily closed, with the mesh acting as a barrier to intra-abdominal organs entering the hernia sac (often known as intraperitoneal onlay mesh repair). The deep surface of the mesh may come into contact with intra-abdominal organs.

The relative merits of each of the mesh placement techniques have been debated for some time, with passionate advocates for each at some point over the past 50 years. The onlay technique is technically easy and versatile, as is the inlay technique (often referred to as "*bridging*"). The retromuscular and intraperitoneal positions are thought to have superior biomechanical advantages, with the meshes being held in the correct positions by intra-abdominal pressure. Ultimately, recurrence rate following hernia repair has been used as the measure for determining which technique offers the optimal outcome.

The inlay technique is now recognized to have an unacceptably high recurrence rate. The reasons for failure of the hernia repair are multifactorial and may be the result of shrinkage of the synthetic mesh, the complex biomechanical forces of the abdominal wall that cause the mesh itself to fail, the mesh–tissue interface, or undue stretching on the ingrowing tissue. Furthermore, many of the meshes originally used with the inlay technique were associated with complications such as erosion into the bowel and enterocutaneous fistulas. Consequently, the technique is no longer advocated. Systematic review of randomized trials failed to demonstrate any superiority of onlay versus sublay mesh placement techniques [49]. Conversely, national registry data suggest that retromuscular repair results in a markedly lower recurrence rate compared with the other techniques [55]. Many authors and the European Hernia Society now regard the retromuscular technique as the reference standard for open repair. It can be combined with posterior component separation to facilitate the closure of large defects.

38.6.2 Laparoscopic Approaches

Laparoscopic approaches are ideally suited to patients who have amenable peritoneal cavities, smaller herniae, and require simpler procedures, usually without concomitant bowel resections or abdominoplasty. Adhesiolysis may be the most technically challenging aspect of the procedure, and avoiding energy devices is advisable; sharp dissection with scissors is preferable. Several reviews of randomized trials concluded that there is no difference in recurrence rates compared with open procedures, but that complications rates are lower, specifically wound infections [56, 57]. Recent data from national registries may suggest a lower crude recurrence rate with laparoscopy, but the data are not risk adjusted for selection bias regarding the surgical approach chosen, and interestingly, laparoscopy was associated with increased rates of the more serious complications [55].

38.6.2.1 Intraperitoneal Onlay of Mesh

The intraperitoneal position of mesh placement is synonymous with the laparoscopic approach. The most prevalent technique is to use the mesh as a bridge across the hernia defect. The optimal size of the mesh depends on the size of defect being repaired, but it needs to account for mesh shrinkage, which may be up to 94 % of the surface area [58]. Consequently, the traditional advice of a 5-cm overlap may not be reliable as defects size increases and the mesh-to-defect ratio becomes smaller. Significant debate exists among surgeons as to the optimal method of fixation, positioning and tension in the mesh when placed during laparoscopic repair. If the mesh placement is not optimal, there is a risk of pseudo-recurrence (defined as a recurrent swelling at the site of the original hernia) as a result of the mesh bulging into the hernia sac or seroma, and which may occur much more frequently than initially thought, with rates of 19–31 % in incisional and ventral hernia repairs [59, 60]. Closure of the defect during laparoscopic repair may reduce the risk of these complications and of true hernia recurrence [61]. Tacker mesh fixation may be associated with quicker surgery and less postoperative pain in the short term, but otherwise there is no difference from suture mesh fixation [62].

38.6.3 Intraoperative Anesthetic Considerations

Anesthetists often favor the use of an epidural anesthetic in conjunction with general anesthesia to facilitate abdominal wall relaxation and postoperative pain relief. As the abdominal wall is being closed, the anesthetist can monitor changes in respiratory physiology (such as airway pressure and tidal volume). If volume-controlled ventilation is being used, increases in airway pressure can be a surrogate for the likelihood of both postoperative respiratory complications and the risk of abdominal compartment syndrome. Communication between the anesthetist and surgeon can help identify at-risk patients, and, if necessary, additional surgical techniques can be used to relax the abdominal wall and reduce the intra-abdominal pressure.

38.6.4 Special Considerations

Some patients may have herniae of such complexity that the techniques described earlier are inadequate to close the abdominal wall. This may be particularly true in patients subject to penetrating trauma, necrotising fasciitis, laparostomy, or tumors invading into the abdominal wall. Furthermore, there may be complexity because of concomitant stoma problems or the effects of profound weight loss. In such circumstances, additional techniques may have to be considered.

