Advanced Colonoscopy and Endoluminal Surgery

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Scott R. Steele
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Editors

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Preface

Advanced endoscopic procedures and endoluminal interventions have continued to experience tremendous growth in both community and academic settings. Many technical advances in endoscopic tools and platforms have transformed the way we treat patients with colon and rectal diseases. As surgeons explore less invasive surgical techniques and gastroenterologists more complex therapeutic endoscopic procedures, the convergence of interests will lead to further innovations and evolution of the way we treat our patients.

Although surgeons such as Hiromi Shinya and William Wolff pioneered therapeutic endoscopy, we have largely relinquished the practice of endoscopy to our gastroenterology colleagues. However, as endoscopic tools become more practical and sophisticated, endoscopy is finding its way back to the operating rooms as an adjunctive surgical tool. The ability to assess the integrity of the surgical anastomosis, locate benign and malignant colonic neoplasms, and control bleeding, among other things, is becoming invaluable during lower intestinal surgery. More and more surgeons are realizing the importance of incorporating endoscopic skills to their surgical armamentarium.

Frank Veith, in his presidential address to the Society for Vascular Surgery in 1996, emphasized that in order for vascular surgeons to adapt to the changing medical environment at the time, they must acquire endovascular skills. At that time vascular surgeons found themselves at a crossroad. Without fully embracing therapeutic endovascular surgical techniques, vascular surgeons were at risk of being left out. As surgeons who care for patients with colon and rectal diseases, we wonder whether we are at the same crossroad. Do we need to fully embrace endoscopic and endoluminal surgery in order to stay relevant?

In this textbook, we try to provide an overview of basic to advanced endoscopic techniques. Each chapter includes a narrative by the authors on his/her technical details and "tips and tricks" that they utilize in dealing with complex technical situations. Additionally, where appropriate, links to online downloadable videos will give an up-front look into technical aspects of EMR, ESD, endoscopic stent placement, and CELS. We feel very fortunate to include many world experts in the area of endoscopy as authors of our textbook. We are truly grateful for their time and contributions. We hope our textbook will stimulate further discussions and lead to better patient outcomes.

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Philadelphia, PA — Howard M. Ross, M.D.
Woodbury, NY — David E. Rivadeneira, M.D.
Cleveland, OH — Scott R. Steele, M.D.
New York, NY — Daniel L. Feingold, M.D.

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Sang W. Lee
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Finally and most importantly, I would like to thank my wife, Crystal, for her support, encouragement, and unwavering love and my sons, Eric and Ryan, for making me a better person and making everything worthwhile.

Howard M. Ross
I am happiest when a group I am involved with truly works together—selflessly, efficiently, and synergistically. My friends, the editors of this book, have made my career so much more rewarding than I would have ever guessed. Thank you all so much. Thanks also to my incredible family. Molly, Leo, Emily, and Stacy you are the best!

Scott R. Steele
I would like to first thank my co-editors for their outstanding work and Sang for coming up with this idea and leading the way. I would again like to thank our developmental editor, Elektra McDermott, for another extraordinary job at seeing this work through to completion and taking care of all the details. Finally to my family for continuing to support me and allow me to pursue these endeavors—Michele, Marianna, Piper, and Flynn.

David E. Rivadeneira

"*Curiouser and curiousers*"
Alice from Alice in Wonderland

To Sang W. Lee for his vision and dedication. To my fellow co-editors Sang W. Lee, Scott R. Steele, Daniel L. Feingold, and Howard M. Ross, I continue to be inspired and learn from all of you. To Elektra McDermott—the ultimate cat herder—thank you for getting us all together. To my family, Anabela, Sophia, and Gabriella, thank you for your unwavering support and love.

Daniel L. Feingold
I dedicate this book to my wife, Tonja, and to our children Judah, Ethan, Noa, and Lily. Your love, support, and inspiration make it all possible.

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History of Colonoscopy

1

Jeanette Zhang and Howard M. Ross

Key Points

- Philipp Bozzini is often credited as the father of endoscopy. He foresaw that direct observation would allow for improved understanding of human physiology and disease processes and enhance the treatment of such diseases.
- Application of advances in upper gastrointestinal endoscopes is largely responsible for the evolution of the current colonoscope.
- Flexible endoscopes and fiber-optic technology were noteworthy breakthroughs in endoscopic designs.
- Numerous endoscopic techniques utilizing the colonoscope have been developed to treat a host of benign and malignant colorectal diseases.

Bozzini and the Lichtleiter

Philipp Bozzini is considered by many the father of endoscopy. Born in Mainz, Germany, in 1773, Bozzini's goal was to examine the inner cavities of the human body in designing the Lichtleiter, or "light conductor." He recognized the importance of direct observation in the ability to understand the physiology and function of human organs [1]. With his design, he also foresaw the ability to perform new procedures and to make existing procedures safer by allowing, for instance, the removal of rectal polyps or cervical tumors to be done under direct visualization rather than to depend on luck.

The original Lichtleiter consisted of a vase-shaped lantern made of tin and covered with leather [2, 3]. Within this housed the light source, a wax candle, on a spring device designed to keep the flame at a constant height. A concave mirror was placed to project light through an aperture, onto which various tubular specula could be attached. The mirror directed light toward the hollow organ and avoided reflection toward the observer's eye [4]. On the opposite side was another fenestration onto which an eyepiece was attached for the observer (Fig. 1.1). The tubular specula were made of brass or silver and modified based of the organ they were meant for: urethra, vagina, rectum, and so on [1]. His conductors were straight to avoid deviating from the straight lines on which light rays travel. In order to observe objects at an angle, for instance behind the nasopharynx, he used a mirror to bend the light. He did note, however, that bending the light compromised the clarity of the image [1].

Dr. Bozzini first introduced his creation to the public in Frankfurt in 1804 [3]. He also sent a description of the Lichtleiter to Archduke Karl of Austria, and with his support, experiments with the instrument were conducted at the Vienna Josephs Academy. These concerned mostly diseases of the rectum and uterus, though in one experiment a stone was visualized in the urinary bladder of a female cadaver. Unfortunately, as a result of political rivalry between medical institutions, Joseph Andreas Stifft, who was at the time the Director of Medical Studies and President of the Vienna Medical Faculty, deemed the Lichtleiter a "mere toy" [2]. With this criticism, Bozzini's invention was soon forgotten. However, the principles embodied by his design would be carried into future endoscopic inventions.

Evolution of Upper Gastrointestinal Endoscopy

Early Advances

The development of colonoscopy would largely not be possible were it not for technologic advances in upper gastrointestinal endoscopy. Therefore, noteworthy breakthroughs

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Fig. 1.1 Bozzini's original Lichtleiter. Courtesy of Archives of the American College of Surgeons, "The Bozzini Endoscope," Online April 6, 2011

will be reviewed here. Early endoscopic advances were largely modifications of instruments based on Bozzini's Lichtleiter. John Fisher in the United States and Segales in France illuminated body cavities using a system of mirrors to reflect candlelight [5]. In 1824 Fisher added a double convex lens to sharpen and enlarge the viewed image [6]. Antonin Desormeaux is credited with developing the first open-tube endoscope [5, 6]. He used a lamp fueled by a combination of alcohol and turpentine for continuous illumination. Another significant advance was the use of a condenser lens to concentrate the illumination on a single spot [7]. However, a significant drawback of this system was the thermal tissue injuries from the heat created by the light source.

In 1877 Maximilian Nitze introduced his cystoscope, which is often considered the first practical endoscopic instrument (Fig. 1.2). He used a platinum wire loop lamp with a water cooling system for illumination [6]. Significant advances he incorporated were placing the light source at the tip of the instrument to improve illumination and enlarging the field of view by using an optical system [8]. After Thomas Edison's invention of incandescent light in 1879, Nitze incorporated a miniaturized version of the filament globe into his device.

Edison's invention proved significant for the future of endoscopes, as the use of incandescent light eliminated the need for the then-used platinum loop lamp and its unwieldy cooling system. Johann von Mikulicz and Josef Leiter in 1881 introduced an esophagoscope that consisted of a straight tube with a small bulb at the distal end of the instrument [6]. Mikulicz also added to Nitze's model by adding a mirror to create an angular field and an air canal to allow for insufflation [7]. The result of this combination was a greater

Fig. 1.2 Examining cystoscope according to Nitze's Kystoskop no II, prograde and sliding optics. Created by Josef Leiter, Vienna. Courtesy Int. Nitze-Leiter Research Society for Endoscopy, Vienna/Reuter Collection © International Nitze-Leiter Research Society for Endoscopy, Vienna. Reused with permission

field of view to examine otherwise collapsed cavities. Six years later Leiter produced what he called the panelectroscope. By reflecting light from an electric lamp built into the handle, the panelectroscope served as a universal light source for all endoscopic tools.

The next series of developments involved inclusion of optical systems to the rigid endoscope. In 1896 Theodor Rosenheim produced a gastroscope with three concentric tubes: the innermost contained an optical system, the middle carried the light source consisting of a platinum wire loop lamp and water cooling system, and the outermost with a scale to demarcate the distance inserted [6]. Hans Elsner built on Rosenheim's design by adding a rubber tip to the end of the straight tube, which facilitated introduction of the instrument. However, its use was hampered by difficulty viewing through the lens once it was soiled. In 1922 Rudolf Schindler created his rigid gastroscope, a later version of which contained an air outlet to clear the lens.

Semiflexible Endoscopes

Beginning in the 1930s came a period that saw the development of semiflexible endoscopes. Schindler was an integral character during this era. The first recorded flexible esophagoscope, however, was by Kelling in 1898 [7]. The lower third of his instrument could be flexed up to a 45° angle. Schindler's breakthrough came about in 1932 in the form of the semiflexible gastroscope (Fig. 1.3). The distal half of this endoscope was constructed from a spiral of bronze with a protective covering of rubber [6]. Key to his design, though, was the discovery that using a tube filled with very thick lenses with short focal distances allowed for bending in several planes without distortion of the transmitted image. Schindler introduced an updated version 4 years later that

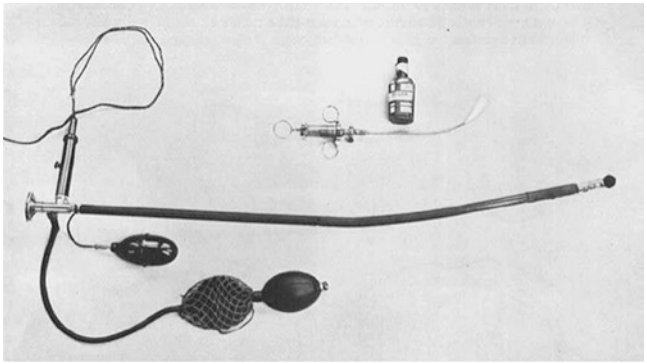

Fig. 1.3 The Wolf-Schindler flexible gastroscope. With permission from Taylor H. Gastroscopy: Its history, technique, and clinical value, with report on sixty cases. British J Surg. 1937 Jan;24(95):469–500. [19] © John Wiley and Sons

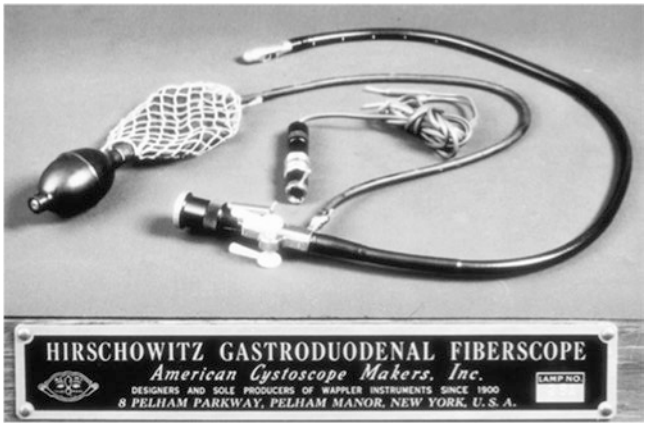

Fig. 1.4 The Hirschowitz Fiberscope. With permission from Wilcox CM. Fifty years of gastroenterology at the University of Alabama at Birmingham: A festschrift for Dr. Basil I. Hirschowitz. Am J Med Sciences. 2009 Aug;338(2):1–5. [20] © Wolters Kluwer

used an electric globe as the light source [7]. The maximal bending angel was only 30°, as greater angles would not allow for image transmission, and thus there were significant blind spots not visualized by the endoscope.

A bevy of productivity by American manufacturers was responsible for a number of advancements over the next decade. William J. Cameron's "omni-angle" flexible gastroscope included a mirror within the scope's tip that could be flipped, allowing the viewer to scan the stomach without moving the endoscope [7]. Donald T. Chamberlin helped create an instrument with a controllable tip. This ushered in an era of endoscopes that could more thoroughly examine the stomach by minimizing blind spots that had been problematic in previous models, such as Schindler's.

Fiber-Optic Endoscopy

The next revolution in endoscopic development came with the discovery of fiber-optic technology. This yielded a portfolio of instruments with improved flexibility, improved light transmission, and greater field of view [6]. Basil Hirschowitz was responsible for the first "fiberscope" in 1957 (Fig. 1.4). Soon several improvements were made using Hirschowitz's model as a foundation. Philip A. LoPresti introduced a channel for suction and air or water to keep the lens clean. Longer versions of the endoscope were created in order to reliably visualize the duodenum. Eventually four-way control of the instrument tip and deflection angles up to 180 ° were possible, further improving the field of vision. In introducing further functionality to the endoscope, the "masterscope" was designed such that a smaller fiberscope could be inserted for use in diagnostic or surgical procedures.

Development of the Colonoscope

Early Lower Gastrointestinal Endoscopy

Inspection of the lower gastrointestinal tract dates back to simple anal and rectal specula found in the ruins of Pompei [6]. The majority of advances beyond that, however, did not come until after the advances in fiber-optic upper endoscopy instruments. The first rigid sigmoidoscope by Howard A. Kelly in 1894 used a simple lamp to reflect light off a head mirror down a tube. James P. Tuttle later integrated an electric lighting system. In general, these rigid instruments were effective in examining the first 20 to 25 centimeters of the lower gastrointestinal tract.

Beginning in the 1960s, fiber-optic technology found its way into sigmoidoscopes and colonoscopes as well. Many of the early prototypes were developed and marketed in Japan. In the United States, Robert Turell was one of the first to create a fiber-optic illumination system for use in rigid sigmoidoscopes [6]. Bergein Overholt introduced a flexible fiber-optic sigmoidoscope with the goal of improving patient comfort during the procedure. As such, his instrument allowed for deeper entry and therefore examination of a greater length of the sigmoid and descending colon. Olympus would soon after introduce a colonoscope that included a four-way controllable tip.

The First Colonoscopies

Oshiba and Watanabe published the first results with colonoscopy in 1965 [4]. Luciano Provenzale and Antonio Revignas are credited with performing the first complete

colonoscopy in Sardinia, Italy in 1965 [6]. Their unique approach involved having a patient swallow the end of a piece of polyvinyl tubing. This eventually exited the anus, to which they then attached a Hirschowitz gastroscope and pulled it through the colon all the way to the cecum. Reports by numerous endoscopists detailing their experiences with colonoscopy and the safety of the procedure were then published. In 1977, Bohlman and colleagues published a trial demonstrating the superior diagnostic yield of flexible endoscopes compared to their rigid counterparts.

Endoscopic Photography

Advances in imaging enhanced the practical applications afforded by the endoscope. Taking photos of hollow organs being examined dates back to the nineteenth century with Nitze creating a cystoscope onto which glass plates with a light-sensitive coating could be mounted [7]. The plates could be moved into the light, and photographs could be created with a 3–5 s exposure time. Lange and Meltzung made attempts with a small internal camera attached to a rubber tube that the patient could swallow [6, 7]. The electric wiring for the globe, mechanical cameral trigger, and air channel for insufflation were all contained within the rubber tubing. Henning and Keilhack in 1938 used a Schindler gastroscope and overburned the globe to create a flash, producing the first color photos of the stomach [4].

Successful endoscopic photography was not achieved until the development of external photographing apparatuses. In 1948, Harry Segal and James Watson created an external device for taking color photographs through a semiflexible gastroscope. The key to this was the development of a system in which changes in light supply, gastroscope prism, and camera shutter could occur in synchrony [6].

The gastrocamera was developed in Japan in the early 1950s and introduced in the United States later that decade [6]. This instrument contained all components of a proper camera attached to a control unit: a lens, flash, air valve, and film capsule. The major disadvantages of the gastrocamera were the inability to directly view what was being photographed and the time required to develop the film. The former was remedied by Olympus in 1963 when they introduced an instrument with features of both fiber-optic technology and a gastrocamera packaged within one [6]. H. H. Hopkins contributed to the emergence of endoscopic documentation by replacing interspersed air in previous optical relay systems with glass rods [4]. His system provided superior light transmission, a wider viewing angle, and improved image quality with higher resolution. Furthermore, his system could be housed within a smaller diameter endoscope. With the improved light transmission, practitioners found that attaching a 35-mm camera to the eyepiece could yield high-quality images, and the gastroscope fell out of favor [6].

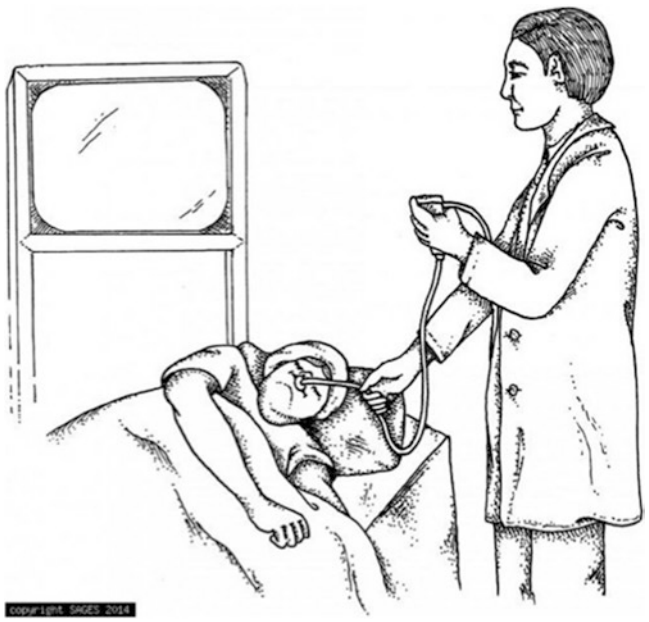

Fig. 1.5 Improved ergonomics with the use of video endoscopy. Endoscopists could view images with both eyes on a screen and work with the endoscope at the waist level. "Video Monitor," online June 16, 2010 © Society of American Gastrointestinal Endoscopic Surgeons (SAGES). Used with permission

Video Endoscopy

Soulas was one of the first to perform video endoscopy in France in 1956 [7]. Prior to the development of miniaturized versions of video equipment, endoscopes were attached to regular television cameras, and through this method images were transmitted to a television monitor. In 1960 Melbourne, Australia, a team created a miniaturized camera 45 mm by 120 mm long that could be attached to a regular endoscope and transmit black and white images to a screen.

Charge-coupled device (CCD) image sensors were a major breakthrough for video endoscopy. The sensor was fitted at the tip of instruments, where the entire imaging process could take place [7]. The old lens and fiber-optic bundles were replaced by wires. It could then transmit the image electronically to a video processor, which was then projected onto a television monitor [6]. These advances allowed for increased flexibility of instruments and improved image quality. This would also become the basis of standard technology for larger flexible endoscopes in the future [4].

Numerous advantages for the practitioner came with video endoscopy, most notably being improved viewing of an enlarged image with both eyes at a convenient distance on a screen, simultaneous viewing by members of an entire team, and improved ergonomics for the endoscopist (Fig. 1.5) [4, 6]. Furthermore, the convenient images and video recordings that could be captured improved documentation not only for medical purposes but also for educational functions.

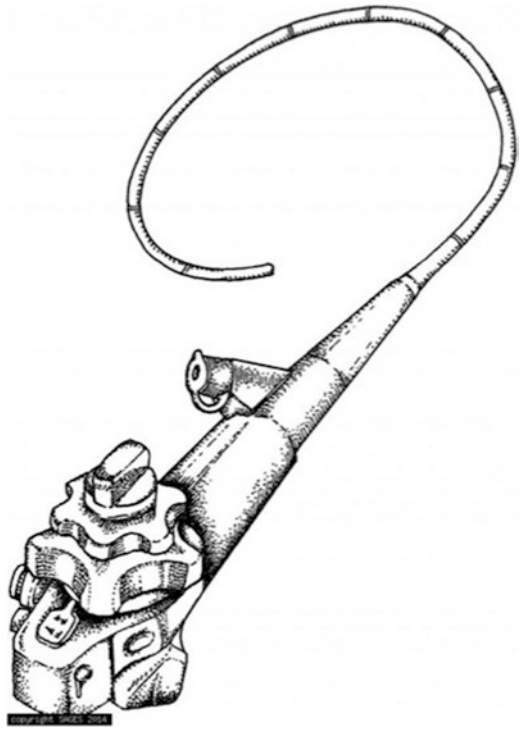

Fig. 1.6 Flexible endoscope with controllable tip. "Rotating wheels on the headpiece of the endoscope," online June 16, 2010 © Society of American Gastrointestinal Endoscopic Surgeons (SAGES). Used with permission

The Modern Colonoscope

The modern day colonoscope uses fiber-optic cables to transmit light to the lumen from a separate light source [9]. Images are retrieved digitally using a CCD chip at the tip of the instrument. It includes suction, air or water insufflation, as well as biopsy capabilities. The shaft of the colonoscope is typically 12 to 14 mm in diameter and consists of a distal flexible portion and a relatively rigid proximal section. The distal-most 9 cm comprises the controllable bending section, allowing 180° of up/down and 160° of left/right angulation (Fig. 1.6). Furthermore, the shaft is torque stable, meaning rotational forces applied by the operator proximally are transmitted distally to the tip of the instrument.

Variations of this standard colonoscope also exist for specific clinical situations [9]. Pediatric colonoscopes are smaller in diameter and are more flexible. The distal bending section is also shorter, allowing the instrument to adapt to the narrower lumen and more angulated colon in children. Pediatric instruments can also be useful in certain adult patients, for instance, in cases of strictures or postsurgical adhesions narrowing the lumen. Colonoscopes with variable stiffness shafts also exist. A dial controls a coiled tensioning wire within the shaft, thereby altering the rigidity. There are mixed reports on whether this feature facilitates insertion of the instrument.

Additional technologic advances have further improved the discriminatory capabilities of endoscopes. For example, the use of narrow band imaging (NBI) to distinguish between vascular patterns of neoplastic vs. non-neoplastic colorectal polyps has recently been investigated. NBI uses blue light with narrow band filters to image superficial tissue structures and emphasizes the vascularity of the mucosa. In a randomized prospective study, Tischendorf and colleagues evaluated colonic and rectal polyps using this technology and compared their classification of polyps with histological findings [10]. Benign polyps were noted to have thin-caliber vessels with a uniform branching pattern, whereas malignant polyps were characterized by dilated, corkscrew vessels with increased vascularity and nonuniform branching patterns. The authors found they were able to identify neoplastic vs. non-neoplastic polyps with high accuracy. Specifically, classification based on vascular patterns visualized with NBI had a sensitivity and specificity of 93.7% and 89.2%, respectively. The implementation of technologies such as NBI could even further expand the diagnostic capabilities of the modern colonoscope.

The Colonoscope as a Therapeutic Instrument

Alongside all advances in the physical design and image quality of endoscopes came attempts to improve their interventional capabilities. Desormeaux was one of the first to conduct operative endoscopic procedures in living patients [7]. Nitze used movable loops for operation within the urinary bladder [8]. Bevan performed esophageal foreign body removals using reflected candlelight [4]. Kussmaul in 1870 achieved the same goal using reflected sunlight. Boisseau de Rocher in 1889 developed an endoscope with separate ocular and sheath components, allowing manipulation techniques needed to perform diagnostic procedures [5]. William Wolff and Hiromi Shinya saw the therapeutic potential of the colonoscope, removing colonic polyps with a wire loop snare in the 1970s [6].

Endoscopic Resection of Early-Stage Malignancies

Developments in endoscopic technique have established the colonoscope as more than a mere screening or diagnostic tool. Endoscopic mucosal resection (EMR) has been used, largely in East Asia, for removal of premalignant lesions and superficial malignancies of the gastrointestinal tracts. Several variations of this technique exist, but all begin with marking the periphery of the lesion with electrocautery then performing a submucosal injection to lift and help identify the lesion [11, 12]. Normal saline with epinephrine is the most

frequently used injection [11]. In the "strip biopsy" technique, forceps are used to lift the lesion followed by excision using a polypectomy snare. A double-channel endoscope is required for this. Similarly, a double snare polypectomy technique has also been described, where one snare is used to lift and strangulate the lesion while the second is used to resect [12].

Use of EMR can often be limited by the size of the lesion, as en bloc resection of larger lesions may not be feasible with available instruments, and the lesion may require piecemeal removal. Endoscopic submucosal dissection (ESD) is a more technically challenging approach that can be used in such situations. ESD also begins with marking the periphery of the lesion and lifting via a submucosal injection. A circumferential incision is then made around the margin, into the submucosa [13]. A variety of knives are available to accomplish this [14]. Electrocautery is then used to free the lesion from the underlying deep layers. Larger lesions can be resected as there is no size limitation from the use of snares as is the case with EMR.

The indications for EMR and ESD are similar, namely, premalignant lesions or early-stage adenocarcinomas without nodal involvement [11, 14]. Complete resection via endoscopic means should be technically possible. These approaches may be considered in certain cases of advanced cancer in which patients may be poor candidates for a larger operation, or for palliation of an obstructing or bleeding mass. Both techniques allow for histological examination of the specimen, an advantage over ablative techniques.

A recent meta-analysis compared the outcomes and safety profiles of EMR and ESD. The group found that ESD was associated with higher en bloc resection and curative resection rates compared to EMR, regardless of lesion size [13]. On subgroup analysis, these findings also held true specifically with colorectal lesions and when broken down by size categories (<10, 10–20, and >20 mm). ESD was also found to have a lower local recurrence rate compared to EMR. The main reported complications of both techniques are procedure-related bleeding and perforation. ESD was associated with a longer operative time and higher rates of bleeding and perforation. Cao and colleagues reported the management of most perforations required a true operation. Others report experiencing mostly microperforations that were definitively managed endoscopically via closure of the defect with a clip [14].