38.6.4.1 Domain Loss

When significant amounts of tissue have been lost, techniques are available that may expand the amount of tissue within the abdominal wall. This has been achieved by the use of progressive preoperative pneumoperitoneum, tissue expanders, and botulinum toxin [63–65]. Preoperative pneumoperitoneum involves the induction of pneumoperitoneum using a Veress needle or endoperitoneal catheter that is maintained over a period of days or weeks [66]. Pneumoperitoneum is sustained using regular insufflation of gases such as oxygen or nitrous oxide until sufficient abdominal wall expansion has been achieved or the hernia has reduced. Tissue expanders are placed in a specially created pocket between the external oblique and the superficial aspect of the internal oblique fascia. The expanders have remote ports that allow the injection of saline on a weekly or biweekly basis over a period of months, depending on the size of the defect, until there is adequate lengthening of the musculature to allow primary fascial closure [67]. Botulinum toxin is a potent neurotoxin produced by the anaerobic gram-positive rod *Clostridium botulinum*. It blocks the release of acetylcholine at the presynaptic cholinergic nerve terminal and results in flaccid muscle paralysis [68]. Injections of botulinum toxin into the lateral abdominal wall muscles essentially separate chemical

components by allowing the muscles to achieve maximum relaxation, facilitating closure. When none of the adjuncts are sufficient, tissue transfer, via either free or pedicled flaps, is required [69].

38.6.4.2 Concomitant Parastomal Hernia

Results of parastomal hernia repair have been disappointing, with high recurrence rates regardless of the type of mesh or technique used [70]. When a parastomal hernia occurs concurrently with an incisional hernia, repairing only one may lead to exacerbation of the other because of the alteration of abdominal wall biomechanics. Treating each hernia in isolation is unwise except in the most comorbid of patients. It is better to have a holistic approach to abdominal wall structure, function, and pathophysiology and to repair all defects during one operation. Evidence from randomized trials is lacking in this situation, and the optimal method seems to be open retromuscular mesh repair [71]. If the midline incisional hernia is small, a laparoscopic Sugarbaker approach may offer the opportunity to treat both herniae simultaneously; this method has encouraging reports of low recurrence rates for the parastomal hernia [72]. There is no robust evidence to confirm the superiority of any one type of mesh in this situation.

38.6.4.3 Abdominoplasty/ Panniculectomy

In some patients the hernia to be repaired is so large that the overlying skin and fat have been stretched to the extent that concomitant abdominoplasty is required as part of the repair. If the fat and skin are left alone and merely closed primarily, a massive seroma often results. There are numerous techniques for abdominoplasty, which can be broadly categorized according to the incision used: horizontal, vertical, or a combination of the two (fleur de lis). Several kilograms of tissue may need to be excised, particularly after significant weight loss (Fig. 38.6). A multidisciplinary team working with plastic surgery colleagues is strongly advocated, not just to help with the intraoperative nuances of the technique but also to manage complications, most notably infection and flap necrosis/wound dehiscence.

38.6.5 Postoperative Management

There are few areas of surgical practice as highly variable among surgeons as the area of postoperative management after complex abdominal wall reconstruction. Evidence is usually derived from generic studies across areas of surgical practice. There is no doubt that prophylaxis against venous thromboembolism should be undertaken according to local guidelines (antiembolic stockings/calf compression devices/low molecular weight heparin). The quality of evidence in other areas is variable at best. Most surgeons recommend planned admission to a critical care unit postoperatively in order to optimise respiratory care and fluid balance monitoring.

38.6.5.1 Dressings and Drains

The value of wound dressings continues to provoke debate among the surgical community, but robust evidence of the benefit of any type of wound dressing in the generic postoperative setting is lacking [73]. Novel technologies such as topical negative-pressure wound therapy applied to wounds healing by primary intention have focused on claims of reduced infection rates. Evidence of benefit from high-quality randomized controlled studies of generic surgical disciplines are lacking [74], but individual case series specific to complex abdominal wall reconstruction show promise [75]. Drains are often used to remove excess fluid from the surgical field and help prevent infection and seroma formation. The advocated duration of drainage is highly variable, ranging from set periods of time to volumes drained over time. While part of surgical tradition, evidence of benefit is absent [76].

38.6.5.2 Abdominal Binders

Use of abdominal binders in the postoperative setting is advocated by some surgeons to reduce complications, specifically reductions in the rates of excessive pain, seroma, and wound dehiscence [77]. There are, however, few data to support these assertions, and in one randomized trial no benefit was seen other than a subjective benefit reported by the patients [78].

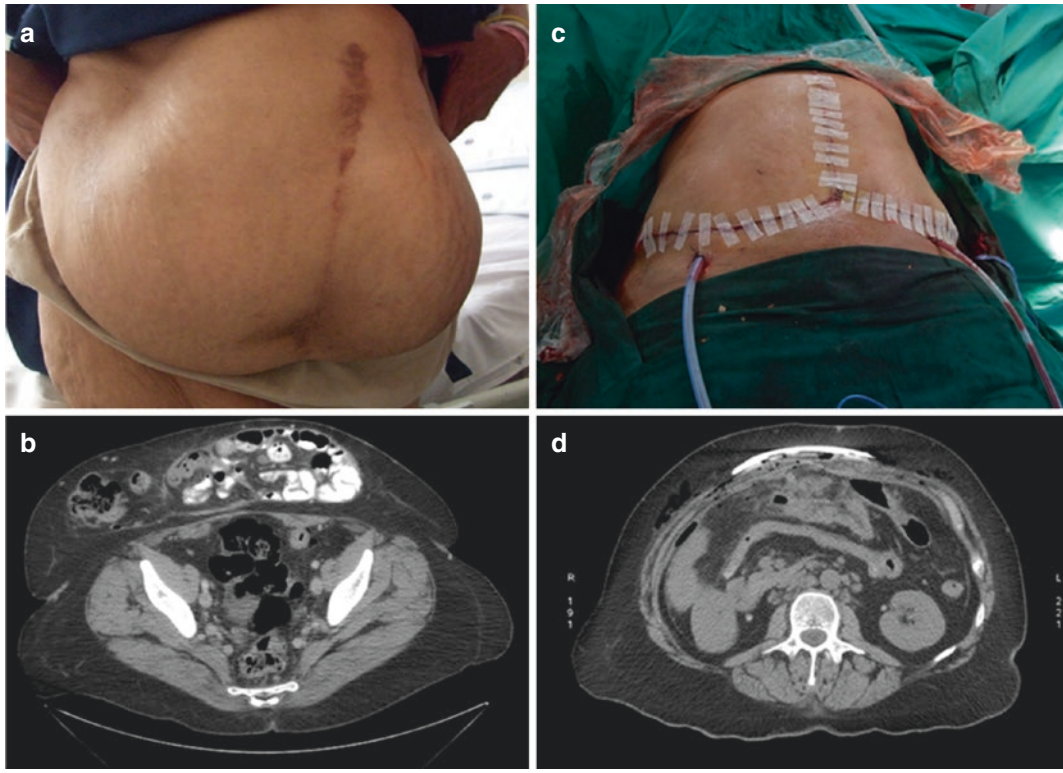


Fig. 38.6 Preoperative photograph (**a**) and computed tomography scan (**b**) of a patient with a large incisional hernia. Immediate postoperative photograph (**c**) and computed tomography scan (**d**) of the same patient following open retrorectus repair with biologic mesh and fleur-de-lys abdominoplasty

38.7 Meshes

The superiority of mesh repair over simple suture closure in terms of hernia recurrence rates is now supported by high-quality evidence [11, 49]. Furthermore, the prophylactic role of mesh placement in midline wounds for the prevention of hernia formation is also established in high-risk patients [79–81]. The search for the ideal mesh, however, is over a century old, and the qualities desired in an ideal mesh for hernia repair have been defined by the European Hernia Society [82]. Although there are over 200 meshes on the market, the ideal mesh has yet to be found. Multiple attempts to classify mesh types have been made, and no universal standard of classification has been agreed on. The easiest approach is a dichotomous division into synthetic (derived from human-made chemicals) or biological (either allograft or xenograft) meshes. A four-category classification was recently proposed that allows a more nuanced appreciation of the range of meshes available [83] (Table 38.2).

38.7.1 Synthetic Mesh

Modern synthetic meshes derive from the seminal work of Francis Usher in the 1950s and 1960s. The meshes may be made from a variety of different compounds, either a single compound or in combination, by weaving, knitting, coating, or applying with an antiadhesive backing. Meshes can be further subclassified according to chemical polymer, porosity, weight (although *density* may be a more accurate term), absorbability, and pre-implantation or explantation characteristics. The plethora of prostheses on the market alludes to the fact that different meshes may have characteristics that lend themselves to superior performance

Table 38.2 A summary of a four-category mesh classification

	1. Simple	2. Composite	3. Combined	4. Biologic
Description	One pure synthetic material	Two layers of simple mesh and an antiadhesive backing	Two synthetic materials knitted, woven, or coated	Derived from tissue
Subclasses	Weight Porosity Resorbable vs. nonresorbable Mono- vs. multifilament	Nonresorbable Resorbable	Nonresorbable Partially resorbable Resorbable	Allograft vs. xenograft Animal of origin Dermis vs. nondermis Cross-linked vs. non-cross-linked
Examples	Polypropylene Polyester Polytetrafluoroethylene Polyurethane Polyglycolic acid Polyglactin 910	Composix Dulex Dualmesh Proceed Physiomesh Parietex PCO Sepramesh	Titanized polypropylene Polypropylene and monocryl Polypropylene and polyglycolic acid Gore Bio-A	Alloderm Periguard Permacol Strattice Surgisis/Biodesign Veritas Xenmatrix

Based on Coda et al. [83]

in certain situations, depending on exactly which outcome is being measured. In open complex abdominal wall reconstruction, synthetic meshes have the data from the longest follow-up in terms of recurrence and complications. The newer synthetic meshes with antiadhesive backings have shorter durations of follow-up.

Polypropylene is the polymer with the most widespread use as a surgical mesh and has over 50 years of use in the clinical setting of hernia repair. Polyester is a polymer favored by some surgeons because of its pliability. It also has hydrophilic properties, but the clinical relevance of this is poorly understood. Polytetrafluoroethylene meshes are available as sheets and as monofilament meshes. Antiadhesion barriers designed to prevent adhesions to viscera when the mesh is placed intraperitoneally may comprised a variety of chemicals, including (but not limited to) hyaluronic acid, cellulose, and polyethylene glycol. Numerous meshes combine a nonabsorbable polymer with an absorbable fiber, such as polyglactin, to produce meshes that reduce the amount of material left in the patient after complete resorption. Newer meshes comprising delayed-absorption copolymers have properties more akin to the biologic meshes discussed below, although even short-term clinical data for such "*biomimetic*" meshes is lacking.