Transanal Techniques

Transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS) are newer techniques available for the local excision of rectal lesions. Use of these techniques has been advocated in benign rectal neoplasms as well as select T1 rectal cancers with favorable histology and low risk of nodal metastasis [15]. Similar to purely endoscopic techniques, they may also be used with more advanced disease in patients unable to tolerate a more extensive procedure, such as low anterior resection or abdominoperineal resection, and for palliative purposes.

TEM involves dilation of the anal sphincter with a 4 cm operating sigmoidoscope that can accommodate optics, suction, and ports for instruments [16]. The rectum is insufflated using carbon dioxide to improve the field of view. Various endoscopic surgical instruments are available, and they allow the surgeons to reach further into the rectum than possible with traditional transanal excision. The technique has a steep learning curve and requires significant setup and rather expensive equipment.

TAMIS evolved as a hybrid between TEM and single-incision laparoscopy that was meant to be more affordable and technically feasible than TEM [15]. Transanal access is achieved with the SILS Port (Covidien, Mansfield, MA) or Gel-POINT Path (Applied Medical, Rancho Santa Margarita, CA). As with TEM, pneumorectum is established to improve the field of view. The procedure can then be carried out using standard laparoscopic instruments. Some have reported using a colonoscope or another flexible tipped scope for visualization rather than a standard laparoscope [15].

A meta-analysis found that TEM had higher rates of negative margins and en bloc resection and lower rates of local recurrence compared to traditional transanal excision [17]. Similar findings have been reported for TAMIS [15]. Though the data thus far has been promising, large-volume randomized controlled trials are still lacking.

Colonic Stenting

Colonic stents can be used in the management of acute large bowel obstructions. Briefly, possible indications for colonic stenting include inoperable obstructing colorectal tumors, obstruction from mass effect by pelvic tumor, malignant fistulae, anastomotic leaks or strictures, and recurrent benign strictures [18].

Self-expanding metal stents (SEMS) are inserted through the anus under endoscopic or sometimes fluoroscopic guidance. They have a predictable shape after deployment and come in several variations. Covered stents are more rigid and resist tumor ingrowth [18]. Uncovered stents, on the other hand, are more flexible and easier to place, but are more prone to tumor ingrowth. All are designed to prevent migration.

Overall, stenting is a relatively low-risk procedure [18]. Technical failure mostly comes in the form of the inability to pass the guidewire across the strictured area. Early complications include perforation and bleeding, which is often self-limiting. Late complications include stent migration,

re-obstruction, erosion or fistulization. The benefits include providing palliation to patients with inoperable tumors or providing a bridge to surgery. The latter allows for preoperative stabilization and optimization of the patient, potentially avoiding the high morbidity and mortality associated with an emergent operation. Palliative stenting can improve quality of life in patients with obstructing tumors who are poor surgical candidates.

Conclusions

Endoscopic instruments have come a long way since Bozzini introduced his Lichtleiter. Modern diagnostic and therapeutic applications of colonoscopy are numerous, and as technological advances and novel instruments continue to be produced, the potential continues to grow.

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Anatomic Basis of Colonoscopy

2

Ron G. Landmann and Todd D. Francone

Key Points

- Critical knowledge of colorectal anatomy is imperative to performing appropriate endoscopic examinations.
- Appreciation for anatomic variations can help in progress during colonoscopy.
- Mural findings and internal clues are appropriate adjuvants in helping the endoscopist proceed with forward advancement and eventual cecal intubation.
- Looping during colonoscopy is common. Various types of loops can be encountered, and appreciation of these formations is mandatory. Having a standardized protocol for preventing and reducing these loops is fundamental in assurance of forward progression and intubation while minimizing patient discomfort and morbidity.
- Observation and verification of certain anatomic landmarks throughout the colon are helpful for providing a roadmap to continued intubation. Similarly, photography of some of these landmarks is required to document successful complete colonoscopy.

Background

Colonoscopy is an effective and efficient tool in the diagnostic and therapeutic management of colon and rectal diseases and allows for complete mural examination and management of the anus, rectum, colon, and terminal ileum. First described by Drs Wolff and Shinaya in 1971 [1–3], numerous exponential advancements in optics, imaging modalities, mechanics, techniques, and instrumentation have made colonoscopy a gold standard in detection and prevention of deaths from colorectal cancer [4–7]. Indeed colonoscopy has also been found to have particular advantages in colorectal cancer screening, surveillance of inflammatory bowel diseases, and management of volvulus and other benign diseases [8]. Mastery of anatomic landmarks and impressions during the procedure is fundamental to the performance of endoscopy and allows for improved and optimal maneuverability, insertion and withdrawal, and also maximizing enhanced diagnostic and subsequent therapeutic yield. Knowledge of normal anatomy and its variants are critical to the appreciation of pathological changes or abnormalities, including polyps, diverticuli, carcinomas, and fistulae, among other findings (Fig. 2.1).

Recent advancements in CT colonography and fluoroscopy have been helpful in better defining anatomic landmarks and in facilitating colonoscopy by reducing looping and straightening and shortening maneuvers [9]. Furthermore, utilization of good basic technique and an appreciation and implications of standardized approach to difficult intubation (redundancy, difficult sigmoid, poor tolerance to sedation) help to yield improved maneuverability and successful colonoscopy [9–11].

Technique for colonoscopic advancement will be further discussed in other chapters in greater detail, particularly as it relates to interventions such as biopsy, polypectomy, endoscopic mucosal resections and endoscopic submucosal dissections, and also tattooing.

Above all, certain standards in endoscopy should be followed to assure patient safety and successful colonoscopy. These including being gentle, minimal blind pushing, keeping the lumen within view, periodic and frequent withdrawal motions for straightening, and avoidance of mucosal whitening or reddening ("redout") by scraping or sliding by the wall of the colon. Pain and incomplete colonoscopy are generally due to loop or bowing formation and resultant mesenteric

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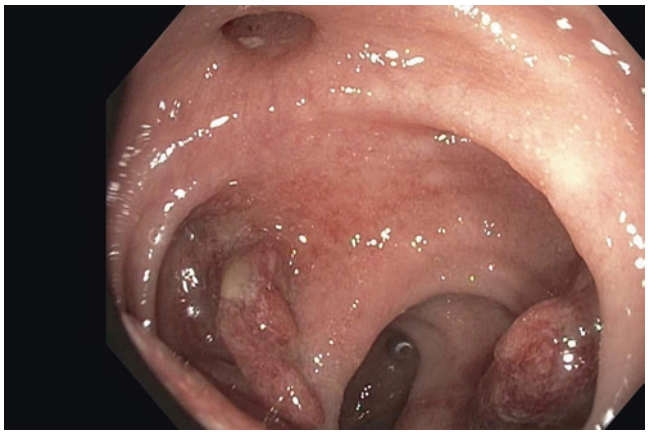

Fig. 2.1 Pseudopolyps and diverticuli. This is a picture taken during evaluation of the sigmoid colon in a patient with long-standing ulcerative colitis. Note the inflammatory appearance of the enlarged polyps, the excavating diverticuli, and the burnt out appearance of the wall of the remaining colon

stretching and, in some occasions, irritable bowel disease. Abdominal pressure to prevent and reduce looping with patient repositioning is a useful sometimes necessary adjunct in successful colonoscopic advancement.

Anatomic Variations

Difficulty in successful colonoscopy is generally related to anatomic variations as it relates to redundancy in the colon or its retroperitoneal attachments leading to looping of the instrument. This looping can lead to stretching of the mesentery and significant pain, and occasionally incomplete colonoscopy. One study of 100 patients reported looping in 73% of patients with a total of 165 loops noted [9]. A fundamental understanding of the anatomy and variations thereof can aid the operator in achieving a maximal rate of successful cecal intubations.

Using intraoperative assessments, Saunders and his group found that colonic length is significantly greater in women (155 vs. 145, $p = 0.005$), with the most pronounced difference noted in the transverse colon, where the colon may dip into the pelvis more often in women than in men (62% vs. 26%, $p < 0.001$) [12, 13].

Similarly, portions of the colon that are typically presumed to be fixed (ascending and descending colon and the hepatic and splenic flexures) have been noted to have variable degree of mobility and freedom. Roughly 8–9% of the descending and ascending colons were mobile as a result of a redundant and non-fixed mesentery. One-fifth of patients had a mobile splenic flexure. The transverse colon reached the symphysis pubis in 29% of patients. Lastly, in approximately 20% of patients, the sigmoid colon had variable adhesions as a result of diverticular disease or pelvic surgery or congenital adhesions [13]. The redundancy in the sigmoid and transverse colon can lead to difficulty in successfully advancing and overcoming these portions as a result of looping or bowing. Indeed, this can occur in up to 91% of patients, with N-type bowing of the sigmoid in 79% and deep transverse bowing in up to 34% [14, 15].

Lastly, based on operative findings, ethnic variations in colonic length have been suggested with patients from Asia and the Far East noted to have longer colons (P = NS), but Caucasians/Western populations observed to have more sigmoid adhesions ($p < 0.05$), longer descending mesocolons ($p = 0.01$), more mobile splenic flexures ($p < 0.016$), and longer transverse colons reaching the symphysis pubis or lower ($p < 0.001$) [16].

Interestingly, when comparing CT colonography and colonoscopy, considerable variance in overall length were noted, with a shorted distance observed on colonoscopy (167 cm vs. 93.5 cm), though this may be related to experience of the endoscopist and also the accordion-like effect of successful intubation. Furthermore, colonography was able to observe and document a higher number of acute angle flexures and tortuosity. In the same cohort of patients undergoing both modalities, while looping occurred in 73 of 100 patients, fluoroscopic-assisted straightening maneuvers were successful in 95%. Successful cecal intubation was precluded in only 2 of 100 patients due to an obstructing sigmoid carcinoma and a redundant colon [9].

Mural Findings and Internal Cues Helpful in Advancement

Small clues can be helpful in locating the lumen and directing forward advancement of the colonoscope. The lumen is located at the center of converging/radially oriented folds (not seen around diverticular orifices). The darkest side of a mucosal view or the darkest area of a fluid-filled colon should be nearest to the center of the colon and lumen. Aiming toward these areas with gentle insufflation should help in achieving proximal progression.

Curved arcs on inspection can also provide clues in determining where to progress within the channel of the colon. Arcs may be caused by haustral folds or reflections of the circular muscles fibers under the mucosal surface or highlights reflected off the surface of the microscopic innominate grooves. Enlarged muscle fibers run longitudinal along the colon (tenia coli) and may be used as a direction of orientation (similar to a white line/stripe along a highway). These are prominent and can be most easily seen along the transverse colon, splenic flexure, and particularly in the cecum.

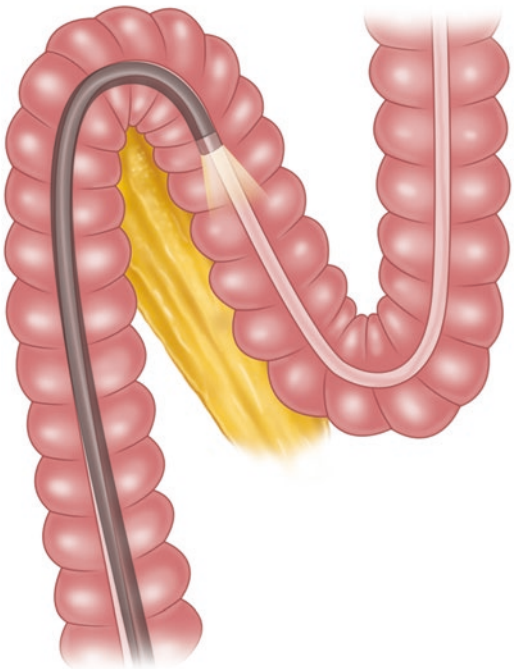

Fig. 2.2 Formation of sigmoid N-loop during colonoscopy. Note how the long mesentery allows stretching of the sigmoid colon. Minimal angulation of the tip will be helpful in advancement of the scope until the loop can be reduced

While progressing through difficult angulation or tortuous folds, a phenomenon called "redout" may be observed—with complete loss of any anatomic landmarks available to guide forward travel. To overcome this, standard guidelines in procedural endoscopy recommend additional gentle insufflation while pulling back with maintenance of current. This will generally smooth out the bend, shortening the colon that is past the tip, and straightening the forward colon while decreasing disorientation (the latter due to reduction of angulation). One exception to the rule may be encountered during creation of N-loops of the sigmoid, where steep/acute angulation of the tip with forward advancement may lead to exacerbation of the bowing/looping distal to the tip (walking-stick phenomenon). In these cases, a slight reduction in angulation may be helpful during forward pushing (Fig. 2.2).

Positioning

Traditionally, colonoscopy is generally performed in the left lateral decubitus position with the hips and knees flexed at 60°–90°. Rare exceptions exist—including intubation and endoscopy through ileostomies or colostomies—and in these situations, the patient is usually in the supine position. Occasionally, as noted above and detailed further throughout the manuscript, application of manual pressure and repositioning into the right lateral or occasionally supine and/or prone positions may help with preventing looping and ultimate cecal intubations [17, 18].

In the left lateral position, the descending colon is typically fluid filled. In the right lateral position, the descending colon is more air filled. With this knowledge, positioning into the supine or right lateral position while navigating the sigmoid and descending colon can lead to forward progress. Once progress has been made, repositioning into the standard left lateral decubitus position may allow continued intubation.

Stool and fluid can also be helpful in determining location of the lumen in the colon. Liquid effluence is generally dependent. Articulation of the tip away from a flat air fluid level will generally guide the operator toward the lumen. Similarly, stool coming through an orifice is generally coming through the main lumen. Care should be taken, however, not to confuse a scybalum-filled diverticulum with the lumen of the colon.

Looping

Looping is very common during forward progression of colonoscopy. These are generally formed due to redundancies in the colon and/or hypermobile mesenteries, typically seen in the sigmoid and transverse colon [19]. Paradoxical movement and loss of 1:1 relationship of tip/shaft advancement are generally caused by sharp angulation and loop formation and are the first signs of loop formation. Typical findings include slippage with paradoxical motion and loss of sensitivity or resistance changes on advancement. Forward pushing at this stage will only increase the size of the loop, cause distention of the colon, further stretch the mesentery, and subsequently increase pain experienced by the patient.

Appreciation of the formation and direction of these loops with an understanding of the underlying anatomy will allow the operator to subsequently reduce these loops, straighten the bowel, and continue with forward progression. The most typical loop is the N-loop (or spiral loop) formed during advancement through the sigmoid colon (80%). The alpha (α)-loop is encountered in about 10% of cases with an anterior/ventral-oriented sagittal loop formation (Fig. 2.3). Lastly, deep transverse looping is noted in approximately 30% of cases (Fig. 2.4). More atypical loops caused by mobile colonic attachments include the reverse α-loop (5%, posterior/dorsal counterclockwise looping of the sigmoid or descending colon requiring strong counterclockwise torque retraction for reduction), reverse splenic flexure loop (3%, ventral left sided angulation and then reorientation to the right), gamma-loop of the transverse colon (1%), and a reverse sigmoid spiral (1%, with the scope oriented initially

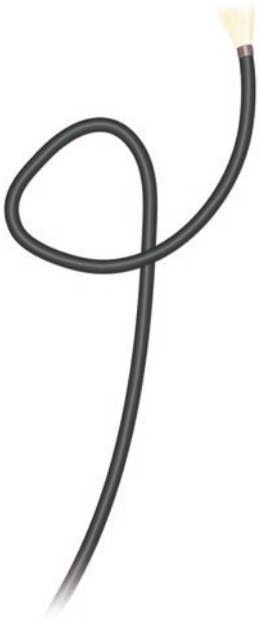

Fig. 2.3 Scope view image of an alpha (α)-loop. Note the appearance typical of a sigmoid volvulus. Pushing through this loop until the descending colon is reached and then reduction with clockwise torqueing and withdrawal will lead to a straightened path for the colonoscope and future ease in progression and navigation of the splenic flexure

Fig. 2.4 Common loops formed during colonoscopy include the (**a**) sigmoid N-loop (sometimes called bowing), (**b**) α-loop with medialization of the sigmoid colon by volvulus formation, and (**c**) deep transverse colon loop

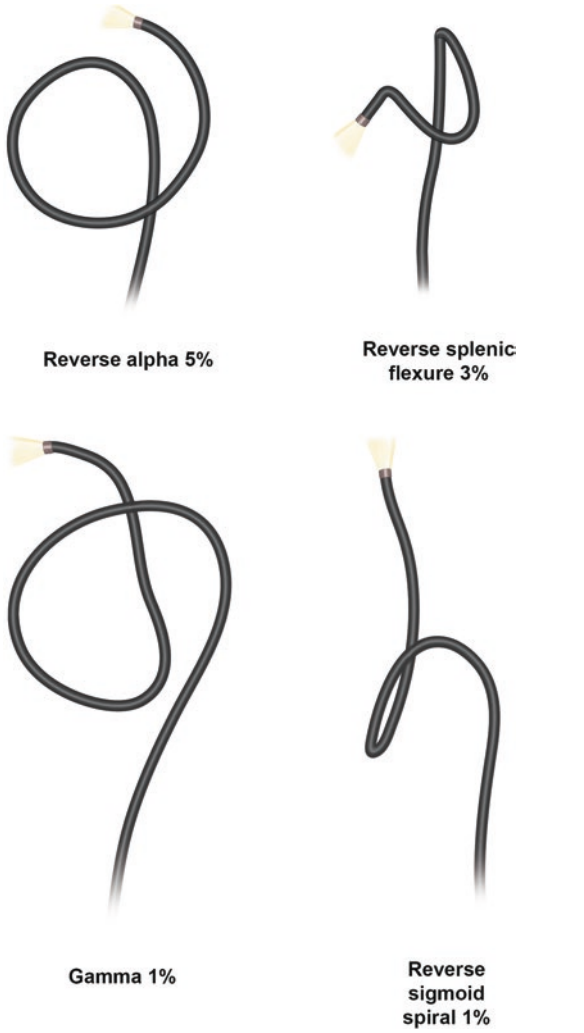

Fig. 2.5 Less common and difficult loops encountered during colonoscopy. These include (in counterclockwise order from top left) (**a**) reverse α-loop, (**b**) deep gamma (γ)-loop of the transverse colon, (**c**) reverse splenic flexure loop, and (**d**) reverse sigmoid spiral loops. Approach to reduction is discussed in the text

anterior and ventral in the caudal orientation and then followed in a cephalad posterior dorsal position leading to medialization, rather than lateral positioning of the sigmoid and descending colon) (Fig. 2.5).

Reduction of Loops

An appreciation loop formation and protocoled regimen to reduce these loops are imperative in allowing continued progression and reduction of pain and other morbidities associated with colonoscopy. These loops are generally overcome by gently withdrawing of the colonoscope and while maintaining the angulation (up-down/left-right), detorqueing the scope in clockwise direction with the wrist. This maneuver prevents slippage. On subsequent advancement, the operator should then try clockwise torqueing. Occasionally, anticlockwise torqueing and retraction followed by anticlockwise torqueing and advancement may be necessary if the above maneuvers are repeatedly unsuccessful. Lastly, changing positioning or abdominal pressure application may be useful with incorporation of the above steps [17]. Successful manipulation of these loops will be met by forward 1:1 or great advancement of the tip and the shaft of the colonoscope. Real-time magnetic image-guided endoscopy can sometimes be used as an adjunct to help visualize and subsequently reduce looping during scope

advancement [14, 15]. This tool may be particularly helpful in the early learning phases of colonoscopy.

Additional steps pertinent to progression of the colonoscopy procedure as they relate to the particular segment of anatomy will be discussed below.

Anatomy

The following will describe various key anatomic landmarks that should be appreciated during advancement and progression of the procedure leading to a successful colonoscopy.

Anus

The first landmark to be visualized and assessed is the perianal area and anal canal. This area of the intestinal canal is frequently overlooked and, in the case of colonoscopy, poorly visualized. Care should be made to grossly evaluate for any external diseases perianally and exclude noteworthy entities such as anal carcinoma (squamous cell, melanoma, etc.), fissures, fistulae, and abscesses. Hemorrhoids are typical findings and should be documented accordingly. In the setting of suspected inflammatory bowel disease, careful visual inspection for waxy elephant ear Crohn's tags should be performed and documented. These are commonly mistaken for benign hemorrhoids. A digital rectal examination of the anorectal canal is then performed to assure no significant mass or excavating lesion exists, as well as provides an assessment for any stricture or stenosis. These can be related to intrinsic inflammatory bowel disease such as Crohn's disease, or may be related to postoperative healing, or carcinoma. If any of these are found, cautious biopsies may be indicated. Care should be utilized however to prevent fistula formation in this vicinity. In some cases, a bimanual examination may be warranted if a mass or penetrating lesion or fistula is suspected. Once visual and digital rectal examination is performed, the colonoscopy can then be initiated.

Once the tip of the colonoscope is inserted within the anorectal canal, using variations of either air, carbon dioxide (CO_2), or water insufflation/instillation, the rectum is then visualized. Typically, there may be residual stool or fluid in the rectal vault from the preparation. This should be sufficiently suctioned out for appropriate evaluation of the anorectal and rectal mucosa.

Rectum

Key Landmarks

- Dentate line
- Rectal valves/folds

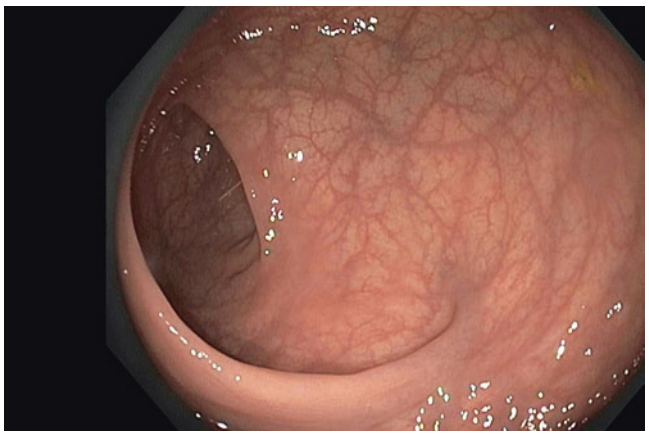

Fig. 2.6 Rectal fold/valves—in this colonoscopic image, the mid and distal folds can be appreciated on the left and right side, respectively. The upper/proximal rectum is in the background, while the mid and then upper portions of the distal rectum are seen in the foreground

The rectum is approximately 15 cm long and, for clinical descriptive purposes, can be divided into approximately 5 cm thirds (proximal, mid, and distal). These portions of the rectum will be demarcated by incomplete haustral valves or folds of Houston (upper/proximal/first, middle/second, lower/distal/third) that can be used as landmarks when describing any atypical lesions (carcinomas, polyps). The proximal/upper fold is considered the uppermost/cephalad extent of the rectum and denotes the rectosigmoid junction (Fig. 2.6). The authors recommend not utilizing only numerical designation but rather descriptive terms (distal or lower instead of first) as this avoids confusion in terms of location and orientation. When commenting on findings, it is helpful to both note the location of these lesions based on distance from the anal verge (or preferably dentate) and also the location related to these rectal folds or valves (i.e., "6 cm above the anal verge, on and distal to the lower/distal rectal fold"). This is significantly important when surgical approaches are to be considered or when imaging is later performed and needs to be correlated to endoscopic findings.

Occasionally, lesions may not be able to be endoscopically managed at the time of index colonoscopy. Advanced endoscopic therapeutic interventions such as endoscopic mucosal resection or endoscopic submucosal dissection may benefit the patient with benign polypoid disease. Surgical (or combined endolaparoscopic) management may also be warranted for malignancy or medically refractory disease. Anticipating the need for these above modalities, photodocumentation with location and anatomic landmarks is critical for the referred physician or surgeon. Furthermore, it may be appropriate to inject a submucosal tattoo on the distal/anal side of the lesion. This should be done using three areas of injection circumferentially around the wall of the colon. The only area that would not definitively need tattooing is a

lesion in the cecum. Rectal lesions are helpful to tattoo in case regression is noted after neoadjuvant chemoradiation therapy.

Progression through the retroperitoneal rectum is generally straightforward with mostly forward pushing, insufflation, and gentle clockwise torqueing required at times. Once the proximal rectum has been traversed, it may be helpful to gently pull back and unloop and reduce any redundancy and excess scope previously inserted.

Rectosigmoid and Sigmoid Colon

Key Landmarks

- Upper rectal valve/fold
- Diverticuli
- Tortuosity in women and patients with long-standing constipation
- Stenoses/strictures due to diverticular disease

At approximately 15–20 cm above the anal verge, the endoscopist will encounter the rectosigmoid and then distal sigmoid colon. This is also the area where the colon is now located within the peritoneal cavity above the peritoneal reflection. Care should be taken in this vicinity as there are commonly located and experienced tortuosities and angulations, strictures/stenoses, and significant diverticular disease in this vicinity (Fig. 2.7). Furthermore, redundancy of the colon in this area may lead to excessive looping of the endoscope. Overly aggressive forward movement and/or twisting may lead to mechanical trauma along the wall of the colon. Barotrauma related to over distention with air is also a significant risk in this area. Both of these are common causes of perforation, particularly in this area. The cecum is also a very common area for perforation due to barotrauma as it relates to LaPlace's law with this proximal-most portion of the colon having a larger radius and thinner wall/tension. Perforations rates are typically less than 0.1%, but may reach 18% based on indication for therapeutic procedure being performed in these areas [20–30].