Head-to-head comparisons of different mesh types in randomized trials are rare, and high-quality evidence to recommend specific proprietary brands of one mesh type over another are often lacking. Lightweight mesh seems to provide outcomes similar to those of standard meshes except for a nonsignificant trend toward increased recurrence rates at 24 months [84], although longer follow-up may elucidate a difference as recurrence rates increase with time. In particular, the optimal mesh type for intraperitoneal use is poorly understood. Meshes without antiadhesive backings have been reported to result in complications caused by adhesions, erosion, fistulation, and migration. Which antiadhesive backing is best remains the subject of debate because of a lack of high-quality clinical studies with sufficiently robust outcome measures over an appropriate duration of follow-up. Findings at repeat laparoscopy have been reported, but only with subjective ratings of the adhesions found [85].

Synthetic meshes are ideal for use in clean cases in either open or laparoscopic surgery. They are cheap, reliable, and effective, with well-characterized benefits and risks. They should form the overwhelming majority of prostheses used in hernia repair. The problem is in clean-contaminated or contaminated fields. Outcomes from synthetic mesh implantation in these circumstances are far from ideal and may cause

more harm than good [86]. The debate over what to do in these situations continues to rage between those who favor a staged approach of a sutured repair initially, with control and treatment of infection according to best practices, followed by a subsequent synthetic mesh repair if/when the hernia recurs, versus those who favor a single-stage approach with a biologic mesh.

38.7.2 Biologic Mesh

Biologic meshes were introduced in the 1990s and essentially provide an extracellular scaffold necessary for the reconstruction of healthy tissue. They allow in-growth of new blood vessels and infiltration of native stromal cells, including fibroblasts and myocytes, which ultimately result in the deposition of new extracellular matrix. The hypothesis, therefore, has been that in contaminated or high-risk situations, biologic meshes are safer than synthetic materials for hernia repair. Biologic meshes may be derived from human (allograft) or animal (xenograft; usually porcine or bovine) tissues. Dermis is the most common tissue used because of the size of mesh that can be manufactured, but prostheses derived from intestinal submucosa and pericardium are also available. Xenografts are manufactured by tissue harvesting followed by a variety of proprietary decellularization and delipidation techniques. This leaves behind the three-dimensional collagen structure, which may then undergo further proprietary processing steps before a terminal sterilization process. More than a dozen different xenografts are currently on the market, with more being developed, and the influence of processing differences is poorly understood, particularly in the context of influence on clinical outcome.

The high cost of xenografts compared with synthetic meshes means that their use in clean, simple cases cannot be justified. The Ventral Hernia Working Group made recommendations as to when to consider the use of biologic mesh [6]. This simplified approach to classifying the complexity of hernia repair has enabled crude comparisons between reports of biologic mesh use, but ultimately, despite the plethora of recommendations and guidelines, there remains no consensus of when to use biologic materials in abdominal wall reconstruction among practicing surgeons [87].

Much of the data on biologic mesh use currently derives from retrospective case series from single institutions, and prospective randomized trials are lacking. The data are often limited by inconsistent use of definitions and/or classification systems for hernia defect, wound contamination, recurrence, follow-up, and complications. Despite this, two recent systematic reviews, each with data from more than 1,000 patients, suggested that biologic meshes have recurrence rates comparable to synthetic meshes but with fewer infective complications, and when infection is present, the salvage rate is higher with biologic meshes [88, 89]. The lack of head-to-head studies means that there are insufficient clinical data to provide recommendations on which biologic mesh to use. Furthermore, the quality of evidence is such that many surgeons still question whether biologic materials are justified given their high costs [90, 91].

Conclusion

Abdominal wall reconstruction presents a challenge for surgeons who decide to undertake this work and for patients who wish to proceed with it. A detailed understanding of the disease, surgical options, and preoperative planning in particular are imperative for optimizing outcomes. Multidisciplinary teamwork is essential.

References

1. Jensen KK, Kjaer M, Jorgensen LN. Abdominal muscle function and incisional hernia: a systematic review. Hernia. 2014;18(4):481–6.
2. Chevrel JP, Rath AM. Classification of incisional hernias of the abdominal wall. Hernia. 2000;4(1):7–11.
3. Korenkov M, Paul A, Sauerland S, Neugebauer E, Arndt M, Chevrel JP, Corcione F, Fingerhut A, Flament JB, Kux M, Matzinger A, Myrvold HE, Rath AM, Simmermacher RK. Classification and surgical treatment of incisional hernia. Results of an experts' meeting. Langenbecks Arch Surg. 2001;386(1):65–73.

4. Ammaturo C, Bassi G. The ratio between anterior abdominal wall surface/wall defect surface: a new parameter to classify abdominal incisional hernias. Hernia. 2005;9:316–21.
5. Muysoms FE, Miserez M, Berrevoet F, Campanelli G, Champault GG, Chelala E, Dietz UA, Eker HH, El Nakadi I, Hauters P, Hidalgo Pascual M, Hoeferlin A, Klinge U, Montgomery A, Simmermacher RK, Simons MP, Smietański M, Sommeling C, Tollens T, Vierendeels T, Kingsnorth A. Classification of primary and incisional abdominal wall hernias. Hernia. 2009;13(4):407–14.
6. Ventral Hernia Working Group, Breuing K, Butler CE, Ferzoco S, Franz M, Hultman CS, Kilbridge JF, Rosen M, Silverman RP, Vargo D. Incisional ventral hernias: review of the literature and recommendations regarding the grading and technique of repair. Surgery. 2010;148(3):544–58.
7. Kanters AE, Krpata DM, Blatnik JA, Novitsky YM, Rosen MJ. Modified hernia grading scale to stratify surgical site occurrence after open ventral hernia repairs. J Am Coll Surg. 2012;215(6):787–93.
8. Slater NJ, Montgomery A, Berrevoet F, Carbonell AM, Chang A, Franklin M, Kercher KW, Lammers BJ, Parra-Davilla E, Roll S, Towfigh S, van Geffen E, Conze J, van Goor H. Criteria for definition of a complex abdominal wall hernia. Hernia. 2014;18(1):7–17.
9. Diener MK, Voss S, Jensen K, Büchler MW, Seiler CM. Elective midline laparotomy closure: the INLINE systematic review and meta-analysis. Ann Surg. 2010;251(5):843–56.
10. Burger JW, Luijendijk RW, Hop WC, Halm JA, Verdaasdonk EG, Jeekel J. Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. Ann Surg. 2004;240(4):578–83; discussion 583–5.
11. Flum DR, Horvath K, Koepsell T. Have outcomes of incisional hernia repair improved with time? A population-based analysis. Ann Surg. 2003;237(1):129–35.
12. Bensley RP, Schermerhorn ML, Hurks R, Sachs T, Boyd CA, O'Malley AJ, et al. Risk of late-onset adhesions and incisional hernia repairs after surgery. J Am Coll Surg. 2013;216(6):1159–67, 1167.e1–12.
13. Fink C, Baumann P, Wente MN, Knebel P, Bruckner T, Ulrich A, et al. Incisional hernia rate 3 years after midline laparotomy. Br J Surg. 2014;101(2):51–4.
14. Baucom RB, Beck WC, Holzman MD, Sharp KW, Nealon WH, Poulose BK. Prospective evaluation of surgeon physical examination for detection of incisional hernias. J Am Coll Surg. 2014;218(3):363–6.
15. Gutiérrez de la Peña C, Vargas Romero J, Diéguez García JA. The value of CT diagnosis of hernia recurrence after prosthetic repair of ventral incisional hernias. Eur Radiol. 2001;11(7):1161–4.
16. Mishra A, Keeler BD, Maxwell-Armstrong C, Simpson JA, Acheson AG. The influence of laparoscopy on incisional hernia rates: a retrospective analysis of 1057 colorectal cancer resections. Colorectal Dis. 2014;16(10):815–21.
17. Deerenberg EB, Timmermans L, Hogerzeil DP, Slieker JC, Eilers PH, Jeekel J, Lange JF. A systematic review of the surgical treatment of large incisional hernia. Hernia. 2014;19(1):89–101. [Epub ahead of print] PMID: 25380560.
18. Henriksen NA, Yadete DH, Sorensen LT, Agren MS, Jorgensen LN. Connective tissue alteration in abdominal wall hernia. Br J Surg. 2011;98(2):210–9.
19. Read RC. Inguinal herniation in the adult, defect or disease: a surgeon's odyssey. Hernia. 2004;8(4):296–9.
20. Read RC. The Nyhus-Wantz lectureship: etiology, herniosis, diverticulosis coli, and cancer. Hernia. 2011;15(5):481–3.
21. Read RC. Signs of herniosis in women with vaginal prolapse and/or stress incontinence. Hernia. 2008;12(5):449–52.
22. Sezer S, Simşek N, Celik HT, Erden G, Ozturk G, Düzgün AP, Coşkun F, Demircan K. Association of collagen type I alpha 1 gene polymorphism with inguinal hernia. Hernia. 2014;18(4):507–12.
23. Barnett C, Langer JC, Hinek A, Bradley TJ, Chitayat D. Looking past the lump: genetic aspects of inguinal hernia in children. J Pediatr Surg. 2009;44(7):1423–31.
24. Burcharth J, Pommergaard HC, Rosenberg J. The inheritance of groin hernia: a systematic review. Hernia. 2013;17(2):183–9.
25. Calaluce R, Davis JW, Bachman SL, Gubin MM, Brown JA, Magee JD, Loy TS, Ramshaw BJ, Atasoy U. Incisional hernia recurrence through genomic profiling: a pilot study. Hernia. 2013;17(2):193–202.
26. Peeters E, De Hertogh G, Junge K, Klinge U, Miserez M. Skin as marker for collagen type I/III ratio in abdominal wall fascia. Hernia. 2014;18(4):519–25.
27. Sørensen LT. Wound healing and infection in surgery. The clinical impact of smoking and smoking cessation: a systematic review and meta-analysis. Arch Surg. 2012;147(4):373–83.
28. Lau B, Kim H, Haigh PI, Tejirian T. Obesity increases the odds of acquiring and incarcerating noninguinal abdominal wall hernias. Am Surg. 2012;78(10):1118–21.
29. Brown SR, Tiernan J. Transverse verses midline incisions for abdominal surgery. Cochrane Database Syst Rev. 2005;19(4):CD005199. doi:10.1002/14651858.CD005199.pub2.
30. Bhangu A, Nepogodiev D, Futaba K. West midlands research collaborative. Systematic review and meta-analysis of the incidence of incisional hernia at the site of stoma closure. World J Surg. 2012;36(5):973–83.
31. Jenkins TP. The burst abdominal wound: a mechanical approach. Br J Surg. 1976;63(11):873–6.
32. Harlaar JJ, van Ramshorst GH, Nieuwenhuizen J, Ten Brinke JG, Hop WC, Kleinrensink GJ, Jeekel H, Lange JF. Small stitches with small suture distances increase laparotomy closure strength. Am J Surg. 2009;198(3):392–5.
33. Millbourn D, Cengiz Y, Israelsson LA. Risk factors for wound complications in midline abdominal