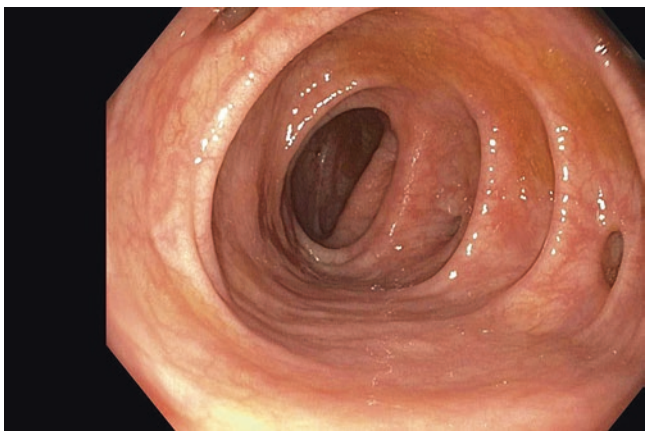

Fig. 2.7 Sigmoid colon with diverticuli. Note the excavating lesions noted on the sides of the wall of the sigmoid colon. Also, the endoscopist should appreciate the larger and darker center lumen that should be used as a guide to advance the scope. In this image, fluid is noted on the upper right, signifying the dependent portion of the colon

During advancement in this area, care should be made to use judicious insufflation and at the same time also aspiration techniques utilized to draw in the more proximal lumen while telescoping and advancing the colonoscope further into the colon. Excessive inflation of the colon can lengthen and distend the colon and, in some cases, enhance twisting or angulation and kinking of the colon and prevent advancement. In general, during advancement, right and left knobs should be used sparingly, and instead, mechanical twisting or torqueing of the shaft of the scope with the operator's wrist is preferred when trying to negotiate turns. Up-down knob manipulation is very helpful however in centering the scope in the lumen and advancing proximally.

First described in 1986 and 2002, the use of carbon dioxide insufflation [31] and/or water instillation [32] has been found to reduce distention and patient discomfort while facilitating advancement of the colonoscope [33–42]. Most recently, the use of warm water irrigation for colonic distention has been shown to aid in navigating through the left colon with extensive diverticulosis by help differentiating the lumen from the mouths of the diverticuli. Warm water colonic distension has also been shown to decrease sedation requirements and patient pain/discomfort [43, 44]. The potential disadvantages associate with water-aided colonoscopy technique is lower adenoma detection rate in the water-filled portions of the colon and longer procedure time [45–49].

In certain cases due to narrowed, angulated, or fixed sigmoid colons, a pediatric colonoscope or a thin upper endoscope can be used in combination of position changes (supine) and abdominal pressure (one or two hands pushing down and to the left and utilizing up to four hands to cover the entire abdomen). In some cases, guidewire exchanges may be utilized. For redundant sigmoid colons, the use of various enteroscopes and/or endoscopic straighteners can also be utilized [11, 50]. Variable stiffness endoscopes have recently been utilized to help in navigating and advancing the scope.

During insertion and navigation through the tortuous rectosigmoid and sigmoid colons and into the otherwise straight descending colon, combinations of right-oriented clockwise wrist twisting/torqueing and de-twisting and pullback/straightening maneuvers may be particularly useful as well. Sometimes, multiple to-and-fro motions may be required to successful navigate through the sigmoid with minimal looping. It is helpful to gain a masterful handling of the colonoscope. Being able to reposition the scope so that pathological

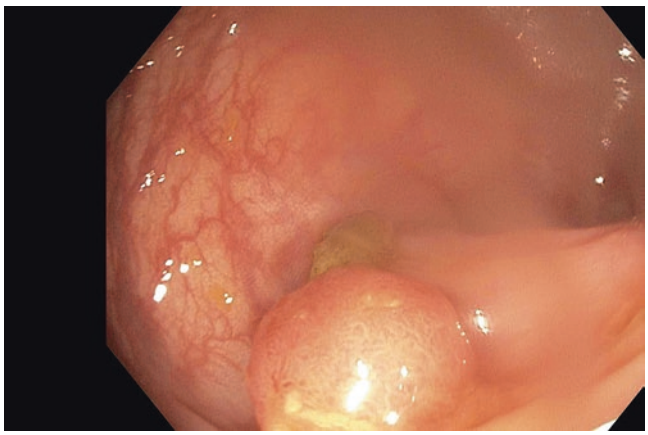

Fig. 2.8 A sessile polyp positioned at 6 o'clock. Note the villous architecture on the mucosal surface and benign appearance of the colon wall

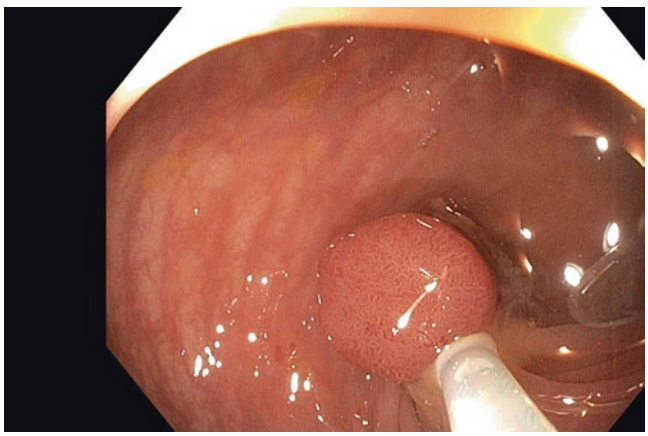

Fig. 2.9 The same polyp being resected with the technique of snare polypectomy

findings and working ports are localized at the 4–8 o'clock position will allow for improved ability for diagnostic and therapeutic interventions, such as biopsy, snare and clip applications (Figs. 2.8, 2.9, and 2.10).

Looping in the sigmoid colon is very common and can lead to difficult if not incomplete colonoscopy. Redundancy of the sigmoid colon leading to looping is correlated with female gender, increasing age, low body mass index, prior hysterectomy, and history of constipation [9, 51–53]. Looping can generally be overcome by following good standard endoscopic procedures without special techniques, using combinations of withdrawal-suctioning torqueing (clockwise vs. counterclockwise rotations of the endoscopy shaft) to straighten out the affected colon [9].

N- or spiral loops are commonly formed with straight pushing advancement motions through a long and mobile sigmoid mesentery. Interestingly there is minimal pain since the long colon is otherwise not particularly stretched. An alpha (α)-loop is endoscopically quite advantageous.

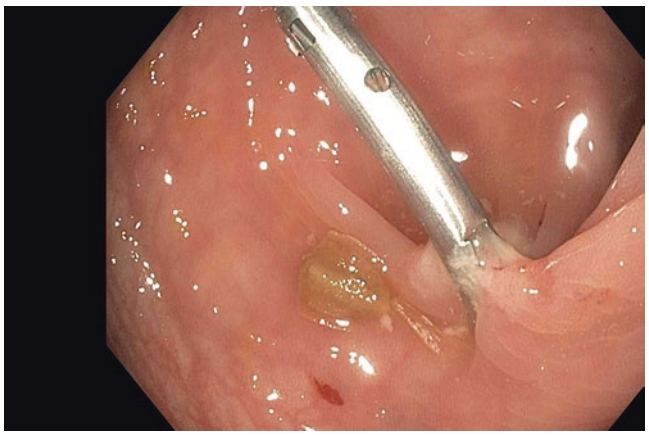

Fig. 2.10 A clip applied to the base of the resection specimen after snare excision of the sigmoid polyp

This α-loop is equivalent to a sigmoid volvulus formation caused during endoscopy due to a very long and mobile sigmoid and a fixed retroperitoneal descending colon. If advancement of the scope is easy without acute bends or discomfort, initially the operator should continue and push through the volvulus or α-loop. Once the proximal to mid-descending colon has been intubated, reduction of an α-loop by withdrawal with simultaneous clockwise rotation will yield a straightened colon that is pressed along the posterior abdominal wall/retroperitoneum allowing for further advancement and forward progress without looping or pain [54, 55]. In rare instances, a longitudinal "split" external straightener or overtube device can be utilized to overcome looping [10, 11]. In general, a median of 2.1 (range 1–6) straightening maneuvers may be necessary to reach the cecum [9].

Care must also be taken to avoid intubation of a diverticulum during insertion. Whenever advancing the endoscope, occasional pullback technique to visualize the central larger lumen may be useful to avoid inadvertent mechanical injury or barotrauma and subsequent perforation in this area.

Descending Colon

Entry into the descending colon is generally accomplished with a back-and-forth motion with clockwise torqueing of the colonoscope [55]. Alpha (α)-loops of the sigmoid colon are suspected when there is more pain than anticipated (secondary to mesenteric twisting and torsion) or paradoxical motion of the tip of the scope. This α-loop needs to be reduced prior to proceeding with scope advancement past the splenic flexure to minimize pain and increase successful cecal intubation rates. This can generally be performed by withdrawing the scope and slowly and gradually rotating the scope clockwise. This should then straighten out the sigmoid and descending colon and aide in further scope advancement

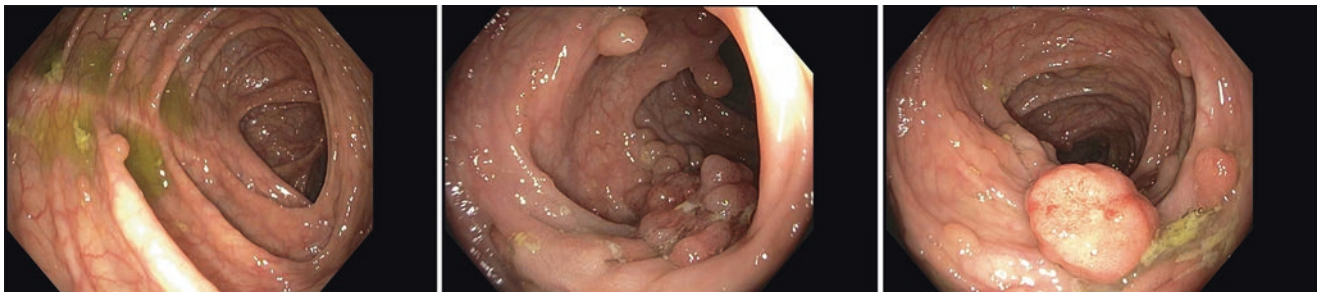

Fig. 2.11 Transverse colon with multiple adenomatous polyps of various sizes. Notice the triangular shape of the colon lumen formed by the thickened muscular teniae coli. This patient has familial adenomatous polyposis and found to have at least 544 adenomatous polyps throughout his colon and rectum

(noted by successful entry into the transverse colon without paradoxical movements).

Typically, once the scope has been manipulated through the sigmoid colon, the descending colon is seen as a straight path lumen with few diverticuli, if any, and generally without angulation. The circular appearance is related to the thick circular muscles lining the wall of the descending colon. This is principally related to the attachments to the retroperitoneal white line of Toldt laterally along the left abdominal wall and the mesentery to the retroperitoneum overlying Gerota's fascia.

Splenic Flexure

Key Landmarks

Sharp turn/angulation

Bluish hue of adjacent spleen

Proximal transverse colon/triangular haustra

Pressure applications are most used and helpful in overcoming the angulations and redundancies in the flexures (splenic and hepatic). The splenic flexure is generally more redundant than the hepatic flexure. In some instances, a bluish-gray hue may be noted through the thin wall of this flexure, and this corresponds to the spleen that may be intimately attached to the colon. Rough forward advancement without appropriate finesse may lead to traumatic splenic rupture and hemorrhage [56–59]. Changing position to the partial right lateral decubitus may help traverse the distal descending colon and splenic flexure.

The best clue signifying successful passage of the splenic flexure is progression from a fluid-filled descending colon to an air-filled, triangular-shaped transverse colon.

Once past the splenic flexure, at the distal transverse colon, attempts should be made to withdraw and reduce any looping or extraneous endoscope within the colon. This is generally helped by the fixation by the phrenocolic ligaments.

The splenic flexure acts as a fulcrum allowing forward progression through the transverse colon while withdrawing, through upward/cephalad lifting of the colon due to a cantilever effect. Similarly, using gravity as an assistant, the right lateral decubitus position helps in forward progression past the splenic flexure and through the transverse colon.

Keys to traversing the splenic flexure involve a few fundamental steps: (1) pull back the shaft to 50 cm with clockwise torque until there's a catapult-like resistance or slippage of the tip; (2) de-angulate the tip; (3) deflate the colon to keep colon short and supple and adaptable; (4) apply hand pressure over the lower abdomen to prevent looping; (5) torque the shaft clockwise to put torsional straightening force on the sigmoid loop while adjusting angulation to keep lumen in view; and (6) gently push in motion. Occasionally positioning the patient on the back and/or right-side down can also be utilized.

Reverse splenic flexure looping occurs when the descending colon is completely mobile and the colonoscope goes the wrong way around the splenic flexure and through the transverse colon. The scope pushes through a deep transverse loop with an acute angulation at the hepatic flexure. By counterclockwise de-torqueing and withdrawal using the splenophrenic ligament as a fulcrum, the descending colon is then twisted back in its typical anatomic lateral position, and the scope is then passed through the flexure in a conventional manner.

Transverse Colon

Key Landmarks

Triangular haustra

Prominent teniae coli

Tortuosity and redundancy noted in women and patients with long-standing constipation.

The transverse colon, proximal to the splenic flexure, is commonly identified by the triangular appearance of the lumen due to the prominent longitudinal muscles of the tenia coli and relatively thin circular muscle fibers (Fig. 2.11). The teniae function as a useful guide for the colonic axis and

direction of progression. The transverse colon is attached and dependent via its retroperitoneal mesentery just caudal to the pancreas. The transverse colon can reach down to the symphysis pubis, particularly in women or those patients with long-standing constipation [55]. Advancement through the mid- and distal-transverse colon is generally aided using various combinations of tip flexion and also abdominal wall compression. Traditionally, once the mid-transverse colon is reached, pulling back with clockwise rotation will lead to advancement through the proximal transverse colon through paradoxical movement as a result of a cantilever-type effect with the splenic flexure functioning as a fulcrum resulting in the shortening, straightening, and elevation of the colon. Repeated in-and-out push-pull movements may be helpful during this phase. In certain cases, a particularly long transverse colon and mesocolon may lead to the formation of a gamma (γ)-loop with a clockwise volvulus. This is particularly difficult to navigate and generally will require careful withdrawal back to the splenic flexure and reinsertion. In some cases, repositioning the patient in supine or prone position may help straighten the colon for advancement.

Hepatic Flexure and Ascending Colon

Key Landmarks

Bluish hue of liver

Once reaching the proximal transverse colon, while the patient is in the left lateral decubitus position, suctioning allows the colon to collapse onto the scope and advancement ensues. The hepatic flexure has an acute hairpin turn and requires masterful steering and manipulation to traverse and steer around. Overcoming the angulation of the hepatic flexure can be typically performed through a combination of torqueing (counter-) clockwise to gain a few additional centimeters of length, suctioning of the distended colon to collapse and shorten the flexure/bend, and pulling/withdrawing back on the endoscope. This generally leads to an accordion-like bowel slipping onto the shaft with prompt scope advancement (in a paradoxical fashion by withdrawal) into the cecum (Fig. 2.12). The application of abdominal pressure at various points (left upper abdomen, centrally, or right sided) may also be helpful. If the patient is lightly sedated, deep inspiration may help lower the diaphragm and flexure. In some cases, even with right lateral decubitus positioning, it may be difficult to overcome the presumed hepatic flexure. With this scenario, one must suspect that indeed, the scope is positioned at the splenic flexure in this case. One common way to determine this is based on fluid contents. In the left lateral decubitus position, the splenic flexure will have dependent fluid, whereas the hepatic flexure should be dry. (see picture "ascending colon from distal hepatic flexure"). Occasionally, the bluish hue from the liver may be seen through the thin-walled hepatic flexure (Fig. 2.13).

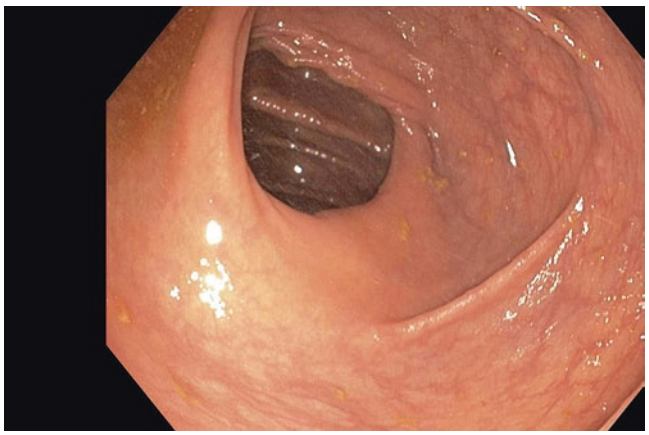

Fig. 2.12 This is a view as the ascending colon is being paradoxically intubated immediately after navigating through the hepatic flexure while withdrawing the scope

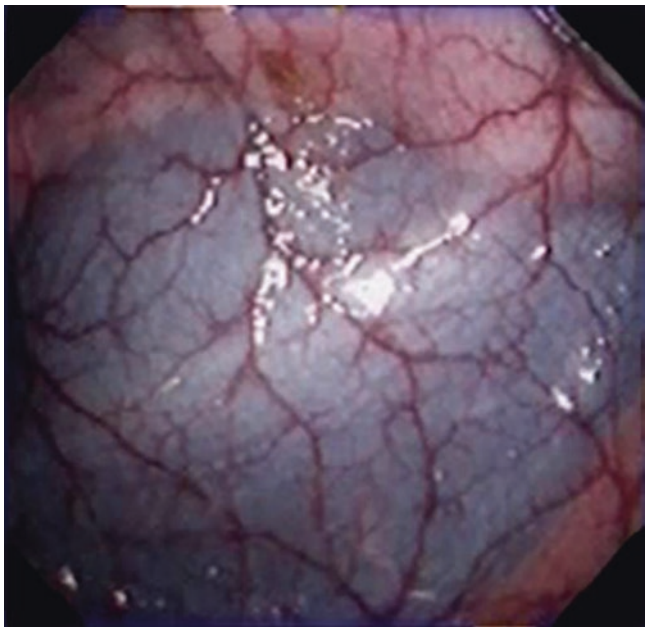

Fig. 2.13 The bluish hue discoloration visible through the thin-walled colon represents blood within the liver as the hepatic flexure is being traversed. A similar appearance can also be noted while traversing the splenic flexure—and this represents the spleen. Particular care should be utilized in these areas to avoid injury to the capsule of these vascular organs and ensuing hemorrhage

Cecum/Ileocecal Valve/Appendiceal Orifice

Key Landmarks

Ileocecal valve (ICV)

Appendiceal orifice (AO)

Once the hepatic flexure has been traversed, suctioning action and simultaneous clockwise rotation during withdrawal will lead to an accordion-like slippage of the ascending colon onto the scope with eventual intubation of the cecum. There may be additional maneuvering required at the

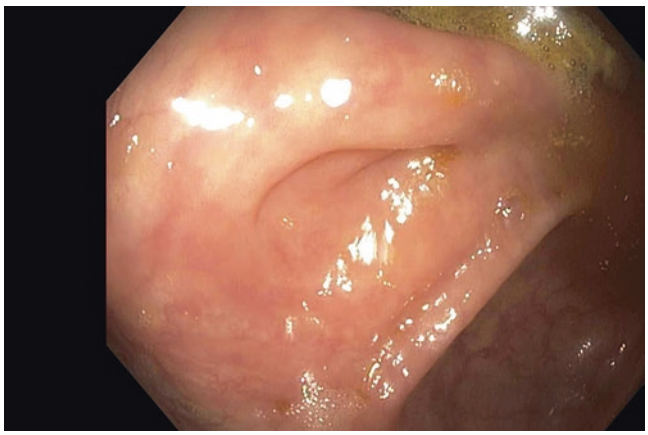

Fig. 2.14 Typical slit-like appearance of the appendiceal orifice. When attempting ileal intubation, the endoscopist should aim the tip toward the mouth of the slit (in this case, up and to the left)

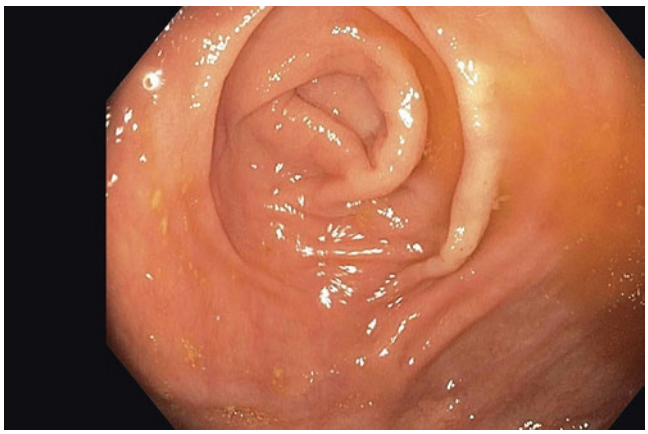

Fig. 2.15 Head on view of the open appendiceal orifice. Dependent fluid on the lateral aspect of the cecum. This fluid should be suctioned clear to evaluate for any small or diminutive polyps

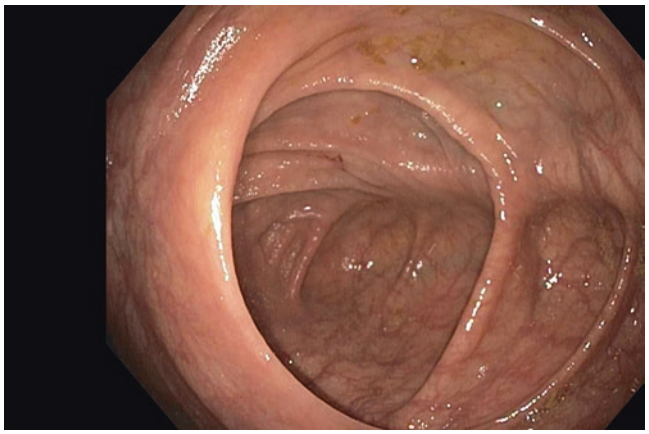

Fig. 2.16 Ileocecal valve and cecum. Note the thickened fold on the left of the picture, corresponding to the ileocecal valve. Hypertrophied and thickened tenia are also noted running longitudinally along the length of the cecum and ascending colon (right of picture). At the apex of the cecum, convergence of tenia is noted in the caput or cecal strap

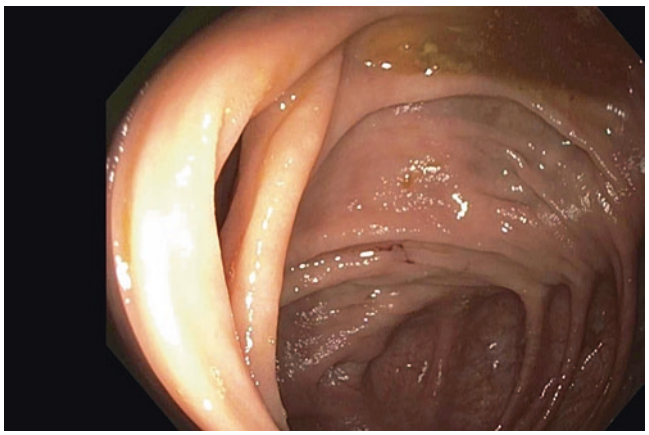

Fig. 2.17 The ileum is seen through the twofolds of the ileocecal valve on the left with the cecum and cecal strap noted in the background

end to successfully overcome the last of the haustral folds and get the ICV and AO in view. Occasionally a tight turn may be confused with the cecum. The absence of the AO and/or ICV is a precaution again making this error.

The AO is typically a very small curved slit or a hole in a circular whirl of folds. There may be ring-like lymphoid aggregate follicles surrounding the AO on close inspection. Some fluid may be noted coming from the orifice (Figs. 2.14 and 2.15).

The ICV is best seen as a bulge on the last and most prominent proximal haustral fold, approximately 5 cm proximal to the cecal caput/strap. Occasionally both lips of the valve may be seen (Figs. 2.16 and 2.17).

Photo documentation of key landmarks including the ileocecal valve (ICV) and the appendiceal orifice (AO) at the terminal end of the cecum is now mandated to be included with all endoscopy reports.

Terminal Ileum

The most straightforward method of intubation of the terminal ileum is by positioning the end of the scope adjacent to the appendiceal orifice; tipping the colonoscope toward the lip of the AO (presuming the ileum would follow a medial course in the peritoneal cavity and the enlarged aspect of the lip also points medially) and then with slow, gentle withdrawal toward the direction of the ileocecal valve, the scope will naturally then "hook" or fall into the valve and the ileum. The operator will quickly notice the marked variation in the appearance (both luminal surface and diameter) of the ileum. Otherwise, direct visualization of the ileocecal valve at the 6 o'clock position and forward and downward motion through this (slit-like opening on the cecal side of the) ICV can be similarly attempted. Occasionally, the scope may need to be positioned just proximal to the ICV and then with downward tipping,

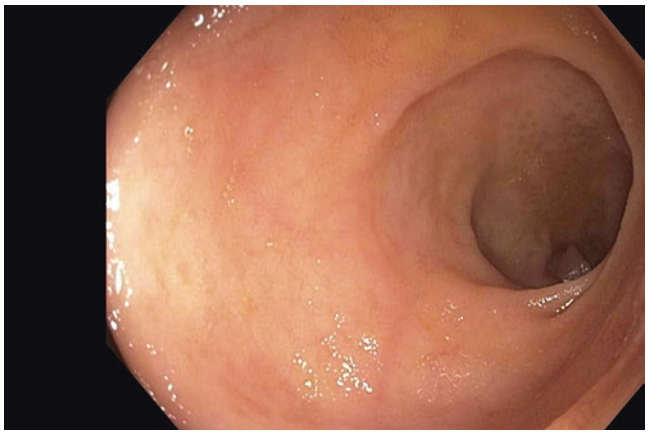

Fig. 2.18 The ileum is intubated. Note the change in appearance of the lining of the intestinal wall. Lymphoid aggregates are appreciated as circular dots in the upper aspect of this image

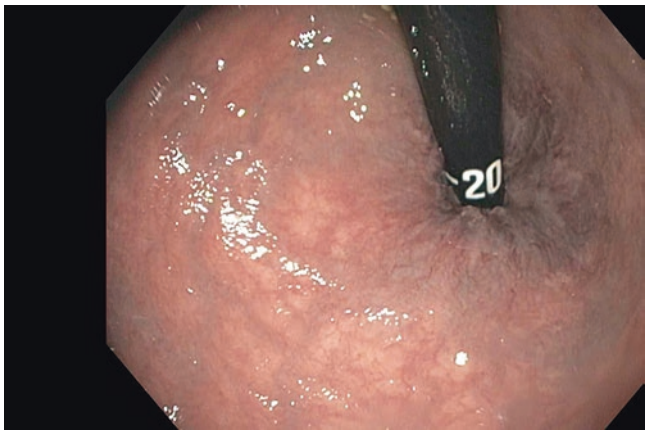

Fig. 2.19 Retroflexed view of the distal rectum and proximal anal canal. The 20-cm marking on the colonoscope is visible. The interface between the pink rectal mucosal line and the white-purplish squamous wall of the anal canal is demarcated by an irregular white dentate line

slowly withdrawn. A "redout" view with subsequent gentle insufflation or water instillation will yield an appropriate view of the terminal ileum villi and occasional hypertrophic lymphoid follicular aggregates (Fig. 2.18). In some cases, this may not be able to be performed due to sharp angulation, stricture or stenosis due to postoperative changes or Crohn's disease, or extraluminal adhesions.