incisions related to the size of stitches. Hernia. 2011;15(3):261–6.
34. Harlaar JJ, Deerenberg EB, van Ramshorst GH, Lont HE, van der Borst EC, Schouten WR, Heisterkamp J, van Doorn HC, Cense HA, Berends F, Stockmann HB, Vrijland WW, Consten EC, Ottow RT, Go PM, Hermans JJ, Steyerberg EW, Lange JF. A multicenter randomized controlled trial evaluating the effect of small stitches on the incidence of incisional hernia in midline incisions. BMC Surg. 2011;11:20.
35. Sanders DL, Kingsnorth AN. The modern management of incisional hernias. BMJ. 2012;344:e2843.
36. Yao S, Li JY, Liu FD, Pei LJ. Significance of measurements of herniary area and volume and abdominal cavity volume in the treatment of incisional hernia: application of CT 3D reconstruction in 17 cases. Comput Aided Surg. 2012;17(1):40–5.
37. Haney M, Löfvenberg R, Svensson O. Optimize perioperative health and begin with insistence on preoperative smoking cessation. Acta Anaesthesiol Scand. 2014;58(2):133–4.
38. Sauerland S, Korenkov M, Kleinen T, Arndt M, Paul A. Obesity is a risk factor for recurrence after incisional hernia repair. Hernia. 2004;8(1):42–6.
39. Fischer JP, Wink JD, Nelson JA, Kovach SJ. Among 1,706 cases of abdominal wall reconstruction, what factors influence the occurrence of major operative complications? Surgery. 2014;155(2):311–9.
40. Chan G, Chan CK. A review of incisional hernia repairs: preoperative weight loss and selective use of the mesh repair. Hernia. 2005;9(1):37–41.
41. Geletzke AK, Rinaldi JM, Phillips BE, Mobley SB, Miller J, Dykes T, Hollenbeak C, Kelleher SL, Soybel DI. Prevalence of systemic inflammation and micronutrient imbalance in patients with complex abdominal hernias. J Gastrointest Surg. 2014;18(4):646–55.
42. Ozdemir S, Ozis ES, Gulpinar K, Aydin SM, Eren AA, Demirtas S1, Korkmaz A. The value of copper and zinc levels in hernia formation. Eur J Clin Invest. 2011;41(3):285–90.
43. Swart M, Carlisle JB. Case-controlled study of critical care or surgical ward care after elective open colorectal surgery. Br J Surg. 2012;99(2):295–9.
44. Harari D, Hopper A, Dhesi J, Babic-Illman G, Lockwood L, Martin F. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. Age Ageing. 2007;36(2):190–6.
45. Shander A, Van Aken H, Colomina MJ, Gombotz H, Hofmann A, Krauspe R, Lasocki S, Richards T, Slappendel R, Spahn DR. Patient blood management in Europe. Br J Anaesth. 2012;109(1):55–68.
46. Shander A, Goodnough LT. Why an alternative to blood transfusion? Crit Care Clin. 2009;25:261–77.
47. Fischer JP, Nelson JA, Wes AM, Wink JD, Yan C, Braslow BM, Chen L, Kovach SJ. The use of epidurals in abdominal wall reconstruction: an analysis of outcomes and cost. Plast Reconstr Surg. 2014;133(3):687–99.
48. Hughes LE. The results of incisional hernia repair: a twelve year review. Ann R Coll Surg Engl. 1987;69(1):40–2.
49. den Hartog D, Dur AHM, Tuinebreijer WE, Kreis RW. Open surgical procedures for incisional hernias. Cochrane Database of Syst Rev. 2008;16(3):CD006438. doi:10.1002/14651858.CD006438.pub2.
50. Halvorson EG. On the origins of components separation. Plast Reconstr Surg. 2009;124(5):1545–9.
51. Ramirez OM, Ruas E, Dellon AL. "Components separation" method for closure of abdominal-wall defects: an anatomic and clinical study. Plast Reconstr Surg. 1990;86(3):519–26.
52. Slater NJ, van Goor H, Bleichrodt RP. Large and complex ventral hernia repair using "components separation technique" without mesh results in a high recurrence rate. Am J Surg. 2015;209(1):170–9.
53. Heller L, McNichols CH, Ramirez OM. Component separations. Semin Plast Surg. 2012;26(1):25–8.
54. Krpata DM, Blatnik JA, Novitsky YW, Rosen MJ. Posterior and open anterior components separations: a comparative analysis. Am J Surg. 2012;203(3):318–22; discussion 322.
55. Helgstrand F, Rosenberg J, Kehlet H, Jorgensen LN, Bisgaard T. Nationwide prospective study of outcomes after elective incisional hernia repair. J Am Coll Surg. 2013;216(2):217–28.
56. Sauerland S, Walgenbach M, Habermalz B, Seiler CM, Miserez M. Laparoscopic versus open surgical techniques for ventral or incisional hernia repair. Cochrane Database Syst Rev. 2011;3:CD007781.
57. Zhang Y, Zhou H, Chai Y, Cao C, Jin K, Hu Z. Laparoscopic versus open incisional and ventral hernia repair: a systematic review and meta-analysis. World J Surg. 2014;38(9):2233–40.
58. Brown CN, Finch JG. Which mesh for hernia repair? Ann R Coll Surg Engl. 2010;92(4):272–8.
59. Tse GH, Stutchfield BM, Duckworth AD, de Beaux AC, Tulloh B. Pseudo-recurrence following laparoscopic ventral and incisional hernia repair. Hernia. 2010;14(6):583–7.
60. Carter SA, Hicks SC, Brahmbhatt R, Liang MK. Recurrence and pseudorecurrence after laparoscopic ventral hernia repair: predictors and patient-focused outcomes. Am Surg. 2014;80(2):138–48.
61. Nguyen DH, Nguyen MT, Askenasy EP, Kao LS, Liang MK. Primary fascial closure with laparoscopic ventral hernia repair: systematic review. World J Surg. 2014;38(12):3097–104.
62. Sajid MS, Parampalli U, McFall MR. A meta-analysis comparing tacker mesh fixation with suture mesh fixation in laparoscopic incisional and ventral hernia repair. Hernia. 2013;17(2):159–66.
63. Dumont F, Fuks D, Verhaeghe P, Brehant O, Sabbagh C, Riboulot M, Yzet T, Regimbeau JM. Progressive pneumoperitoneum increases the length of abdominal muscles. Hernia. 2009;13(2):183–7.
64. Carr JA. Tissue expander-assisted ventral hernia repair for the skin-grafted damage control abdomen. World J Surg. 2014;38:782–7.