At this point, once successful intubation of the cecum and/or ileum has been performed, a careful withdrawal should be performed. This portion of the procedure should generally take as long as insertion. Insufflation should be judiciously utilized to distend the colon enough so as to be able to attain a good 360° evaluation of the colon for any pathology. In certain cases, back-and-forth motions may be required to look around folds and exclude pathology on the proximal aspects. While going around flexures or bends, it may be similarly necessary to use these to-and-fro motions and also preemptively turn the tip to keep the colon distended and the lumen and walls well visualized. Pathological changes and management of these findings will be discussed later in the text.

Anorectal Canal

Key Landmarks

Retroflexed view of distal rectum, dentate, and proximal anal canal

At the termination of withdrawal during the colonoscopy, a retroflexed view should then be performed and photodocumented. This is typically performed by having the scope inserted about 15–20 cm from the verge, then turning the dial maximally in the "up" position (toward the operator), and then manually torqueing the endoscope to the right (Fig. 2.19). This should allow an appropriate, and with twisting, circumferential 360° view of the very distal anorectal canal. The squamocolumnar junction, known as the dentate line, should be well visualized (Fig. 2.20). Occasionally, it may be helpful to localize the presence of an abnormality (including tumor) with reference to distance proximal or distal to the dentate line. Typical findings may include internal hemorrhoids and in rare occasions very distal rectal carcinomas, condylomatous lesions of the proximal anal canal, squamous cell carcinomas, and fistulous openings. The dentate line will be visualized, separating the typical pink appearance of the epithelial mucosa of the rectum from the purplish hue of the squamous cell anal canal and vascularized hemorrhoid tissue.

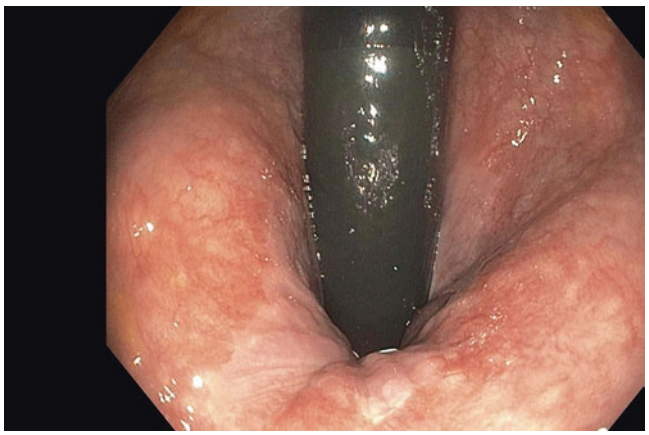

Fig. 2.20 A close-up view of the dentate line. The bulge noted to the left may be a result of the rectum being insufflated and distended from the abdominal side over the puborectalis and sphincter complex. The irregular white dentate line is also visible circumferentially

Pearls and Pitfalls

Appreciation of anatomy and its variations is integral in achieving maximal benefit while performing diagnostic and therapeutic colonoscopy. Careful technique with a structured protocol

to intubate the colon and rectum and also prevent and reduce looping is critical to being able to perform successful and iterative diagnostic procedures and therapeutic interventions. A mastery of instrumentation and insertion and withdrawal techniques, with emphasis on torqueing, allows for enhanced progression with minimal discomfort of the patient. Pain experienced by the patient, paradoxical movement, or loss of 1:1 progression during scope advancement are clues that significant looping has occurred, and reduction of the colonoscope is required. Most loops can be reduced with simultaneous gentle withdrawal and clockwise torqueing action. Maintenance of tip angulation is helpful to prevent disorientation.

Appreciating the key anatomic landmarks with photodocumentation is helpful in both achieving complete colonoscopy and performing therapeutic interventions. Keeping the lumen centered during intubation is critical in avoiding injury and/or perforation of the colon. Water instillation rather than carbon dioxide may be helpful in navigating through the sigmoid and left colon by its gravitational actions. Using internal luminal findings and mural appearance of folds will help keep the operator targeted on the center of the colon. Classic findings to help the endoscopist include the three rectal folds, occasional tortuosity of the sigmoid colon with frequent N- or alpha-looping, the circular/tubular appearance of the descending colon, the triangular appearance of the lumen of the transverse colon caused by the thickened muscular teniae coli, the bulbous and the cavernous cecum with the appendiceal orifice, and ileocecal valve (both of the latter requiring photodocumentation). Occasionally, the hepatic flexure or mid-ascending colon may be confused for the cecum. Without appropriate verification of the above two landmarks, it should be presumed that further advancement is required to successfully intubate the cecum.

Documenting atypical findings with combinations of distance from the anal verge and also anatomic landmarks is helpful for future endoscopic and surgical planning. Tattooing lesions on the distal/anal side in a circumferential pattern may be helpful for the surgeon during future interventions.

Conclusion

Colonoscopy is a very practical tool in the management and welfare of patients. A fundamental appreciation of the anatomic landmarks, variations encountered during advancement, and reduction of looping can yield a successful, pain-free colonoscopy for the surgeon and patient alike.

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Colonoscopy Photo Atlas

3

Daniel L. Feingold

Clinicians rely on colonoscopy as an invaluable diagnostic and therapeutic tool. While video colonoscopy delivers high-definition dynamic streaming imaging of the colorectal mucosa photo documentation is an integral part of present-day colonoscopy and facilitates patient care and operative planning. Reviewing colonoscopic images can confirm tumor localization and helps determine the feasibility of endo-luminal therapy and allows the surgeon to better understand pathology. It is helpful to review still colonoscopy images like those included here as the ability to diagnose pathology and synthesize information from performing endoscopy, and reviewing patients' endoscopic photographs heavily relies on pattern recognition. This atlas by no means comprehensive offers examples of colorectal anatomy and pathology. For illustrative purposes the following images are representative photographs of relevant normal anatomy (Figs. 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 3.10, and 3.11), pathology (Figs. 3.12, 3.13, 3.14, 3.15, 3.16, 3.17, 3.18, 3.19, 3.20, 3.21, 3.22, 3.23, 3.24, 3.25, 3.26, 3.27, 3.28, 3.29, 3.30, 3.31, 3.32, 3.33, 3.34, 3.35, 3.36, 3.37, 3.38, 3.39, 3.40, 3.41, and 3.42), and postoperative anatomy (Figs. 3.43, 3.44, 3.45, 3.46, 3.47, 3.48, 3.49, 3.50, 3.51, 3.52, 3.53, 3.54, 3.55, 3.56, 3.57, 3.58, and 3.59). All photos are courtesy of Daniel L. Feingold M.D. unless otherwise noted.

Normal Anatomy

Figures 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 3.10, and 3.11

Pathology

Figures 3.12, 3.13, 3.14, 3.15, 3.16, 3.17, 3.18, 3.19, 3.20, 3.21, 3.22, 3.23, 3.24, 3.25, 3.26, 3.27, 3.28, 3.29, 3.30, 3.31, 3.32, 3.33, 3.34, 3.35, 3.36, 3.37, 3.38, 3.39, 3.40, 3.41, and 3.42

Postoperative Anatomy

Figures 3.43, 3.44, 3.45, 3.46, 3.47, 3.48, 3.49, 3.50, 3.51, 3.52, 3.53, 3.54, 3.55, 3.56, 3.57, 3.58, and 3.59

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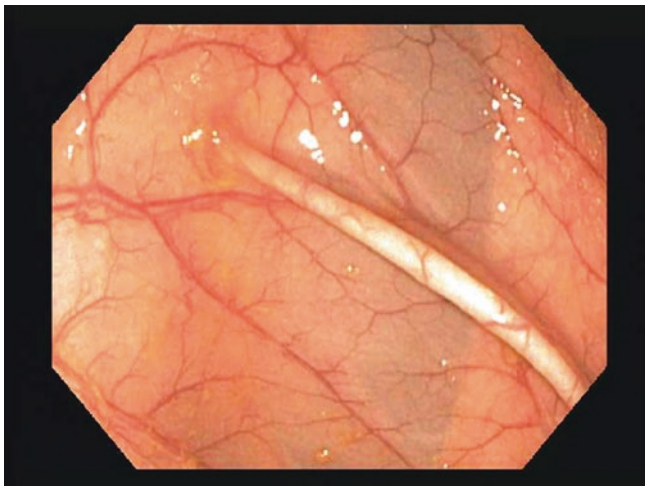

Fig. 3.1 Endoscopic appearance of the splenic flexure. Note the shadow of the spleen

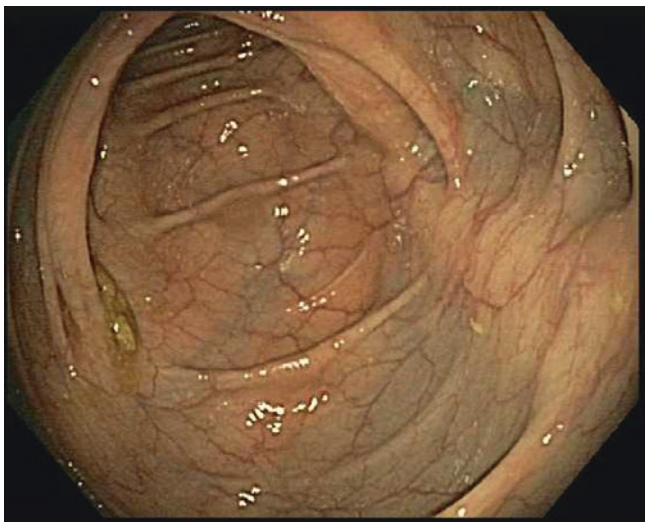

Fig. 3.3 The hepatic flexure colon. Note the typical blueish shadow of the liver

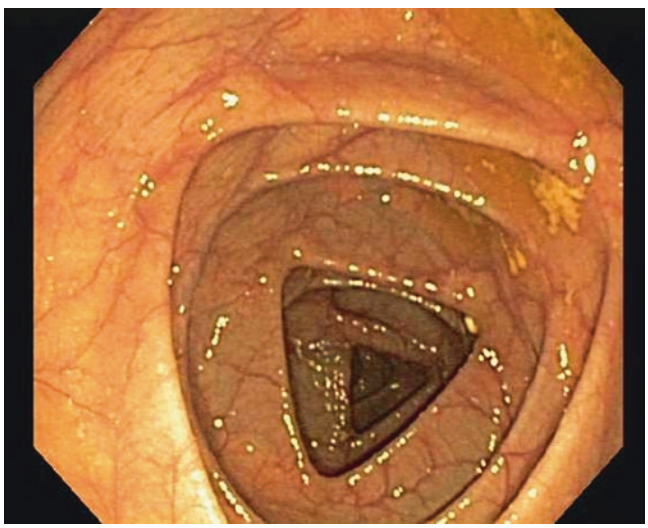

Fig. 3.2 Typical triangular appearance of the transverse colon as seen during colonoscope insertion

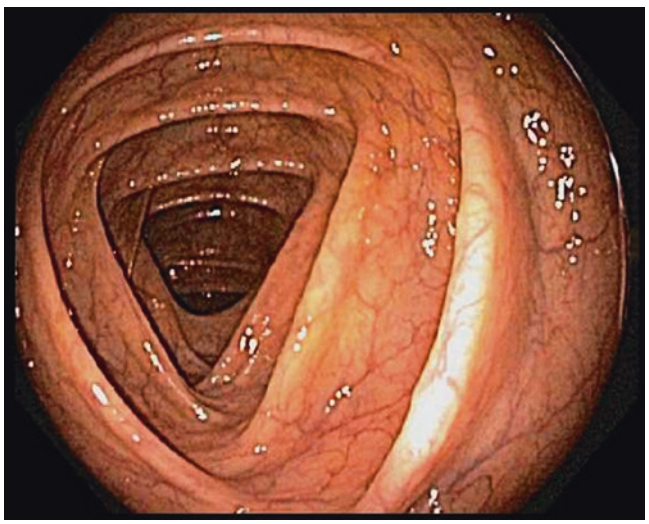

Fig. 3.4 Looking down the ascending colon with the ileocecal valve in the distance

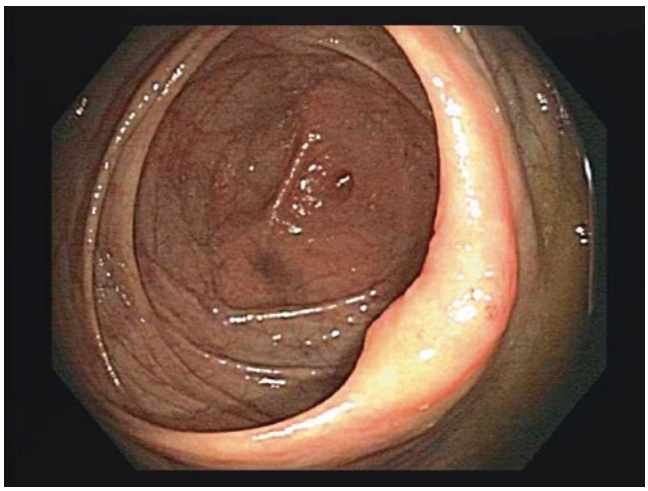

Fig. 3.5 Appearance of the ileocecal valve with the caput of the cecum beyond

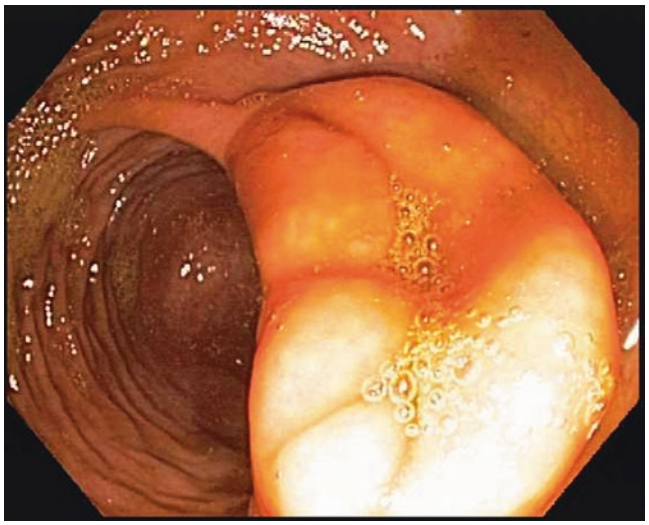

Fig. 3.7 Appearance of the ileocecal valve en face with bubbling bile coming up through the valve

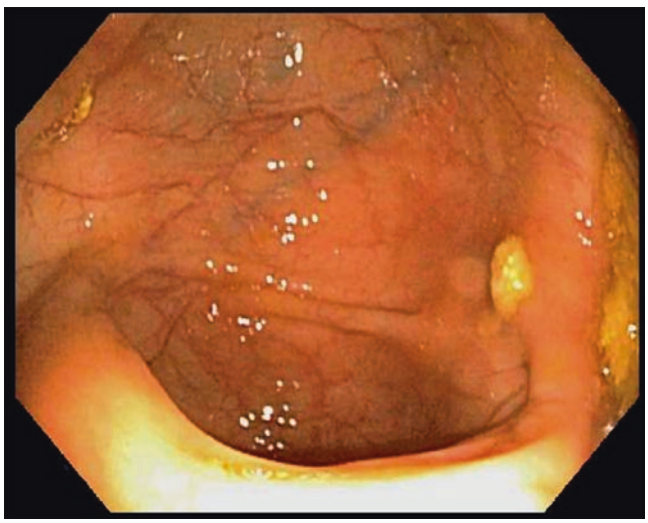

Fig. 3.6 Appearance of a "fool's cecum." The colonoscopist should be wary of relying only on pattern recognition of a thickened mucosal fold as evidence of reaching the ileocecal valve as a bend near the hepatic flexure colon can mimic the appearance of the valve

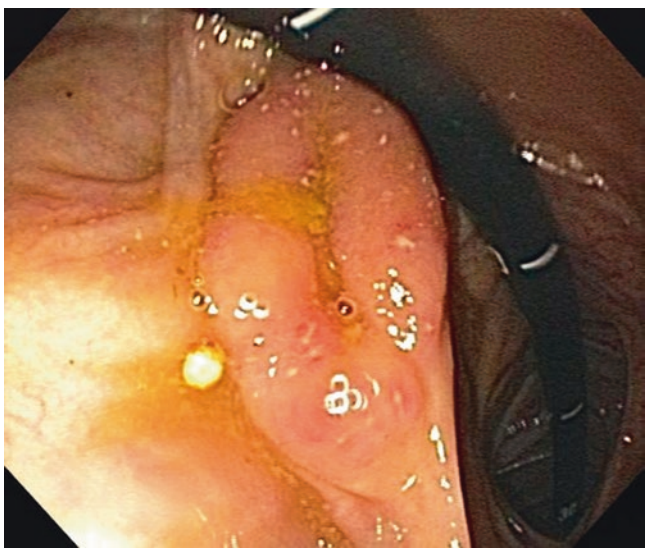

Fig. 3.8 Retroflexion in the cecum visualizing the ileocecal valve

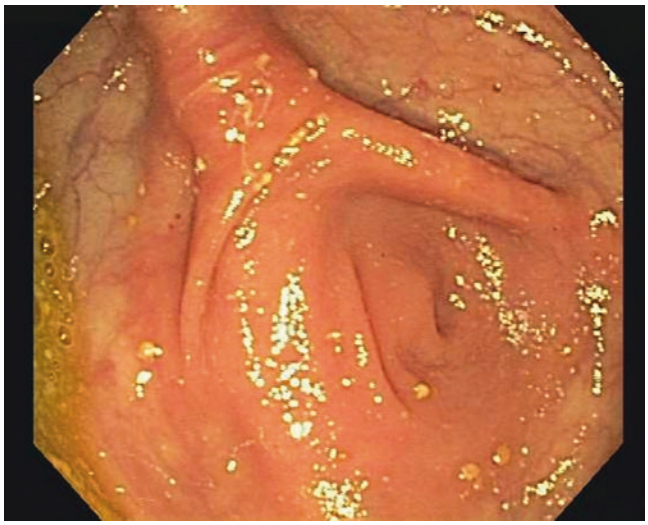

Fig. 3.9 The cecal strap is the endo-luminal appearance of the confluence of the tenia in the caput of the cecum. Note the appearance and location of the appendiceal orifice

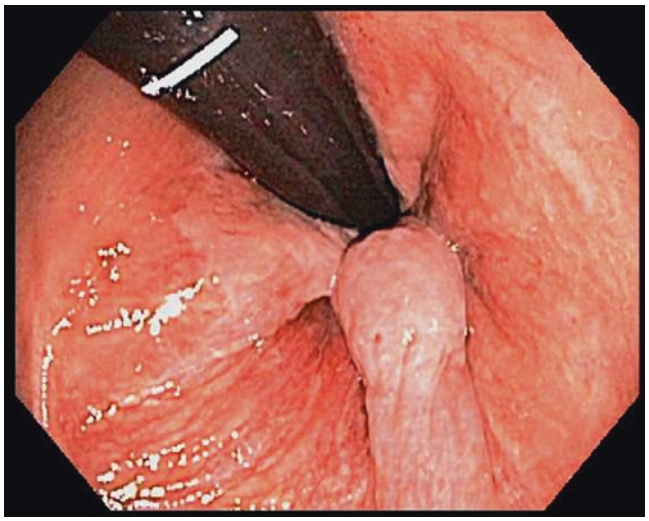

Fig. 3.11 Retroflexion in the rectum observing internal hemorrhoids

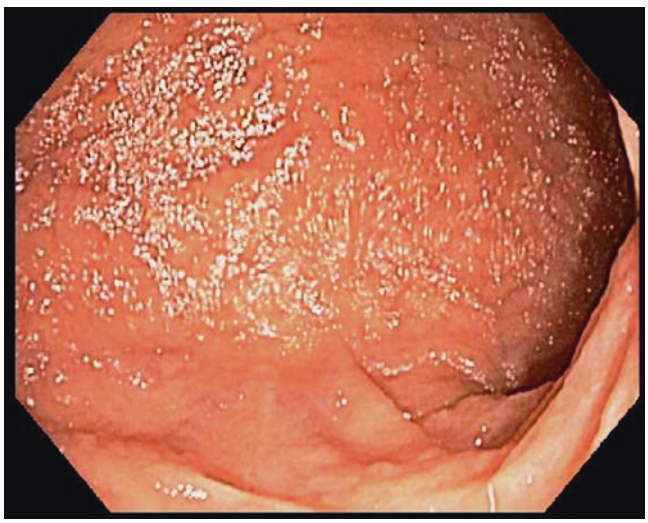

Fig. 3.10 Typical appearance of healthy terminal ileum mucosa. Note the granular, fine, villous appearance of the mucosa

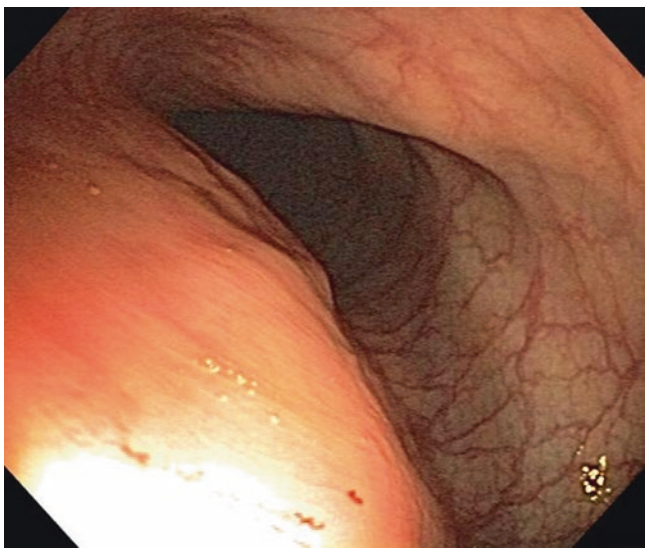

Fig. 3.12 Extrinsic compression of the rectosigmoid by a large uterine mass

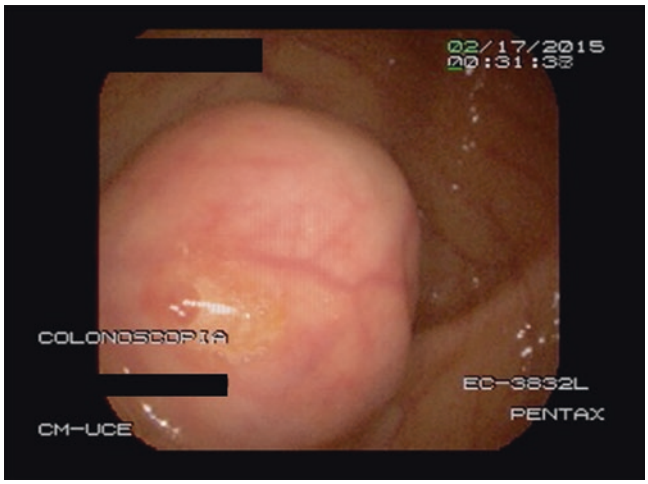

Fig. 3.13 Appendiceal mucocele with bulging of the area of the appendix. Note the slit of the appendiceal orifice

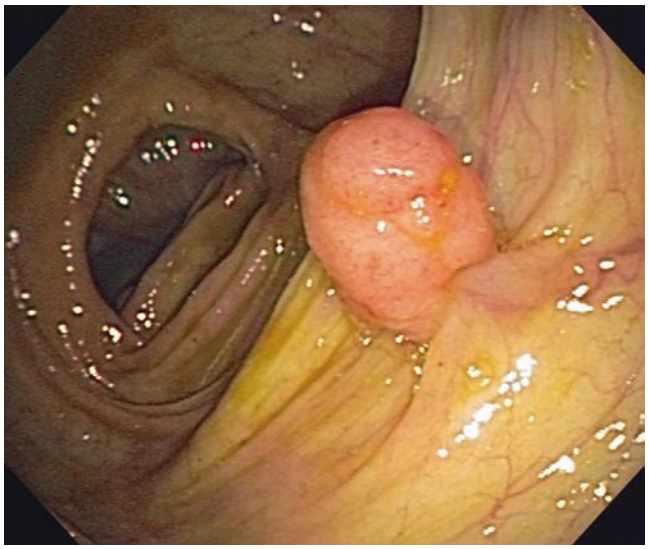

Fig. 3.15 Pedunculated polyp in the ascending colon. For localization purposes, note the ileocecal valve in the distance

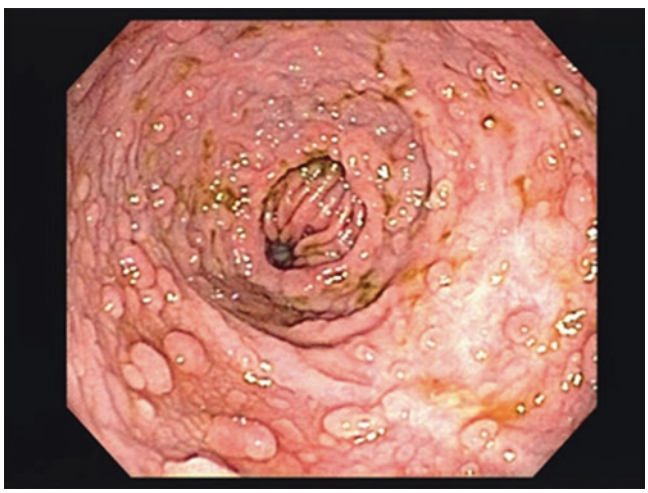

Fig. 3.14 The typical appearance of a patient with familial adenomatous polyposis with innumerable polyps

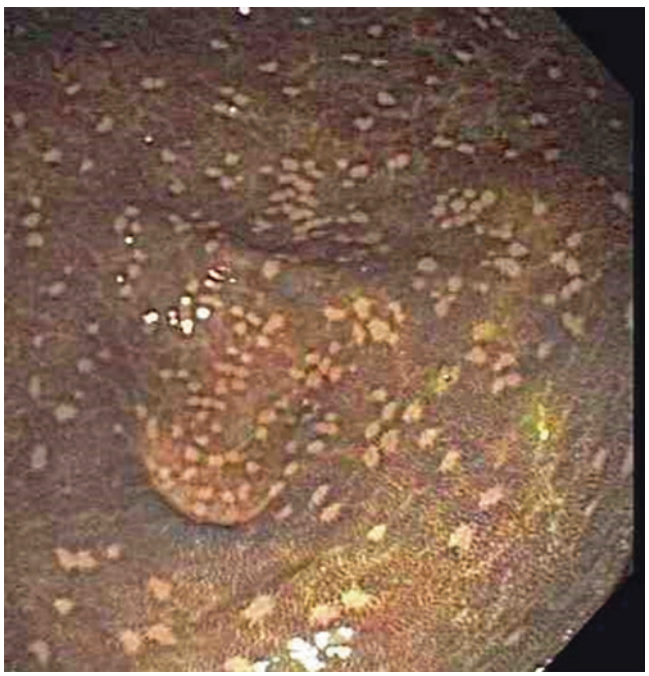

Fig. 3.16 Melanosis of the colon. The pigmentation manifests as a variety of dark colored mucosal patterns

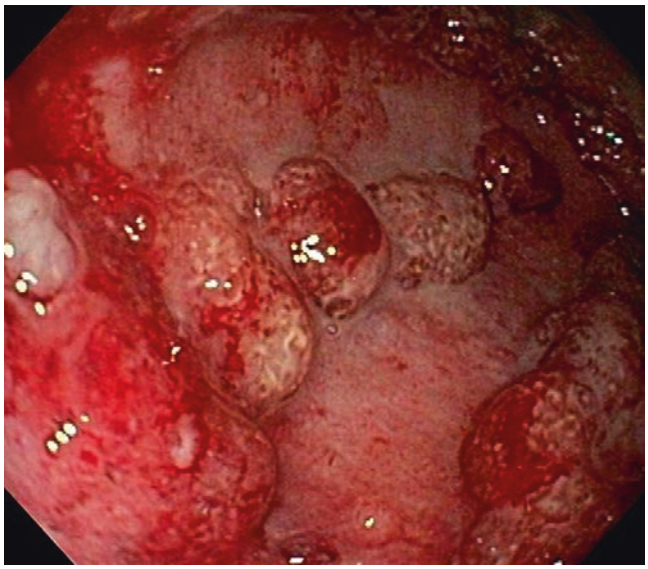

Fig. 3.17 Severe chronic inflammatory bowel disease with "bear claws" in areas of mucosal inflammation

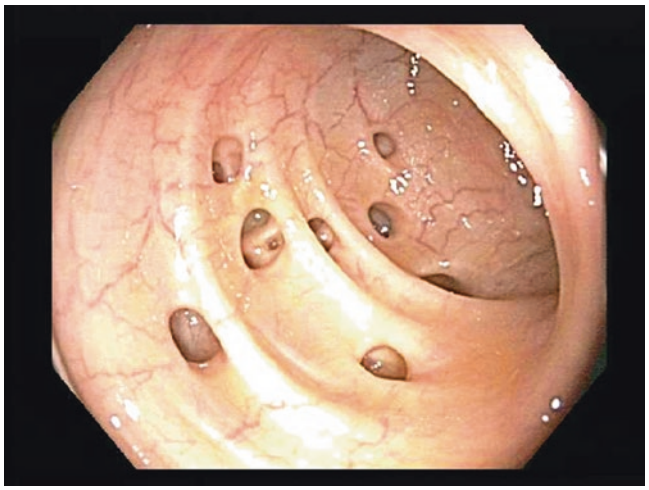

Fig. 3.19 Typical appearance of sigmoid colon diverticulosis

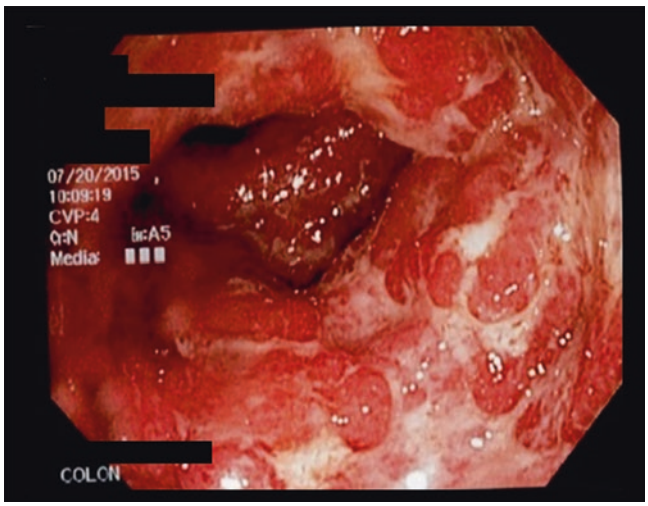

Fig. 3.18 Ulcerative colitis. Photo courtesy of David E. Rivadeneira, M.D.

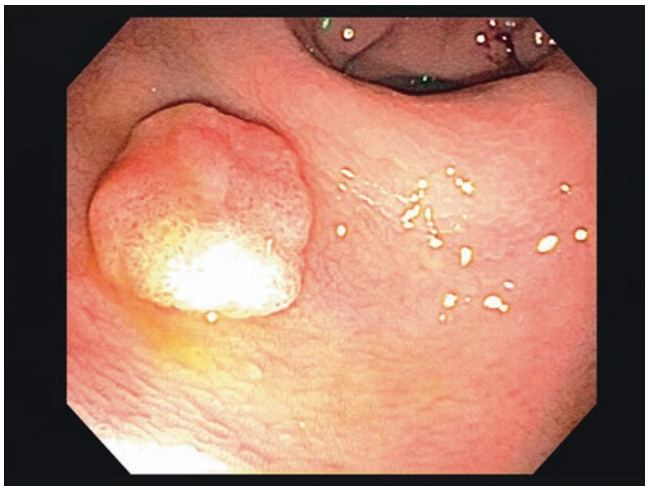

Fig. 3.20 Small sessile polyp

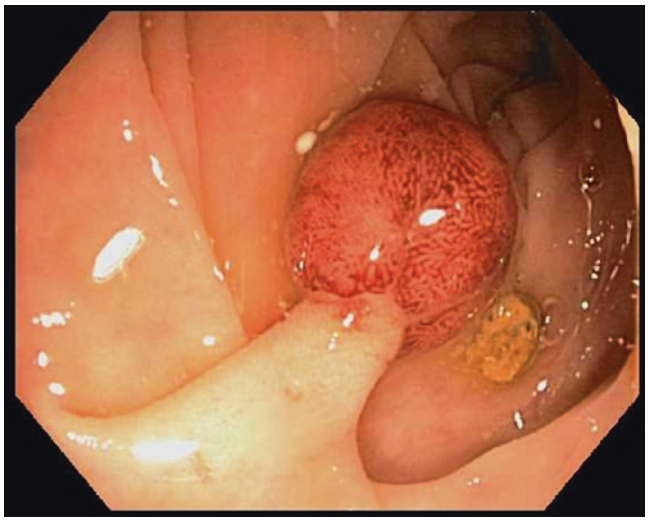

Fig. 3.21 Small pedunculated polyp

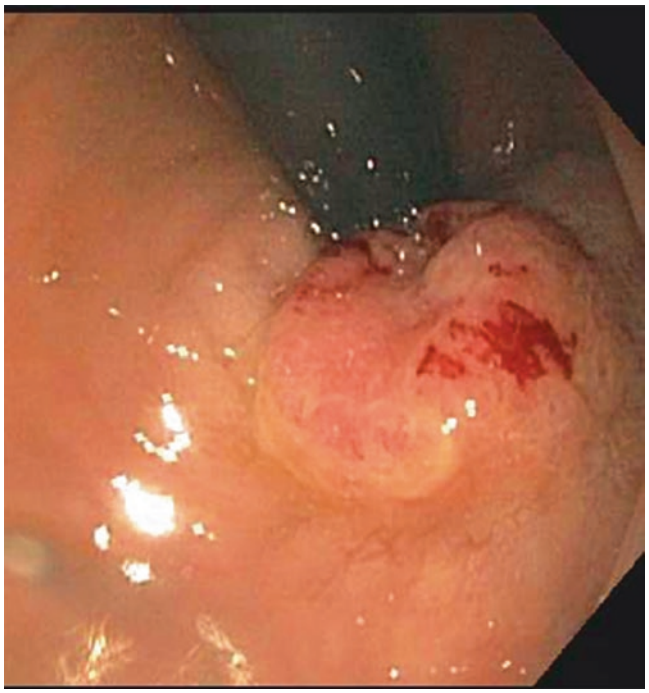

Fig. 3.23 Retroflexion in the rectum reveals a small neoplasm

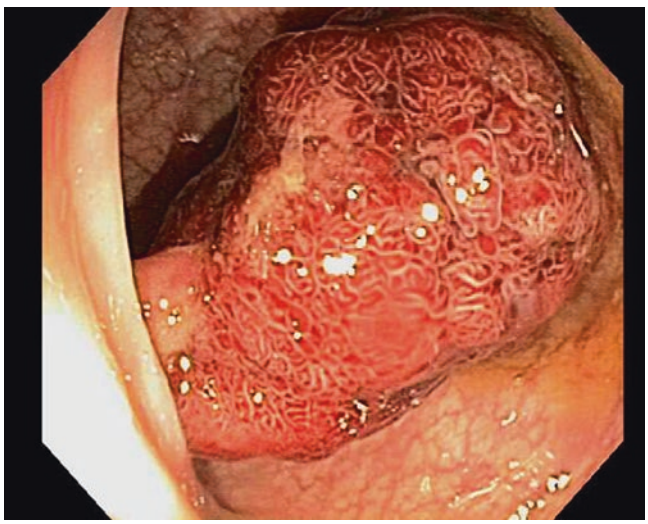

Fig. 3.22 Large pedunculated polyp

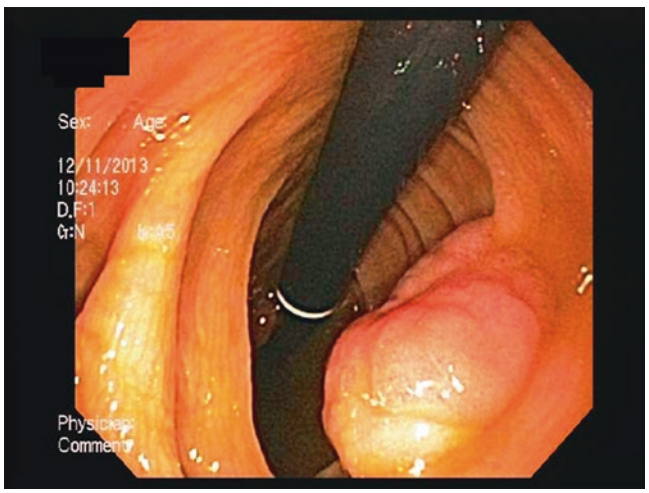

Fig. 3.24 Retroflexion in the right colon reveals the proximal extent of a tumor laying over a fold

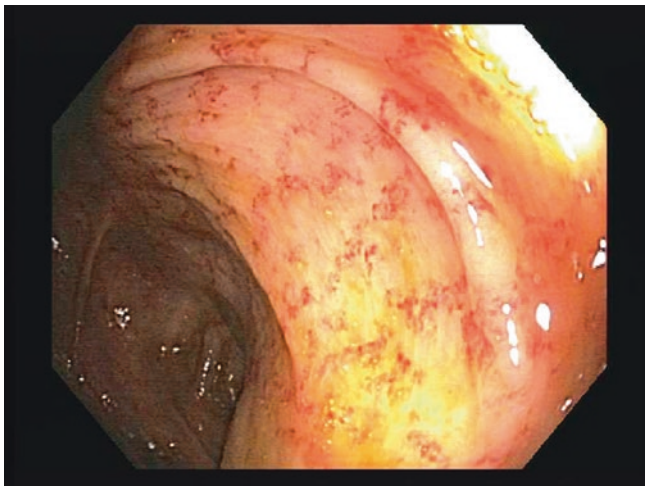

Fig. 3.25 Arteriovenous malformations (AVMs) are seen as flat, distinct, bright red mucosal vessels

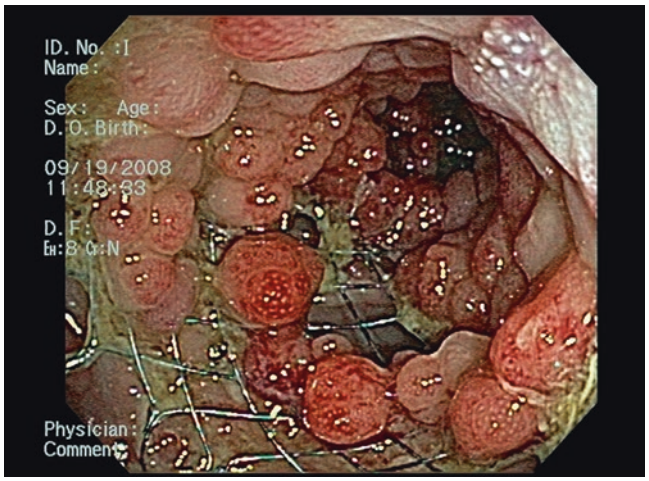

Fig. 3.27 Rectal cancer growing through the interstices of an endoluminal stent

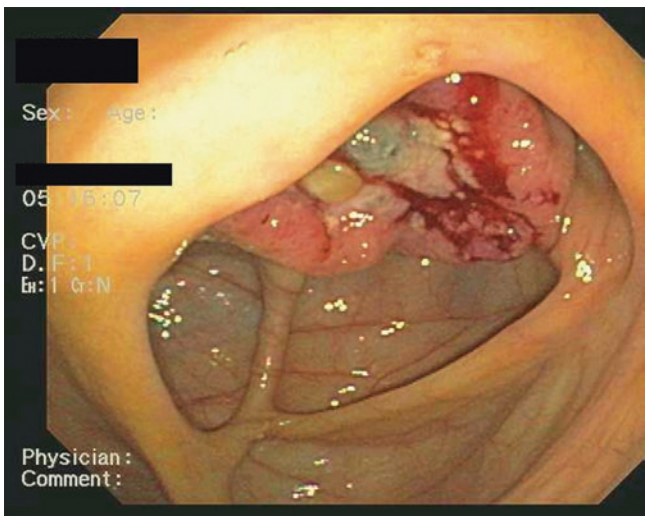

Fig. 3.26 Cecal neoplasm with preoperative localization confirmed by the presence of the ileocecal valve

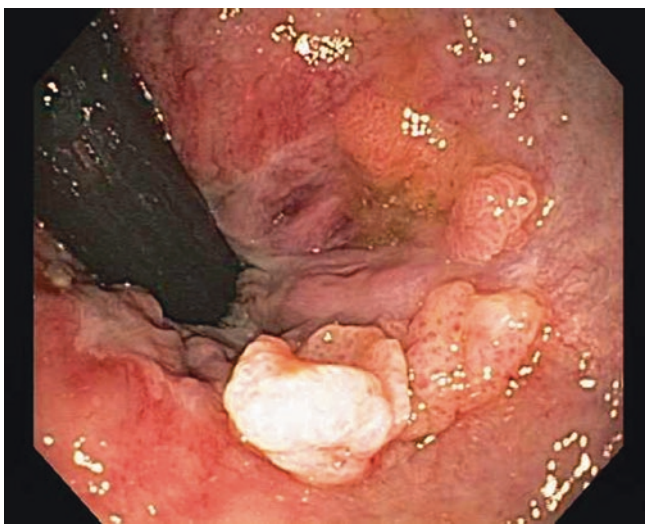

Fig. 3.28 Retroflexion revealing anal warts

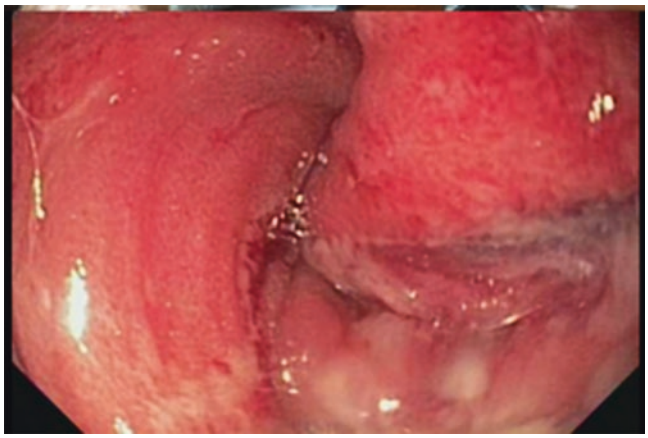

Fig. 3.29 Spiraled view of a sigmoid volvulus before endoscopic reduction. Photo courtesy of Scott R. Steele, M.D.

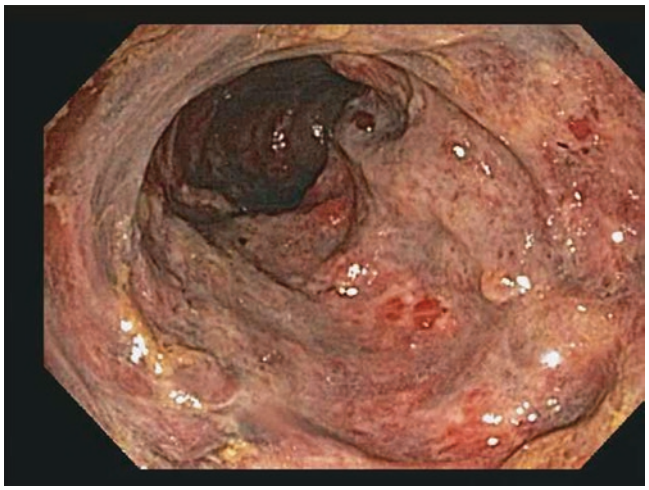

Fig. 3.31 Severe ischemic colitis with sloughing, nonviable mucosa. Photo courtesy of Anjali S. Kumar, M.D.

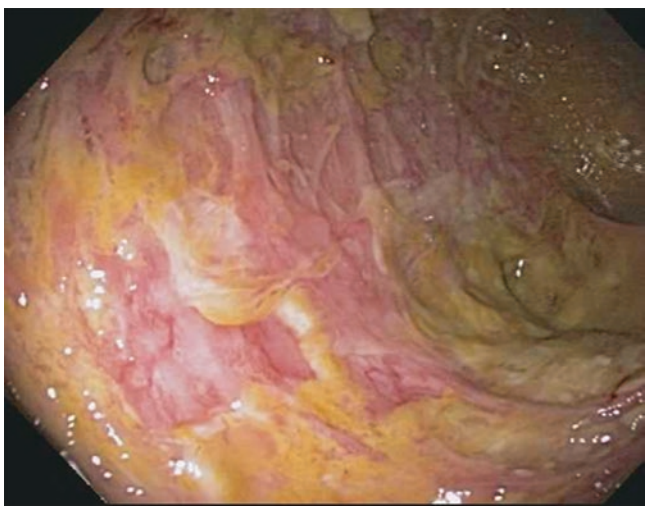

Fig. 3.30 Clostridium difficile colitis with typical grayish yellow pseudomembranes. Photo courtesy of Anjali S. Kumar, M.D.

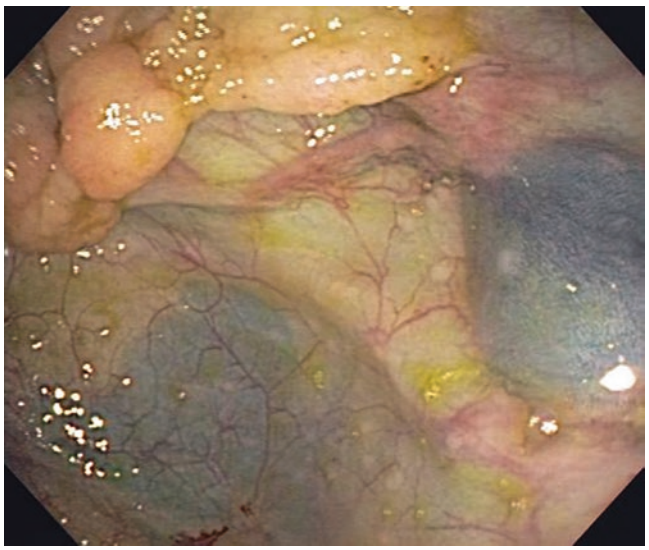

Fig. 3.32 Example of mucosal tattooing just distal to a colon neoplasm. To increase the likelihood of successful intraoperative localization, it is recommended to tattoo in three quadrants

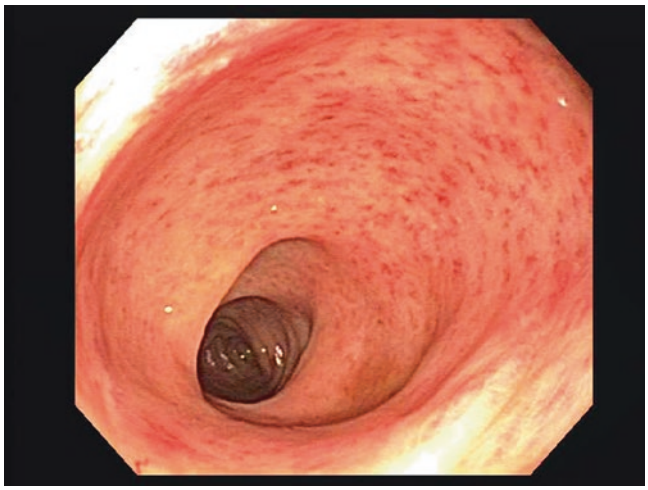

Fig. 3.33 Mild radiation proctitis

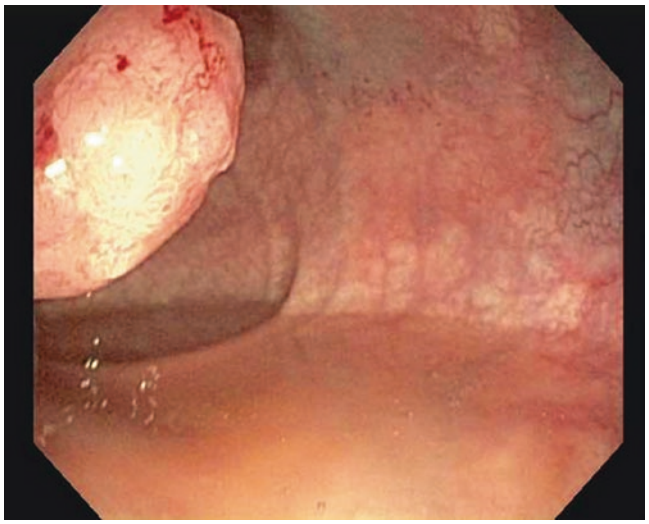

Fig. 3.35 Rectal cancer. With the patient in left lateral decubitus position, the water level demonstrates the left lateral side of the rectum and localizes this cancer to the posterior midline

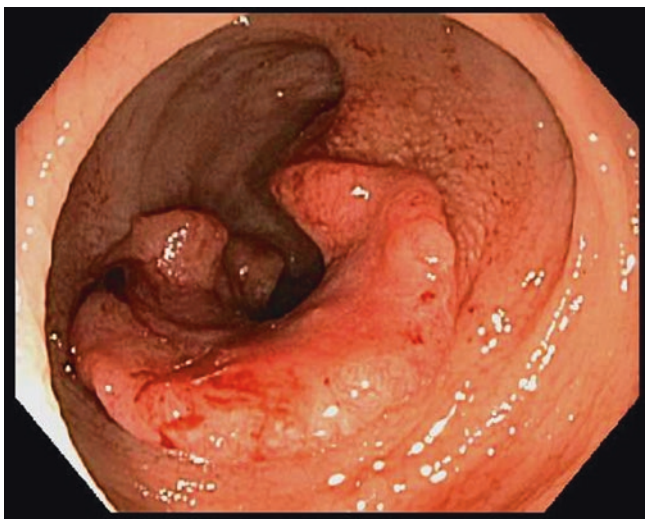

Fig. 3.34 Rectal cancer

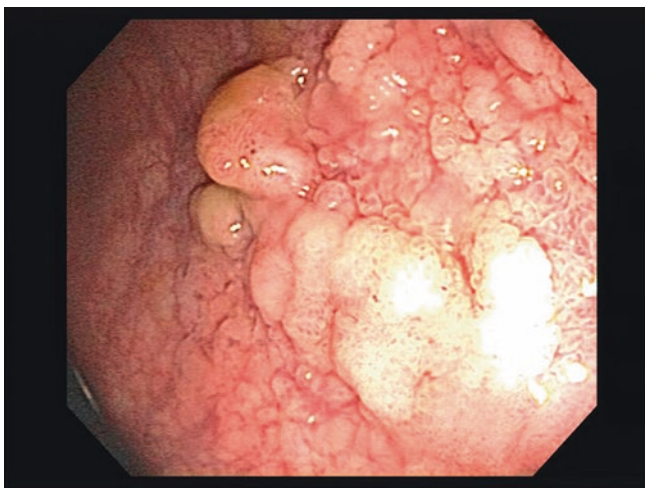

Fig. 3.36 Carpeting of a colon polyp with non-discrete borders between adenomatous and normal mucosa

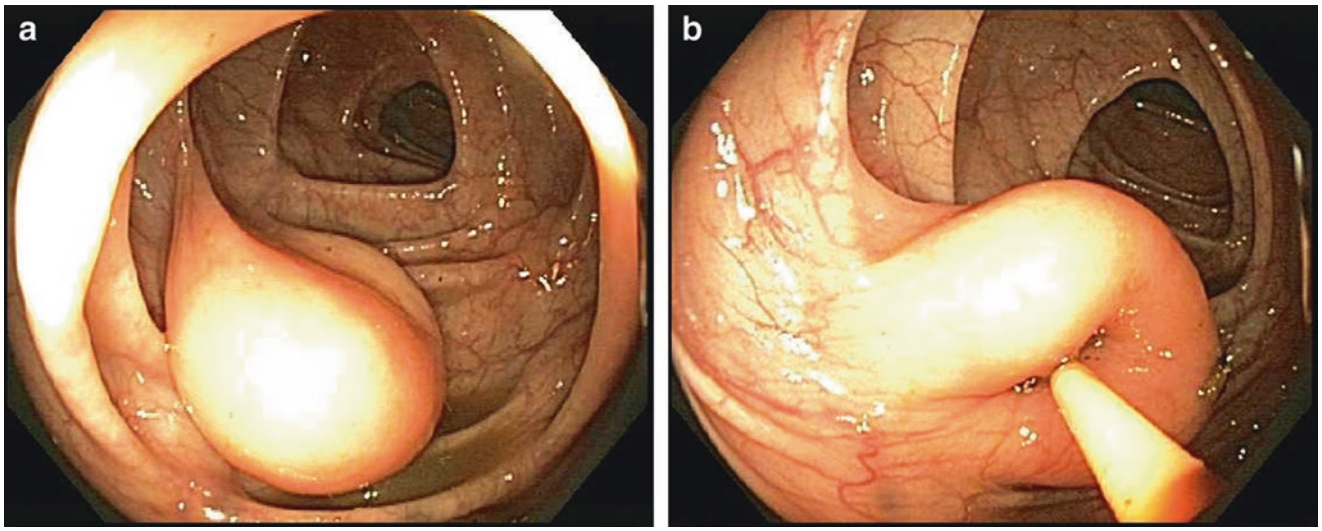

Fig. 3.37 (**a**) Large colon lipoma. (**b**) "Pillow test" of a colon lipoma helps differentiate this submucosal lesion from a carcinoid

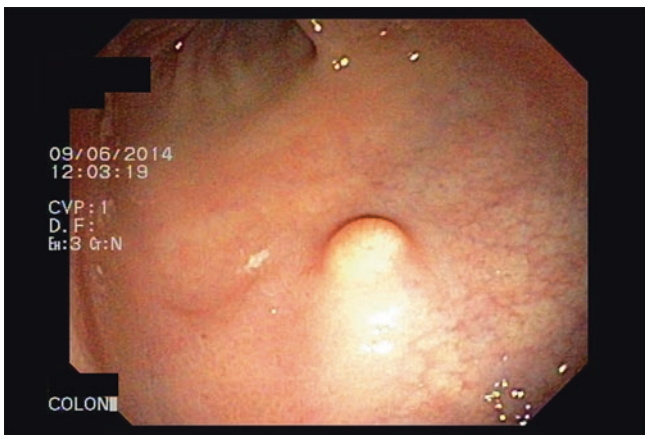

Fig. 3.38 Rectal carcinoid. Note the intact overlying mucosa with the yellowish hue. Photo courtesy of David E. Rivadeneira, M.D.