65. Ibarra-Hurtado TR, Nuño-Guzmán CM, Echeagaray-Herrera JE, Robles-Vélez E, de Jesús González-Jaime J. Use of botulinum toxin type a before abdominal wall hernia reconstruction. World J Surg. 2009;33(12):2553–6.
66. Caldironi MW, Romano M, Bozza F, Pluchinotta AM, Pelizzo MR, Toniato A, Ranzato R. Progressive pneumoperitoneum in the management of giant incisional hernias: a study of 41 patients. Br J Surg. 1990;77(3):306–7.
67. Admire AA, Dolich MO, Sisley AC, Samimi KJ. Massive ventral hernias: role of tissue expansion in abdominal wall restoration following abdominal compartment syndrome. Am Surg. 2002;68(5):491–6.
68. Jankovic J, Albanese A, Atassi MZ, Dolly JO, Hallett M, Mayer NH, editors. Botulinum toxin therapeutic clinical practice and science. Philadelphia: Saunders; 2009.
69. Kuo YR, Kuo MH, Lutz BS, Huang YC, Liu YT, Wu SC, Hsieh KC, Hsien CH, Jeng SF. One-stage reconstruction of large midline abdominal wall defects using a composite free anterolateral thigh flap with vascularized fascia lata. Ann Surg. 2004;239(3):352–8.
70. Hansson BM, Slater NJ, van der Velden AS, Groenewoud HM, Buyne OR, de Hingh IH, Bleichrodt RP. Surgical techniques for parastomal hernia repair: a systematic review of the literature. Ann Surg. 2012;255(4):685–95.
71. Raigani S, Criss CN, Petro CC, Prabhu AS, Novitsky YW, Rosen MJ. Single-center experience with parastomal hernia repair using retromuscular mesh placement. J Gastrointest Surg. 2014;18(9):1673–7.
72. Hansson BM, Morales-Conde S, Mussack T, Valdes J, Muysoms FE, Bleichrodt RP. The laparoscopic modified Sugarbaker technique is safe and has a low recurrence rate: a multicenter cohort study. Surg Endosc. 2013;27(2):494–500.
73. Dumville JC, Gray TA, Walter CJ, Sharp CA, Page T. Dressings for the prevention of surgical site infection. Cochrane Database Syst Rev. 2014;9:CD003091.
74. Webster J, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention. Cochrane Database Syst Rev. 2014;10:CD009261.
75. Soares KC, Baltodano PA, Hicks CW, Cooney CM, Olorundare IO, Cornell P, Burce K, Eckhauser FE. Novel wound management system reduces surgical site morbidity after ventral hernia repairs: a critical analysis. Am J Surg. 2014. pii: S0002–9610(14)00380-8. doi:10.1016/j.amjsurg.2014.06.022. [Epub ahead of print].
76. Gurusamy KS, Allen VB. Wound drains after incisional hernia repair. Cochrane Database Syst Rev. 2013;12:CD005570.
77. Bouvier A, Rat P, Drissi-Chbihi F, Bonnetain F, Lacaine F, Mariette C, Ortega-Deballon P. Pour La Federation de Recherche en Chirurgie (FRENCH). Abdominal binders after laparotomy: review of the literature and French survey of policies. Hernia. 2014;18(4):501–6.