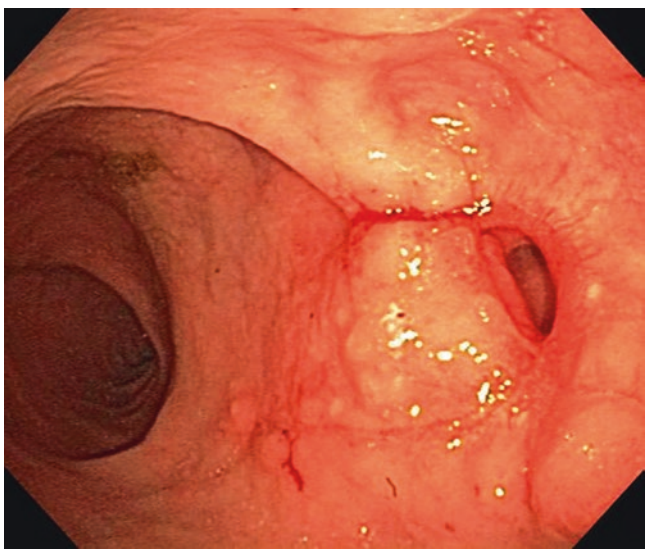

Fig. 3.39 A rectourethral fistula

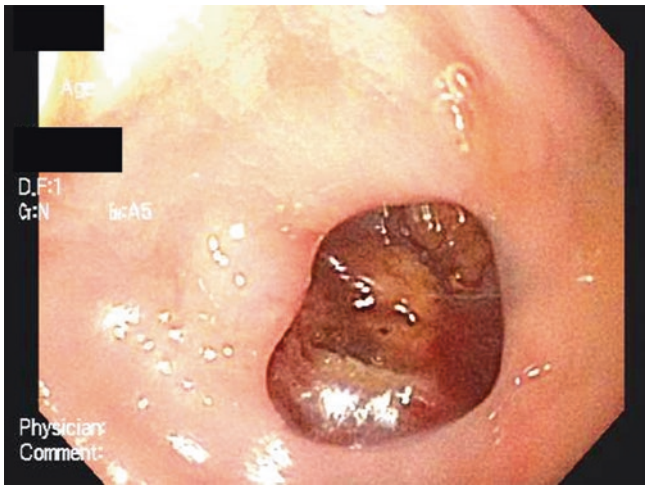

Fig. 3.40 Colonoscopic perforation with mesenteric fat behind the perforated diverticulum

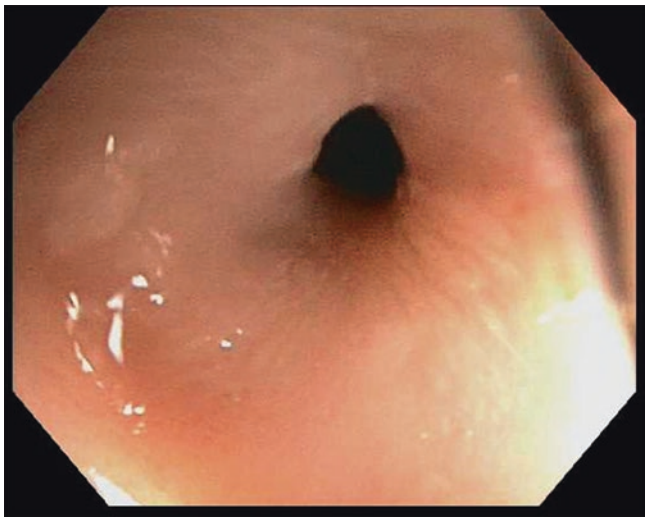

Fig. 3.42 Vaginoscopy in a woman status post hysterectomy demonstrating a colovaginal fistula at the apex of the vaginal cuff from diverticulitis

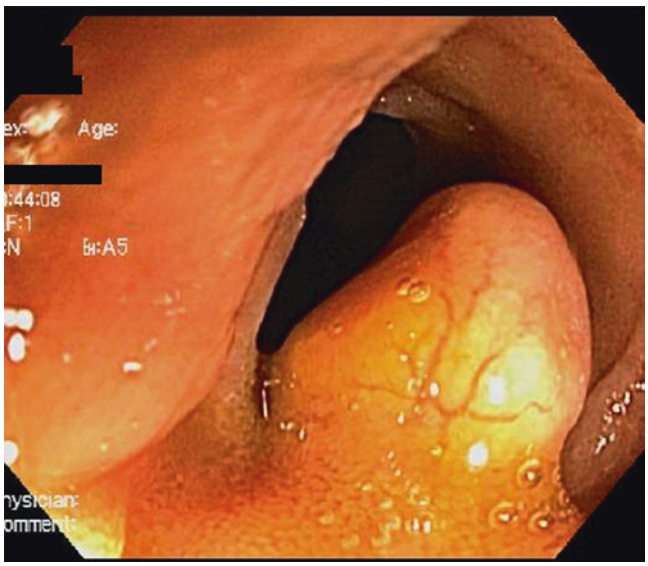

Fig. 3.41 Ileal carcinoid found incidentally on screening colonoscopy. Note the submucosal mass with intact overlying mucosa

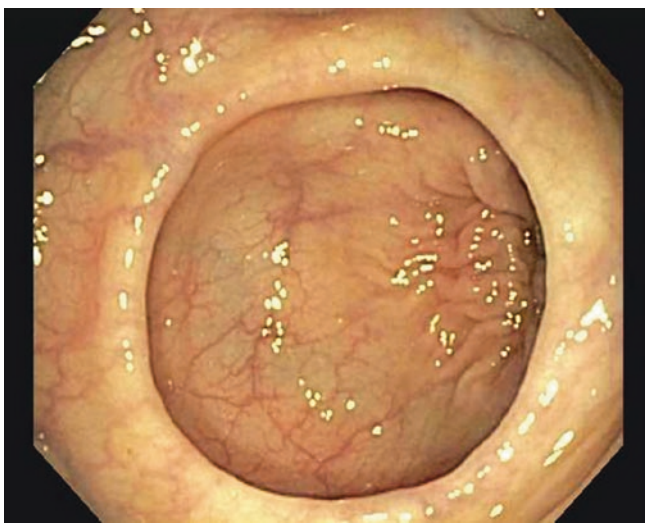

Fig. 3.43 Healed hand-sewn end-to-end colo-colonic anastomosis

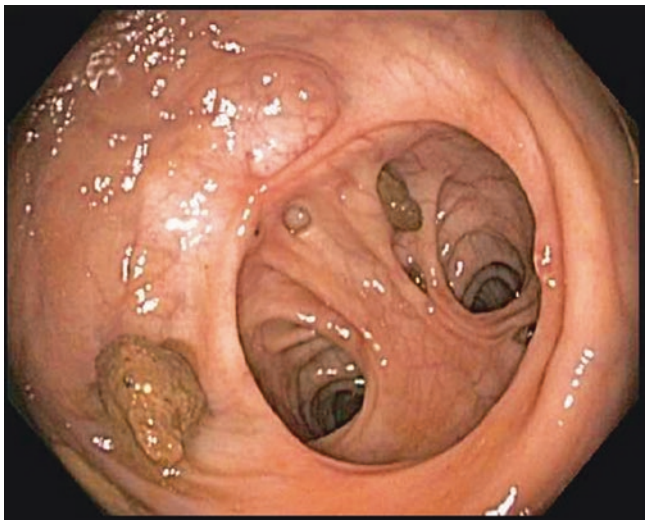

Fig. 3.44 An example of a colorectal "Baker" anastomosis. Note the side-to-end configuration of the anastomosis with one lumen leading to the proximal colon and the other leading to the stapled off end of the colon

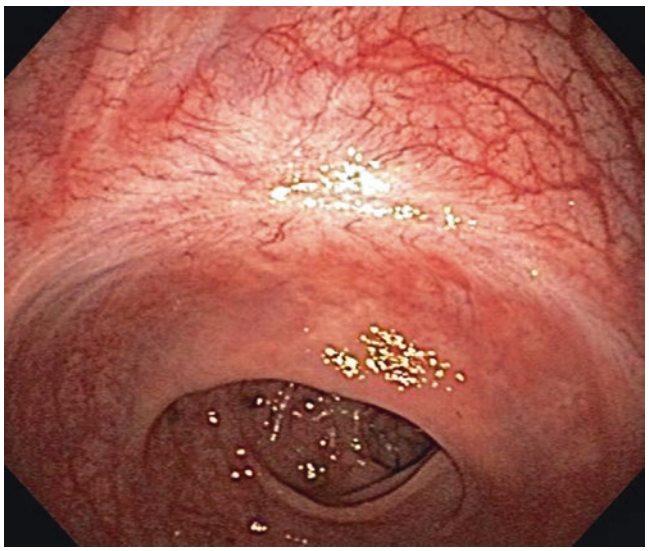

Fig. 3.47 Scar observed on surveillance colonoscopy after conventional trans-anal excision of a rectal tumor

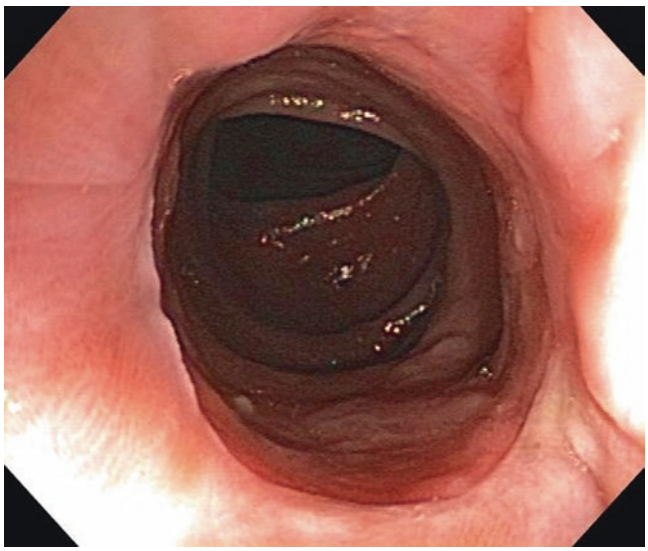

Fig. 3.45 View of a stapled colo-anal anastomosis looking up from the anal canal

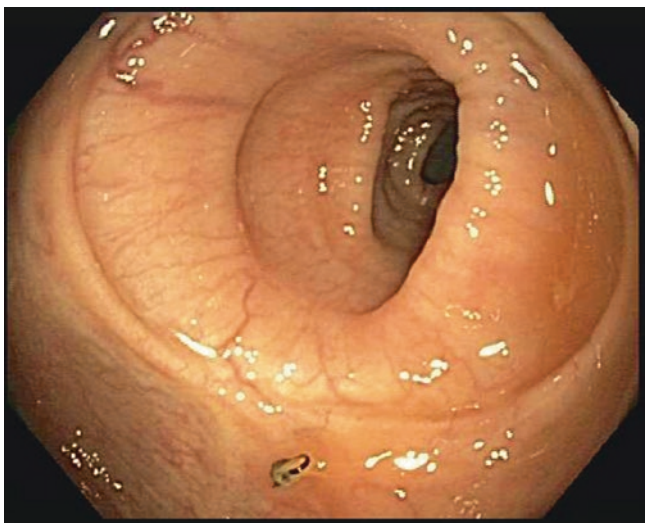

Fig. 3.48 A healed, stapled end-to-end anastomosis. Note the presence of retained staples

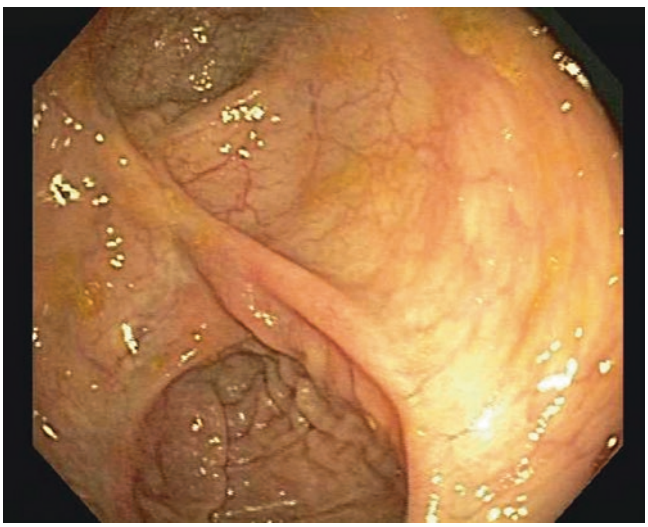

Fig. 3.46 Typical appearance of a side-to-side ileocolic anastomosis

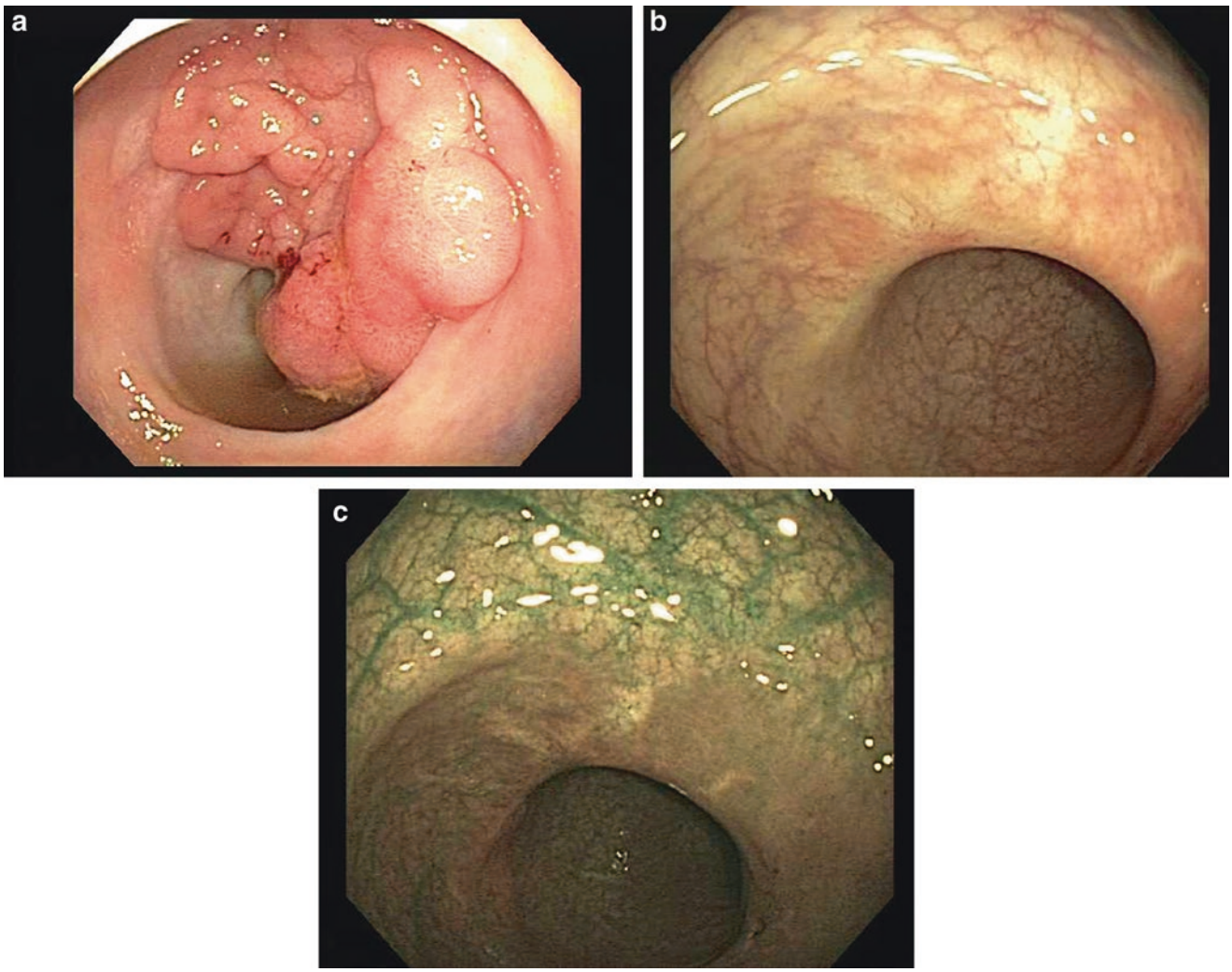

Fig. 3.49 (**a**) Large villous adenoma in the mid-rectum before TEMS excision. (**b**) Appearance of the post-TEMS excision scar observed on surveillance colonoscopy using white light endoscopy. (**c**) Appearance of the post-TEMS scar visualized with narrow band imaging (NBI)

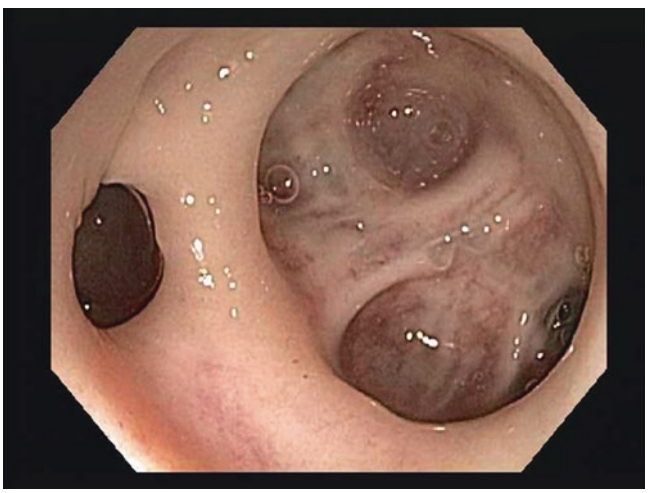

Fig. 3.50 The rectal cuff after a Hartmann procedure for complicated diverticulitis. Note the staples at the end of the cuff and the retained colon diverticulum. This patient required completion colectomy at the time of Hartmann reversal

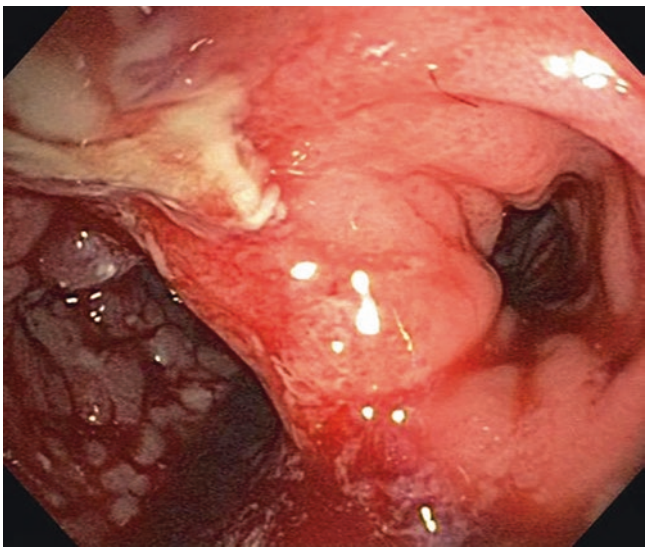

Fig. 3.51 A disrupted colo-anal anastomosis

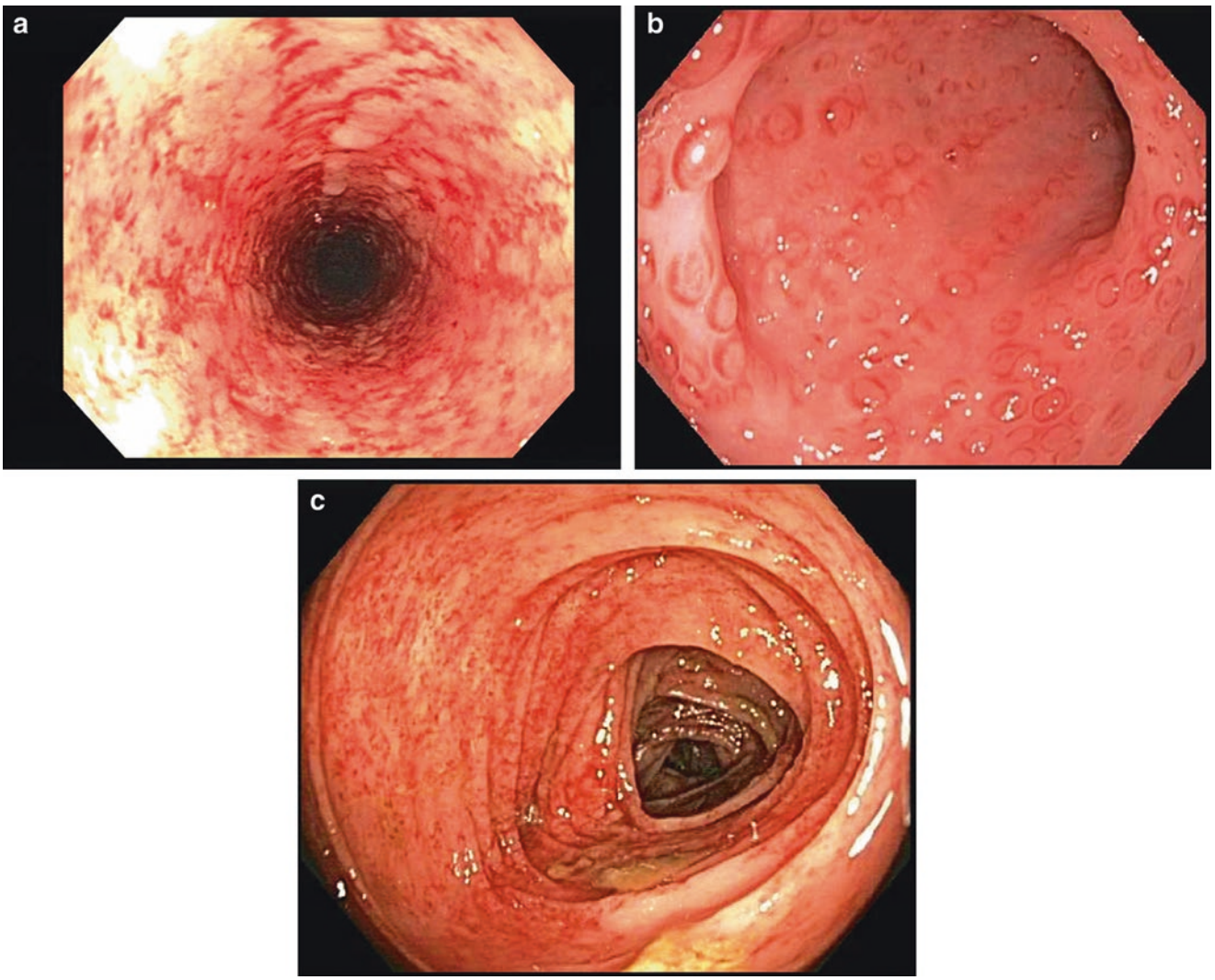

Fig. 3.52 (**a**) Diversion ("disuse") changes in the colon can present with a variety of appearances. (**b**) Diversion changes in the colon. (**c**) Diversion changes in the colon