78. Christoffersen MW, Olsen BH, Rosenberg J, Bisgaard T. Randomized clinical trial on the postoperative use of an abdominal binder after laparoscopic umbilical and epigastric hernia repair. Hernia. 2015;19(1):147–53.
79. Timmermans L, de Goede B, Eker HH, van Kempen BJ, Jeekel J, Lange JF. Meta-analysis of primary mesh augmentation as prophylactic measure to prevent incisional hernia. Dig Surg. 2013;30(4–6):401–9.
80. Nachiappan S, Markar S, Karthikesalingam A, Ziprin P, Faiz O. Prophylactic mesh placement in high-risk patients undergoing elective laparotomy: a systematic review. World J Surg. 2013;37(8):1861–71.
81. Bhangu A, Fitzgerald JE, Singh P, Battersby N, Marriott P, Pinkney T. Systematic review and meta-analysis of prophylactic mesh placement for prevention of incisional hernia following midline laparotomy. Hernia. 2013;17(4):445–55.
82. Bringman S, Conze J, Cuccurullo D, Deprest J, Junge K, Klosterhalfen B, Parra-Davila E, Ramshaw B, Schumpelick V. Hernia repair: the search for ideal meshes. Hernia. 2010;14(1):81–7.
83. Coda A, Lamberti R, Martorana S. Classification of prosthetics used in hernia repair based on weight and biomaterial. Hernia. 2012;16(1):9–20.
84. Conze J, Kingsnorth AN, Flament JB, Simmermacher R, Arlt G, Langer C, Schippers E, Hartley M, Schumpelick V. Randomized clinical trial comparing lightweight composite mesh with polyester or polypropylene mesh for incisional hernia repair. Br J Surg. 2005;92(12):1488–93.
85. Chelala E, Debardemaeker Y, Elias B, Charara F, Dessily M, Allé JL. Eighty-five redo surgeries after 733 laparoscopic treatments for ventral and incisional hernia: adhesion and recurrence analysis. Hernia. 2010;14(2):123–9.
86. Choi JJ, Palaniappa NC, Dallas KB, Rudich TB, Colon MJ, Divino CM. Use of mesh during ventral hernia repair in clean-contaminated and contaminated cases: outcomes of 33,832 cases. Ann Surg. 2012;255(1):176–80.
87. Harth KC, Krpata DM, Chawla A, Blatnik JA, Halaweish I, Rosen MJ. Biologic mesh use practice patterns in abdominal wall reconstruction: a lack of consensus among surgeons. Hernia. 2013;17(1):13–20.
88. Darehzereshki A, Goldfarb M, Zehetner J, Moazzez A, Lipham JC, Mason RJ, Katkhouda N. Biologic versus nonbiologic mesh in ventral hernia repair: a systematic review and meta-analysis. World J Surg. 2014;38(1):40–50.
89. Slater NJ, van der Kolk M, Hendriks T, van Goor H, Bleichrodt RP. Biologic grafts for ventral hernia repair: a systematic review. Am J Surg. 2013;205(2):220–30.
90. Harris HW. Biologic mesh for ventral hernia repair: a cautionary tale. Ann Surg. 2013;257(6):997–8.
91. Petter-Puchner AH, Dietz UA. Biological implants in abdominal wall repair. Br J Surg. 2013;100(8):987–8.

Index

© Springer-Verlag Berlin Heidelberg 2017
A. Herold et al. (eds.), *Coloproctology*, European Manual of Medicine,
DOI 10.1007/978-3-662-53210-2

D