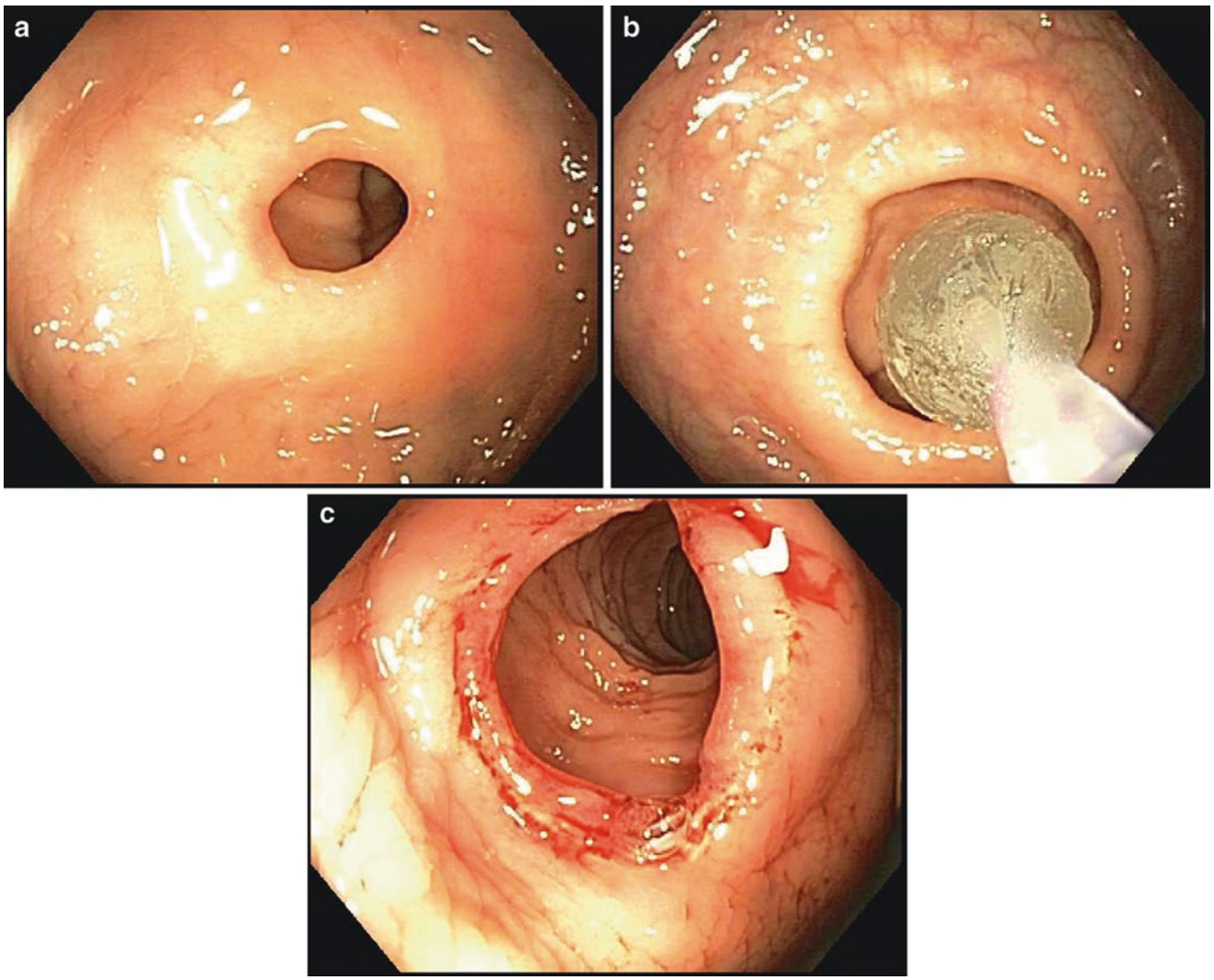

Fig. 3.53 (**a**) Strictured colorectal EEA anastomosis. (**b**) Through-the-scope (TTS) balloon dilation of the stricture. (**c**) Post-dilation anatomy

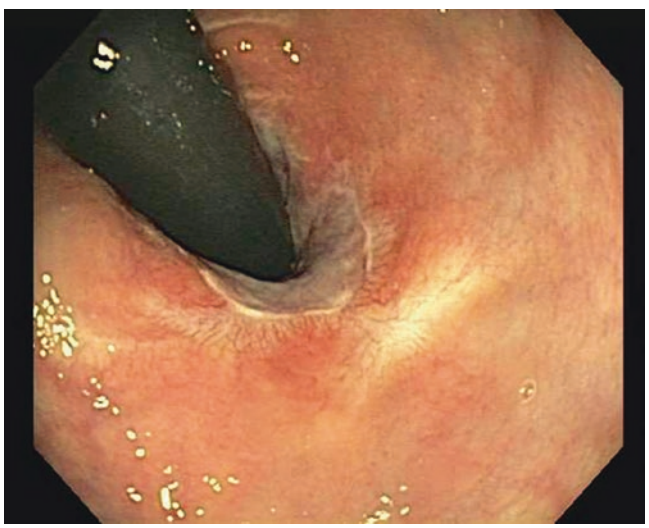

Fig. 3.54 Retroflexion reveals the scar from a conventional hemorrhoidectomy

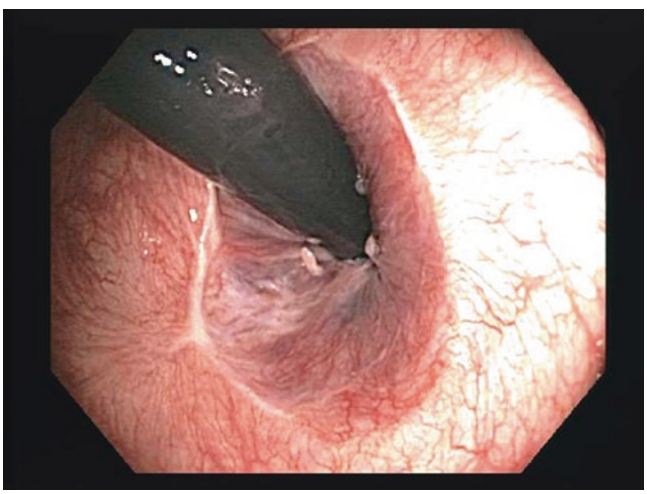

Fig. 3.55 Retroflexion reveals the scar from a stapled hemorrhoidectomy

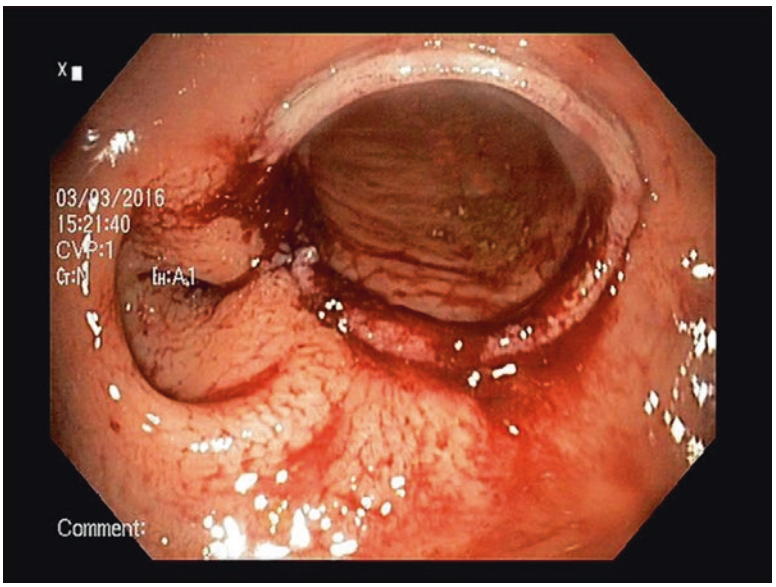

Fig. 3.56 Intraoperative CO_2 colonoscopy demonstrating a fresh end-to-end colorectal anastomosis while performing a leak test with the pelvis under saline. Appreciate the remaining portion of the TA staple line and the well-perfused colon coming down to the anastomosis. Photo courtesy of Steven A. Lee-Kong, M.D.

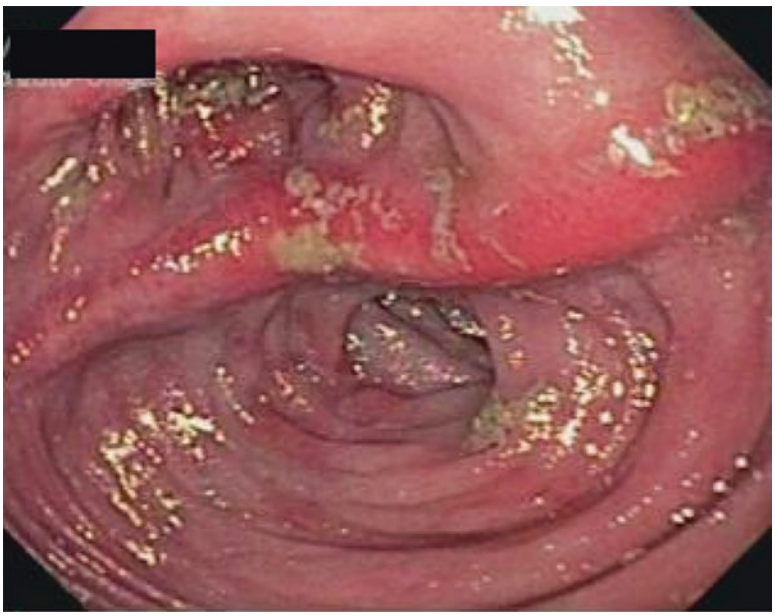

Fig. 3.57 Looking up at the apex of a healthy pouch from the ileal pouch anal anastomosis. Photo courtesy of Scott R. Steele, M.D.

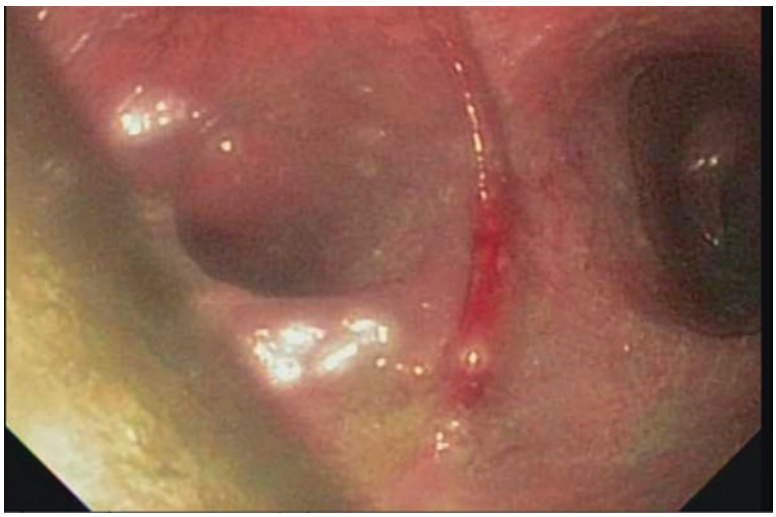

Fig. 3.58 Pouchitis with inflammation and liquid contents in the pouch. Photo courtesy of Scott R. Steele, M.D.

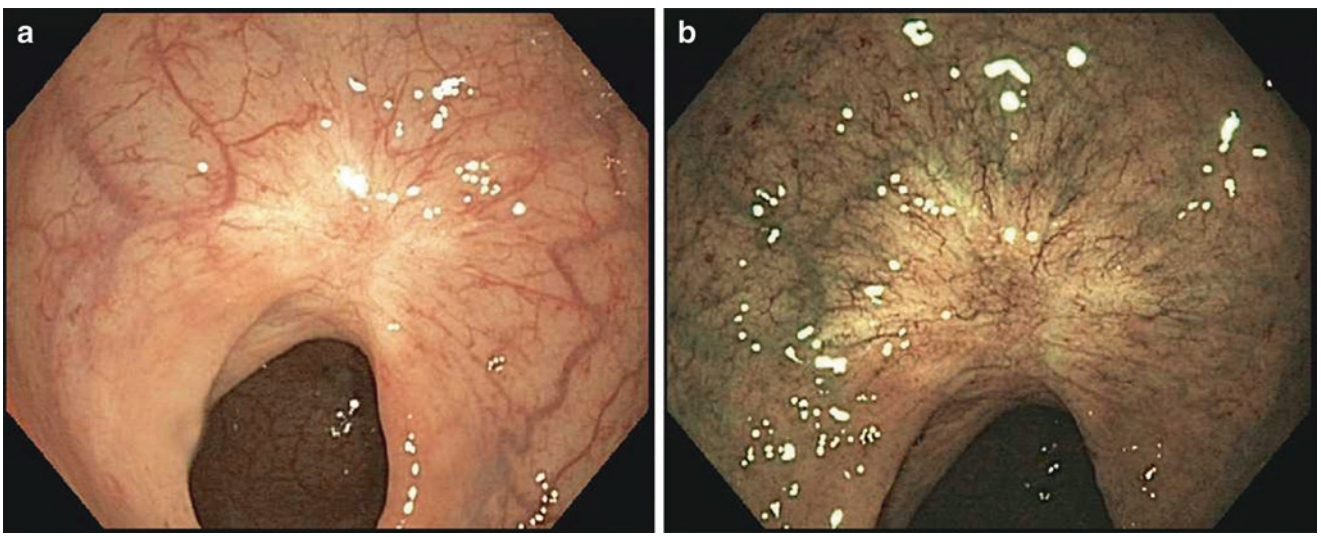

Fig. 3.59 (**a**) White light observing the site of a rectal cancer after chemoradiotherapy. (**b**) Narrow band imaging (NBI) observing the site of a rectal cancer after chemoradiotherapy

How to Achieve High Rates of Bowel Preparation Adequacy

4

Quinton Hatch, Rubina Ratnaparkhi, and Scott R. Steele

Key Points

- Effective colonoscopy is dependent on adequate bowel cleansing; however, inadequate bowel preparations are still reported in up to 30% of all colonoscopies. The reasons for this are multifactorial.
- The gold standard bowel preparation is a 4-L isosmotic solution of polyethylene glycol and balanced electrolytes (PEG-ELS); however, many patients still fail to complete this preparation due to abdominal fullness and cramping.
- Split-dose bowel cleansing, in which half the preparation is given the day before the procedure and the second half is given the morning of the procedure, is the recommended form of preparation administration due to improved efficacy and tolerability.
- Lower volume preparations with 2-L PEG solutions have been advocated, and have generally shown similar efficacy to the gold standard.
- Patient factors associated with poor preparation include inpatient status, older age, male gender, or history of cirrhosis, stroke, colorectal surgery, colonic inertia, dementia, obesity, diabetes, or active use of narcotics, calcium channel blockers, tricyclic antidepressants. These patients may be candidates for a more aggressive bowel preparation, which may include double-preparation, standard 4-L PEG solution with adjuncts, or 24–48 h of dietary restrictions prior to colonoscopy.
- Endoscopic maneuvers and systems are available to salvage an inadequate preparation; however, the most cost- and time-effective strategy is optimizing patient compliance with the preparation.
- Objective characterization of the quality of bowel cleansing is necessary, and should utilize one of the validated grading systems such as the Aronchick scale, the Ottawa Bowel Preparation Scale, or the Boston Bowel Preparation Score.

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Introduction

Achieving high rates of adequate bowel preparation requires consistent application of evidence-based approaches for colon cleansing, engaging patient education, adaptability when faced with challenging patients or inadequate preparations in need of salvage, and attention to detail in documentation. An adequate bowel preparation is defined as sufficient clearing of the colon to allow effective mucosal visualization to detect polyps or other lesions greater than 5 mm in size from the rectosigmoid colon complete to the cecum [1]. Inadequate cleansing can lead to failure to detect adenomas or neoplastic lesions as well as a greater rate of procedural adverse events. Nevertheless, inadequate bowel preparations are still reported in up to 30% of all colonoscopies [2–4]. This remains well above the target set by the US Multi-Society Task Force on Colorectal Cancer [1], which indicates a need for renewed attention in this area.

In this chapter, we will first review the wide variety of available preparations and discuss the most recent recommendations for their use. We will then define criteria to identify patients who may benefit from more aggressive bowel preparations and techniques for salvaging inadequate preparations. We will also summarize cleansing scales appropriate for clinical practice.

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Types of Bowel Preparations

Ideally, a colon preparation solution will quickly evacuate and cleanse the colon with minimal discomfort to the patient, limited physiologic fluid shifting and electrolyte imbalance, and no alteration of the colonic mucosa. To this end, a number of bowel preparations have been FDA-approved available for commercial use (Table 4.1). These agents act as oral cathartics and can be classified based on their osmolarity. Several combination agents have also been introduced. In 2015, the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy issued bowel preparation guidelines, but declined to endorse any specific preparation, and instead recommended individualized prescribing that weighs efficacy, safety, tolerability, cost, and patient preferences [4]. Here we will discuss available agents and review key considerations for determining the appropriate bowel preparation.

The gold standard bowel preparation is an isosmotic solution of polyethylene glycol and balanced electrolytes (PEG-ELS), which is intended to pass through the bowel without fluid and electrolyte shifts. As a result, it is considered safe for patients in whom electrolyte imbalances would be concerning (i.e., heart failure, renal disease, or chronic liver disease with ascites). The gold standard, however, is not without its limitations. In fact, ~5–15% of patients do not complete the preparation due to the large volume of consumption and consequent abdominal fullness and cramping [5]. Patients also complain about the preparation's unpleasant taste that often cannot be made more palatable even with addition of various flavorings.

In response to patient criticisms, a sulfate-free PEG-ELS solution was developed with improved smell and palatability due to altered sodium sulfate, potassium, and chloride concentrations [6]. Studies have demonstrated comparable efficacy of the sulfate-free solution with regard to colonic cleansing, safety, and tolerability when compared to PEG-ELS [7]. This has increased its popularity among physicians despite a slight increase in cost. Unfortunately, this preparation still requires 4 L of fluid consumption and thus does not eliminate the associated abdominal discomfort identified with standard 4-L PEG-ELS use.

Low-volume PEG-ELS solutions have also emerged. A 2-L PEG-ELS solution with ascorbic acid shares the isosmotic nature of PEG-ELS and sulfate-free PEG-ELS solutions, but minimizes fluid consumption (although an additional 1 L of clear liquid is often required). By and large, studies have demonstrated similar efficacy between low-volume and 4-L PEG-ELS solutions [4, 8]. The only safety concern of note arises with use in patients with glucose-6-phosphate dehydrogenase deficiency due to the potential for hemolysis with ascorbic acid.

An over-the-counter low-volume PEG-ELS solution was introduced for use that consists of a powder of a polyethylene glycol powder (PEG-3350) mixed in 2 L of a commercially available sports drink (e.g., Gatorade, Powerade, Crystal Light). In contrast to previously discussed bowel preparations, PEG-SD is hyposmotic, and studies to date have yielded mixed results regarding its comparability in terms of efficacy and safety to FDA-approved preparations. Some studies have suggested associations between PEG-SD and lower adenoma detection rates and higher rates of hyponatremia when compared to 4-L PEG-ELS [9], although other studies have shown comparable preparation quality [10]. Anecdotal data suggests increased compliance due to its lower volume, palatability, and relative availability and affordability. It may thus be a legitimate option, especially in patients who have been noncompliant with other preparation regimens. However, patients using either preparation still may have intolerance, nausea, vomiting, and incomplete use.

Hyperosmotic solutions are also available, although data supporting their efficacy is limited. Of the hyperosmotic solutions, oral sodium sulfate has been evaluated most robustly and has shown comparable results to PEG-ELS [11]. No serious adverse events have been reported, although side effects include mild GI events and vomiting. Magnesium citrate and sodium phosphate, two other hyperosmotic solutions, are not recommended for routine use. Magnesium citrate has been reported to cause magnesium toxicity, bradycardia, hypotension, nausea, and drowsiness, and is contraindicated in the elderly and patients with renal disease. Sodium phosphate has received an FDA warning due to the risk of renal injury and electrolyte abnormalities. At present, it is essentially not being used.

Two combination agents also merit discussion. Sodium picosulfate/magnesium citrate combines sodium picosulfate, which increases the force and frequency of peristalsis, with hyperosmotic magnesium citrate to enhance colonic fluid retention. Clinical trials to date suggest non-inferiority of sodium picosulfate/magnesium citrate when compared to low-volume PEG-ELS regimens [12]. GI adverse events were mild to moderate in nature. The other combination preparation, of note, pairs sodium sulfate with 2 L of sulfate-free PEG-ELS. This regimen also appears to be similar in efficacy to PEG-ELS preparations, although significantly greater rates of abdominal discomfort and vomiting were reported relative to comparator treatments [13].

Administration

Historically, bowel preparations were administered as a single dose on the day or evening before colonoscopy. A body of literature has now emerged in support of split-dose bowel preparations, in which half of the preparation is given the day before the procedure and the second half is given the morning of the procedure. Studies have shown that the split-dose schedule increases adenoma detection rate, possibly due to improved patient tolerance and willingness to take the entire preparation [14, 15]. ASGE recommends administration of the second dose between 3 and 8 h before colonoscopy to

Table 4.1 Commercially available bowel preparations

Type	Preparation	Composition	Volume		Split dosing regimens	Price
			Purgative	Other liquid		
Isosmotic	Polyethylene glycol electrolyte solution (PEG-ELS)	Polyethylene glycol, sodium sulfate, sodium, bicarbonate, sodium chloride, potassium chloride	4 L	None	• 2–3 L day before • 1–2 L day of	$24.56
	Sulfate-free PEG-ELS	Polyethylene glycol, sodium bicarbonate, sodium chloride, potassium chloride	4 L	None	• 2–3 L day before • 1–2 L day of	$26–28
	Low-volume PEG-ELS with ascorbic acid	PEG-3350, sodium sulfate, sodium chloride, ascorbic acid	2 L	1 L clear liquid	• 1 L day before • 1 L day of	$81.17
Hyposmotic	Low-volume PEG-3350 SD	PEG-3350	238 g in 2 L sports drink	Varies	• 1 L day before • 1 L day of	$10.08
Hyperosmotic	Oral sodium sulfate	Sodium sulfate, potassium sulfate, magnesium sulfate	12 oz	2.5 L water	• 6 oz OSS in 10 oz water + 32 oz day before • Repeat day of	$91.96
	Magnesium citrate	Magnesium citrate	20–30 oz	2 L water	• 1–1.5 10 oz bottles day before • Repeat day of	$2.38
	Sodium phosphate	Monobasic and dibasic sodium phosphate	32 tablets	2 L	• 20 tablets day before • 12 tablets day of	$150.84
Combination	Sodium picosulfate/ magnesium citrate	Sodium picosulfate, magnesium sulfate, anhydrous citric acid	10 oz	2 L water	• 5 oz + 40 oz clear liquids day before • 5 oz + 24 oz clear liquids day of	$95.34
	Sodium sulfate/SF-PEG-ELS	Sodium sulfate, potassium sulfate, magnesium sulfate, PEG-3350	6 oz in 2-L PEG-ELS	1.25 L water	• 6 oz OSS in 10 oz water + 32 oz day before • 2-L PEG-ELS day of	$77.94

*Adapted from Saltzman et al. [4]

allow sufficient time to achieve the desired response and avoid potential aspiration with sedation. Split-dose administration remains the preparation schedule of choice in both inpatient and outpatient settings. This recommendation stands regardless of whether the scope occurs in the morning or afternoon, although endoscopists may consider full-dose administration on the morning of the procedure for afternoon colonoscopies.

Criteria for More Aggressive Bowel Preparation

It has been well established that adequate bowel cleansing is essential to achieve high rates of cecal intubation and adenoma detection [16]. While no one regimen has shown superiority to this end, it seems clear that all established bowel preparations work in the majority of patients who are compliant with the instructions [4]. The reasons for inadequate preparation are numerous and likely multifactorial. Interestingly, failure to follow prep instructions only contributes to approximately 20% of inadequate preparations, which suggests a significant number of patients have an inherent difficulty with bowel cleansing [3]. Patient factors associated with poor preparation include inpatient status, older age, male gender, or history of cirrhosis, stroke, colorectal surgery, colonic inertia, dementia, obesity, diabetes, or active use of narcotics, calcium channel blockers, tricyclic antidepressants [2–4]. One model used a number of patient factors (e.g., cirrhosis, Parkinson's, diabetes, male gender, BMI, age, positive fecal occult blood test, and prior colorectal surgery) to predict inadequate preparation, and was able to predict 60% of inadequate preparations. This model could theoretically reduce the rate of inadequate cleansing from 33 to 13% if widely utilized to identify patients in whom a more aggressive preparation would be beneficial [2]. To avoid the waste associated with repeat colonoscopy, it is important that we utilize such models and ensure there is a plan in place to optimize bowel cleansing prior to committing to endoscopy. At a minimum, patients with a history of inadequate preparation should be considered for a more aggressive bowel cleansing regimen.

Types of More Aggressive Preparations: Two-Day Preps/Types

Patient education has been found to be a contributor to inadequate bowel preparation in approximately 20% of patients [3]. Proper teaching is perhaps the easiest and most cost-effective method of ensuring an adequate bowel cleansing. While it is of critical importance to all bowel preparations, it should be a special point of emphasis in those patients who are deemed high risk for inadequate bowel cleansing, to include those who are non-English-speaking, cognitively impaired, or who have risk factors for inadequate preparation. Thus, appropriate education is the first component of any intensive bowel cleansing regimen.

Several aggressive adjunctive measures have been proposed for patients at high risk of inadequate preparation, although the evidence to support these practices is predominantly anecdotal. Most would support a full 4-L PEG solution in split doses (the evening before and the day of colonoscopy) rather than a 2-L dose. Two full days of clear liquids prior to examination or double administration of the preparation over 2 days are often utilized in this setting, although there is no evidence to support these practices. Other options are the addition of magnesium citrate (300 mL) or bisacodyl (10 mg) to a standard PEG preparation [17].

Few formalized aggressive bowel cleansing regimens have been proposed in the literature. The most notable such algorithm consists of (a) low fiber diet for 72 h before colonoscopy; (b) liquid diet the day before colonoscopy; (c) two tablets of 5 mg bisacodyl at 7 p.m. on the day before the colonoscopy; and (d) 1.5 L of PEG at 8 p.m. on the day before the colonoscopy, and 1.5 L of PEG at 6 a.m. on the day of colonoscopy. This regimen was offered to a series of patients who had previously had an inadequate preparation. The authors found improved rates of adequate cleansing (98.8% vs. 0%), cecal intubation (98% vs. 78%), polyp detection (69% vs. 51%), flat lesion detection (63% vs. 43%), and adenoma detection (47% vs. 10%) in the 51 patients who underwent a repeat colonoscopy using the proposed intensive bowel cleansing strategy. Patient compliance was equivalent, and 63% of patients characterized the preparation as easy or very easy to take [18].

Techniques for Salvaging Inadequate Preparations

Prior to starting any colonoscopic examination, the patient should be questioned regarding compliance and characteristics of the effluent. In the 5–30% of patients who present with persistent brown effluent [2, 3, 19], a number of strategies may be employed to "salvage" the preparation. Unfortunately, intraprocedural techniques are costly in terms of time and productivity. In fact, it has been estimated that intraprocedural cleansing accounts for up to 17% of total colonoscopy procedural time [20]. This inefficiency highlights the necessity for identifying and acting on these patients prior to the procedure start time.

The most simplistic method for cleansing an inadequately prepared colon revolves around standard irrigation pumps or saline flushes via the working port on the endoscope. A number of novel irrigation devices have been studied, and initial

reports suggest significant improvement in the preparation and polyp detection rate when compared to standard irrigation alone. The most studied of these is the JetPrep system, which has demonstrated a polyp miss rate of only 26% compared to a 50% miss rate when standard irrigation alone is utilized in an inadequately cleansed colon [21]. Similar devices have shown improvement in bowel cleansing; however, it is at the cost of prolonged withdrawal times [22, 23].

Another strategy involves the infusion of a 500-mL PEG enema in the hepatic flexure via the colonoscope. The colonoscope is then withdrawn and the patient is allowed to proceed to the lavatory to defecate prior to repeat examination. The drawbacks in terms of time are obvious in this case, although the authors did report adequate cleansing in 96% of patients [24].

An alternative to irrigation and enemas is holding off on colonoscopy until additional oral preparation is ingested. One unique approach in this vein involves the administration of 1000-mL PEG-ELS into the second portion of the duodenum on upper endoscopy (in those patients undergoing both EGD and colonoscopy). The patient is then allowed to evacuate their bowels in between procedures. This technique resulted in 85% excellent preparation quality in a series of 152 patients [25].

Any salvage procedure embarked upon will be inefficient in terms of time, and many of these techniques may be completely unrealistic from an administrative or logistic standpoint. Ultimately it is up to the endoscopist to determine the benefit of attempting salvage techniques versus bringing the patient back for a repeat endoscopy at a later date.

Cleansing Scales Appropriate for Clinical Practice

Objective characterization of the quality of bowel cleansing is necessary to determine the adequacy of the colonoscopic examination for detecting polyps. To this end, a number of scoring systems for assessing the quality of bowel cleansing have been validated.

The Aronchick scale, developed in 1999, uses a 5-point scale [1–5] to determine the quality of bowel cleansing on initial colonoscopic exam. It is therefore useful for comparing different bowel preparations before "salvage" maneuvers are undertaken by the endoscopist. The scale accounts for the colon as a whole, and does not discriminate between the prep quality in different segments (Table 4.2) [26, 27].

The Ottawa Bowel Preparation Scale, developed in 2004, similarly uses a 5-point scale (0–4) to determine the adequacy of initial bowel cleansing. The primary difference between the two scoring systems is that the Ottawa scale breaks the examination down into rectosigmoid colon, mid colon, and right colon. The overall score is on a scale of 0 (excellent) to 14 (very poor) and is calculated by adding the three segmental scores and the whole colon fluid score. The Aronchick and Ottawa scales have been compared and validated for interobserver reliability (Table 4.2) [28].

The Boston Bowel Preparation Score, developed in 2010, is unique in that it accounts for endoscopist maneuvers in determining the adequacy of the examination. It is therefore calculated after the examination has concluded. It has been shown to correlate with polyp detection rate, and because it

Table 4.2 Bowel cleansing scoring systems

Aronchick Scale [26, 27]	1	Excellent (>95% of mucosa seen)
	2	Good (clear liquid covering up to 25% of mucosa, but > 90% of mucosa seen)
	3	Fair (semisolid stool could not be suctioned, but >90% of mucosa seen)
	4	Poor (semisolid stool could not be suctioned and <90% of mucosa seen)
	5	Inadequate (repeat preparation needed)
Ottawa Bowel Prep Scale rating for each colon segment [28]	0	Excellent (mucosal detail clearly visible)
	1	Good (minimal turbid fluid in segment)
	2	Fair (necessary to suction fluid to adequately view segment)
	3	Poor (necessary to wash and suction fluid to obtain a reasonable view)
	4	Inadequate (solid stool not cleared with washing and suctioning)
Ottawa Bowel Prep Scale rating for the amount of fluid in the whole colon	0	Small amount of fluid
	1	Moderate amount of fluid
	2	Large amount of fluid
Boston Bowel Preparation Scale rating for each colon segment [29]	3	Entire mucosa of segment well seen after cleaning
	2	Minor residual material after cleaning, but mucosa of segment generally well seen
	1	Portion of mucosa in segment seen after cleaning, but other areas not seen because of retained material
	0	Unprepared colon segment with stool that cannot be cleared

*Adapted from Saltzman et al. [4]

is a validated post hoc assessment, it is the only scale in use that truly determines the adequacy of the examination. As with the Ottawa scale, the adequacy of the preparation is determined in each of three colonic segments (right, transverse, and left). The three segmental scores are determined after inter-procedure irrigation, and are added to give a 0–9 point score, with 0 being very poor preparation and 9 being excellent preparation (Table 4.2) [29].

Pearls and Pitfalls

- In order to optimize patient compliance and adenoma detection rates, the bowel preparation recommendation should be individualized and account for efficacy, safety, tolerability, and cost considerations with attention to patients' comorbid conditions and preferences.
- Split-dose preparations are more efficacious with improved tolerability, and are therefore recommended.
- Patients at high risk for inadequate preparation should be identified before colonoscopy and should be considered for a more aggressive bowel cleansing regimen.
- An inadequate preparation may be salvaged at the time of colonoscopy; however, it is advantageous from cost and time perspectives to ensure the adequacy of preparation prior to the procedure.
- Adequacy of preparation should be documented using a validated scoring system.

Summary

A number of bowel cleansing preparations exist. While a full 4-L PEG-ELS remains the gold standard, the ASGE recommends individualized prescribing that balances efficacy, safety, tolerability, and cost considerations with attention to patients' comorbid conditions and preferences. Split-dose administration, with administration of the first dose the day before the procedure and the second dose given 3–8 h prior to colonoscopy, is considered the schedule of choice regardless of the specific bowel preparation employed. Patients at high risk for inadequate prep should receive thorough education regarding preparation instructions. Two full days of clear liquids prior to examination, double administration of the preparation over 2 days, or the addition of magnesium citrate or bisacodyl to a standard PEG preparation may all be considered for these patients. Salvage of an inadequate preparation may be undertaken during the procedure with the use of systems such as the JetPrep or simply endoscopic infusion of PEG solution directly into the bowel. Finally, the quality of the preparation should be graded and documented using one of the several validated scoring systems.

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Patient Comfort During Colonoscopy

5

Charles B. Whitlow

Key Points

- The vast majority of patients undergoing colonoscopy desire sedation.
- A combination of a benzodiazepine and an opioid is the most common sedation for colonoscopy.
- Insufflation with CO_2 improves patient comfort in the immediate post-procedural period.
- Appropriate monitoring during sedation decreases the risk of sedation-associated complications.
- Variable stiffness colonoscopies improved cecal intubation rates and decrease procedural pain compared to standard colonoscopies.

Introduction

Colonoscopy is a frequently performed procedure in the United States with an estimated frequency of 15 million per year [1]. It is the most common test performed for colon cancer screening and is the procedure of choice for evaluating symptoms referable to the colon and rectum. Fear of pain during the procedure is a barrier to patients undergoing recommended screening and a poor patient experience can have an adverse affect on the willingness to undergo subsequent surveillance exams. The quality of the exam and the ability to perform therapeutic procedures can be impacted by patient discomfort and movement at inopportune times during the exam. While this would at initial glance appear to be a straightforward topic, there are several considerations that are worthy of discussion. Included in this list are issues of risk versus benefits vs. cost of sedation; which drugs to use; who administers the drugs; who monitors the patient and what monitoring is required; and what training is necessary for administration of drugs and monitoring patients. Additionally, in recent years, technical factors such as the use of carbon dioxide (CO_2) for insufflation or water immersion have been touted to improve patient comfort and technical performance of the exam. In the following chapter, the use of the term colonoscopy will specifically refer to standard air insufflation colonoscopy. Studies which pertain to the use of CO_2 insufflation, water immersion, or water exchange will be pointed out as such.

Current Sedation Practices for Colonoscopy

In the USA, the overwhelming majority of patients desire sedation for colonoscopy [2]. A combination of a narcotic (most commonly Fentanyl) and a benzodiazepine (typically midazolam) has been the most frequently used sedation protocol [3, 4]. More recently, propofol (alone or in combination with narcotics or benzodiazepines) has been used in increasing numbers of patients accounting for about 20–25% of colonoscopies performed in 2012. Lawrence Cohen has an excellent statement about the variation of sedation practices in a 2010 review article—"The variation in sedation practices worldwide reflects the diversity of social, cultural, medicolegal, economic, and market forces that influence patient tolerance for colonoscopy as well as the willingness and ability of endoscopists to expend the time, effort, and resources required for the safe and effective use of sedation" [1].

Unsedated Colonoscopy

Unsedated colonoscopy has been an uncommon practice in the United States. A survey of gastroenterologists in 2006 reported 98% of EGDs and colonoscopies were performed with some type of sedation [4]. The advantages of unsedated colonoscopy are multiple: decreased cost, it eliminates the risks of sedation (admittedly these are low for most patients),

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Table 5.1 Studies comparing colonoscopy with and without sedation

Authors	Study design	Total procedures (% sedated procedures)	Difference in CIR	Difference in cecal intubation time	Difference in ADR
Bannert et al. [5]	Retrospective	52,506 (86%)	Yes (1.2%)		No
Radaelli et al. [6]	Retrospective	12,835 (55%)	Yes (8%)		PDR higher with sedation
Crispin et al. [7]	Retrospective	236,087 (97%)	Yes		NA
Paggi et al. [8]	Prospective	964 (44%)	Yes (16%)		No
Petrini [9]	Prospective	2090 (72%)	No	No	No
Aljebreen [10]	Prospective	403 (67%)	No	No	No

Table 5.2 Levels of sedation/analgesia

	Minimal	Moderate	Deep	General anesthesia
Responsiveness	Normal	Purposeful	Purposeful to repeated painful stimuli	Unarousable
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Developed by the American Society of Anesthesiologists; approved by the ASA House of Delegates October 13, 1999, last amended 2014. www.asahq.org—Standards and guidelines, 10.15.14

immediate resumption of normal activity, and decreased inconvenience to patients (missed work, need for escort). Requirements for unsedated colonoscopy include a motivated patient and a skilled endoscopist. However, anatomic factors may prevent successful completion without addition of sedation.

Cecal intubation rates (CIR) vary from 67 to 100% in reports of unsedated colonoscopy from around the world with most CIR reported at >90%. Additionally, time to cecal intubation is typically longer in unsedated patients. There is a lack of high-quality data pertaining to quality metrics and sedation. What data is available, while not universal, favors sedated colonoscopy for CIR with mixed results for polyp detection (Table 5.1) [5–10]. There is also a lack of data showing quality outcome differences based on level of sedation such as moderate vs. deep.

Two groups have reported prospectively collected data on unsedated colonoscopy in their practices. Paggi et al. reported a 56% acceptance rate of unsedated colonoscopy [8]. The CIR was 82% and increased to 97% when on-demand sedation was administered. Adenoma detection rates were similar for sedated vs. unsedated patients. They found that patients who had an absent/low level of self-reported pre-procedure anxiety, no concern about the exam, and first-time procedure were all associated with acceptance of an unsedated procedure. Absence of pre-procedure anxiety was associated with completion of the procedure without medication. Petrini et al. described their experience with unsedated colonoscopy: [9] 28% of 2091 patients elected to start the procedure without sedation and of those 81% completed it without sedation. Cecal intubation rate and time to cecum was the same for patients sedated at the start of the procedure and those who were unsedated throughout the procedure.

Patients should be informed of the option of unsedated colonoscopy. Physicians who use this technique must recognize that it requires an increased amount of communication with the patient and more patience in performance of the procedure. While patient selection is vital to the successful use of this technique, provisions for sedation should be immediately available for those who initially elect to forgo sedation but during the procedure decide they need sedation.

Propofol Versus Benzodiazepine +/− Opioid

The American Society of Anesthesiologists has described different levels of sedation based on patient responsiveness, ability to protect the airway, spontaneous ventilation, and cardiovascular function (Table 5.2) [11]. For endoscopic procedures, propofol is frequently equated with deep sedation and the combination of a benzodiazepine with an opioid (B/O) is equated with minimal/moderate sedation; however, the agent used and the level of sedation are two separate issues—in other words, moderate or deep sedation can be achieved with either agent. For most patients either sedation strategy will provide adequate sedation. Anecdotally, the author's impression is that it seems that there are more patients on anxiolytics, narcotics, and antidepressants than previously and these patients require higher doses of the traditional B/O combination.

The advantages and disadvantages of propofol are outlined in Table 5.3. A meta-analysis confirmed the decreased recovery time and time to discharge, as well as the improved patient satisfaction with propofol over B/O [12]. There were no differences in complication rates between the two types of sedation. The authors note that a limitation of this study is that the vast majority of patients were "generally healthy."

A review of SEER data compared complications in over 165,000 colonoscopies performed with anesthesia assistance vs. those without—the presumption being that those with anesthesia assistance are almost all propofol cases [13]. The authors found overall complications were higher in the anesthesia-assisted group (0.22% vs. 0.16%) as was the rate of aspiration (0.14% vs. 0.10%). Perforations and splenic injuries were similar between the two populations. The authors conclude that depth of sedation may be a risk factor for complications.

I would add (based on personal experience of 10 years experience of B/O sedation followed by 3 years of sedation with propofol) my experience favors propofol as a quicker more reliable form of sedation for colonoscopy. Patients do need more airway attention and I have abandoned routinely moving patients from left lateral to supine on achieving cecal intubation. Since patients who are under deep sedation are generally unable to help in changing positions, I now leave larger patients and those with known sleep apnea in the left lateral position. A small percentage of patients can develop a prolonged cough that is felt to represent micro-aspiration [14]. In addition to the risk of aspiration pneumonia, this cough can cause technical difficulty with examination of the mucosal surface and polypectomy.

Ulmer et al. reported on a randomized trial of nurse administer propofol vs. midazolam/fentanyl [15]. They found that patients who received propofol were sedated faster, to a deeper level of sedation, and were discharged home quicker. They also scored better on a series of post-procedure tests of learning, memory, working memory span, and mental speed.

Several models exist for how sedation is administered for endoscopic procedures (Table 5.4). Barriers to widespread use of propofol include an increase in cost in large part because of the increased use of anesthesia services. There is an FDA/package insert warning with propofol stating it should be "administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure." Other factors which limit endoscopist administered or directed use of propofol include state nursing board regulations, hospital policies/credentialing, lack of familiarity with the drug, and cost/reimbursement issues. Despite these issues, there is ample evidence that non-anesthesiologist-administered propofol can be safely accomplished.

Because colonoscopy is performed so frequently it is a prime target for cost reform and because the socioeconomic landscape is constantly changing it is difficult to know what impact reimbursement will ultimately have on the future use of propofol. The current model of anesthesiologist directed or administered propofol changes the cost-effectiveness of colonoscopy as a screening exam—the question that remains is what the magnitude of that change will be. An additional result of this model is that the physicians and nursing staff lose the skill set of conscious sedation making them dependent on anesthesia services to accomplish their procedures.

Table 5.3 A comparison of some advantages and disadvantages of propofol for colonoscopy

Advantages	Disadvantages
Quick and reliable onset of action	Increased cost
Recovery and time to discharge	Increase personnel
Rapid return to baseline function	Difficulty with positional changes
Patient satisfaction	Increased coughing
Physician satisfaction	Lack of reversal agent
Efficacy in difficult to sedate patients	

Table 5.4 Common sedation models for colonoscopy[a]

Provider role	Targeted level of sedation	Typical agents	Comments
Endoscopist administered	Light to moderate	Benzodiazepine +/− opioid	Nursing personnel must still monitor patient
Endoscopist directed	Light to moderate	Benzodiazepine +/− opioid	
Endoscopist directed—registered nurse administered	Moderate to deep	Propofol	Most institutions require special training/credentialing
Nurse anesthetist administered	Moderate to deep	Propofol	Supervised by anesthesiologist or endoscopist
Anesthesiologist administered	Moderate to deep	Propofol	Most commonly used in higher risk patients

[a]Combinations and modification of these strategies can be made on individual basis. For example—patients being sedated with a benzodiazepine and opioid may experience enough discomfort that deep sedation is required and which can be produced with those agents

Opioids Alone

Fentanyl, remifentanil, and alfentanil have all been described for single agent use for colonoscopy. The benefit of this approach is that less sedation is achieved and therefore the risk of complications from sedation is avoided. The data available are from a small number of trials. In one, patients receiving fentanyl had lower pain scores and shorter times to cecal intubation than patients who were given midazolam [16]. The midazolam group experienced a decrease in O_2 sat in 35% of patients compared to none with fentanyl.

Remifentanil may shorten recovery times compared to B/O with less respiratory depression. Side effects and the need for administration by a separate trained person have limited its use for colonoscopy [17]. Only one small trial of alfentanil in colonoscopy has been performed [18]. This study showed fewer patients given alfentanil alone were less likely to require supplemental oxygen compared to those administered alfentanil with midazolam. No other differences were noted.

CO_2 Insufflation Colonoscopy

Several procedural adjuncts have been described to decrease pain, reduce the amount of sedation required, or enable/facilitate performance of unsedated colonoscopy. The two techniques that seem to have garnered the most attention are CO_2 insufflation and water-aided colonoscopy. There is data for each of these individually and more recent studies have compared them head-to-head or used together.

CO_2 insufflation is believed to decrease pain from colonoscopy due to the rapid absorption of this gas relative to air. This technique requires a CO_2 regulator and a source of the gas—gas line or refillable cylinders. Wu and Hu performed a systematic review and meta-analysis of nine randomized trials with 1577 patients comparing CO_2 vs. air insufflation [19]. Procedural sedation included unsedated patients, B/O, and propofol. CIR and cecal intubation times were similar for the two groups. The methodology in this study involved comparing patient with any pain (visual analog score [VAS] > 0) to those with no pain. Using this criteria, they found a benefit with regard to pain during the procedure, and at 1, 6, and 24 hrs post-procedure. There were no differences in complications and end-tidal CO_2 levels were similar during and after the procedure. The authors come to the over-reaching conclusion that these findings "warrant wide clinical use."

There has been no report that demonstrated an increased complication rate for CO_2 colonoscopy. The additional cost includes the gas regulator that is connected to the colonoscope and the cost of CO_2. The benefits for routine screening colonoscopy appear to be minimal and it does not appear to increase the ability to perform unsedated colonoscopy. However, for patient with suspected obstruction or intestinal distention pre-procedure, CO_2 is an excellent option. It may also have benefit in cases in which advanced polyp resection techniques (endoscopic mucosal resection, endoscopic submucosal dissection) are used as well as intraoperative colonoscopy.

Water-Aided Colonoscopy

Two types of water-aided colonoscopy have been described [20]. The first is water immersion. In this technique, water is infused during insertion of the colonoscope and is removed during scope withdrawal. Use of air insufflation is used as needed to provide adequate visualization. After cecal/ileal intubation, the water is removed and gas insufflation is used for withdrawal, mucosal inspection, and any biopsies or polypectomies that need to be performed. Water exchange is a modification of water immersion that involves complete exclusion of air, thus avoiding the lengthening of the colon caused by insufflated gas moving quickly into the cecum.

Several randomized trials have been performed comparing water immersion or water exchange to air insufflation. A systematic review of these studies was published in 2012 [21]. Eight of the studies compared water immersion, and four compared water exchange. Sedation protocols included no sedation, "minimal" sedation for premedication, and on-demand sedation. In the water immersion studied all but one showed a statistically significant reduction in pain scores. However, it should be noted that in only two studies was the mean pain score over five and the absolute mean reduction was less than 2 on a 10-point VAS for all studies. In the water exchange studies, the differences in pain scores were more pronounced. ADR was similar for water immersion vs. air insufflation, but ADR was greater for water exchange vs. air.

A randomized trial of water exchange vs. CO_2 demonstrated similar rates of moderate/severe pain and adenoma detection rates [22]. CIR were improved for the water exchange group while time to cecum was shorter for the CO_2 procedures. Another randomized trial looked at the possible benefit of left-colon water exchange (LWE) -meaning air insufflation once proximal the splenic flexure on insertion [23]. This study showed decreased cecal intubation times in the LWE groups but with a lower bowel prep score and a lower right colon polyp detection rate (small sample size, not statistically significant).

Other combinations and permutations of air, CO_2, water immersion, and/or water exchange have been examined. Two studies with multiple arms have looked at combinations of water-aided insertion vs. gas insertions (air vs. CO_2) and withdrawal with air vs. CO_2. Falt et al. found that the success rate of minimal sedation colonoscopy was greater in patients who had water immersion insertion [24]. Patients who had

water immersion and CO_2 insufflation for withdrawal had less discomfort in the initial 24 h after the procedure. Another multiarmed study concluded that water exchange was the least painful technique and gave the best chance of completing an unsedated colonoscopy [25].

There is a learning curve with water exchange colonoscopy but no special equipment is required beyond the standard high volume irrigator that is widely available. The majority of the literature on water-aided colonoscopy is from a small group of enthusiastic advocates.

Nonetheless, both CO_2 insufflation and water-aided colonoscopy may be useful adjuncts in patients who desire unsedated or minimal sedation procedures. The possible benefit in adenoma detection rate with water-aided colonoscopy warrants further study.

Other Procedural Adjuncts to Colonoscopy

Magnetic Endoscope Imaging

Magnetic Endoscope Imaging (MEI) provides real-time, non-fluoroscopic feedback of colonoscope configuration. The image is generated by electromagnetic fields detected by coils in the colonoscope and additional ones positioned by the patient. Computer software converts the data from the coils into an image displayed on a monitor.

A meta-analysis of studies comparing MEI to conventional colonoscopy (CC) was published in 2013 [26]. The authors concluded MEI is of benefit in training and educating inexperienced endoscopists and improves the cecal intubation rate of experienced and inexperienced endoscopists. A randomized trial published after that analysis demonstrated that for the subset of more difficult case the time to cecum was shorter for MEI. There were no differences in CIR, insertion distance to cecum, time to cecum, mean pain score, or mean sedation score [27].

The role of MEI is unclear, however it maybe useful in training endocopists by showing how loop formation and reduction correlates with the endoscopists actions. It has been used to show the mechanism of other techniques—for example, that water exchange colonoscopy attenuates loop formation [28]. In a randomized study of difficult colonoscopies, the cecal intubation rate was lower and time to cecum was longer for MEI compared with double-balloon enteroscopy [29].

Type of Colonoscope

Colonoscope technology continues to evolve. Changes that effect function in a way that will allow for more frequent cecal intubation, quicker time to cecum, or less pain include scope diameter and the capability to vary the stiffness of the scope. There is data demonstrating fewer patients experiencing moderate or severe pain during unsedated colonoscopy with a variable stiffness scope compared to a standard colonoscope [30, 31]. Cecal intubation rates and time to cecum may be slightly improved with variable stiffness scopes especially in the hands of inexperienced scopes. When comparing variable stiffness scopes of varying sizes, it appears that adult variable stiffness scopes (12.2 mm diameter) allow for quicker cecal intubation than pediatric variable stiffness scopes. However, pediatric variable stiffness scopes may still be useful in the setting of a difficult exam that has failed with an adult scope. While Chen et al. did not find a difference in pain scores between scopes of 11.3, 12.2, and 13.2 mm diameter, others have found decreased pain in unsedated exams with smaller diameter colonoscopies [30, 32].

Patient Position

The technical description of how colonoscopy is performed in almost every study cited in this chapter begins with the patient in the left lateral position. Patients are moved supine or right lateral as needed. Vergis et al. found that starting the exam with patient right-side down resulted in faster times to reach the cecum and these patients were more comfortable during the exam [33]. Unlike some technical aids, the faster time to cecum was seen for experienced endoscopists. Female patients and patient with prior abdominal surgery showed the greatest difference between right- or left-sided starting position.

Medications

Medication adjuncts or substitutions beyond propofol or B/O have been studied with the goal of analgesia without sedation or with less sedation. Nitrous oxide is an inhalational agent with sedative, anxiolytic, and anesthetic properties with rapid onset and clearance. Its use in colonoscopy has been described in several small trials which have included continuous or on-demand usage. Both a systematic review and a Cochrane review have been published on this topic [34, 35]. The heterogeneity of the literature precludes a true meta-analysis; however, these reviews came to similar conclusions. Namely, that nitrous oxide provides similar efficacy of sedation with similar patient satisfaction as sedation with benzodiazepines and opiates or opiates alone. Return of psychomotor function is quicker with nitrous oxide and it is associated with less post-procedure nausea. Propofol was not used in any of the studies included.

The two most recent trials of nitrous oxide produced differing results. Malsekar et al. randomized patients to nitrous oxide vs. midazolam-fentanyl [36]. They reported that

nitrous oxide was superior in several aspects. Patients who received nitrous oxide had lower pain scores, shorter time to discharge, quicker return of psychomotor function, higher satisfaction, and shorter times to discharge. Løberg et al. randomized patients to oxygen vs. on-demand nitrous oxide [37]. Patients were given midazolam and/or pethidine as needed for pain. They found a similar number of patients in each group required additional sedation and/or analgesia and in similar amounts. Pain scores were similar between the two groups. These authors concluded that nitrous oxide was not able to act as an effective substitute for standard intravenous sedation for colonoscopy.

In the early days of colonoscopy, glucagon was administered routinely to decrease colonic spasm. Some endoscopists continue to use antispasmodics selectively or routinely with the rationale that decreasing colonic spasm facilitates both the exam and polypectomy. Until 2013, no recent trials had looked at glucagon with the most recent one in this period (1995) not showing any benefit [38]. Tamai et al. found a statistically significant decrease in pain scores, acceptance of future colonoscopy, abdominal fullness score, and scope manipulation score [39]. All of these are 10-point VAS. The clinical significance of these differences is questionable since none was greater than 1.6 on a 10-point scale. Additionally, they reported a difference in salivary amylase at time of cecal intubation—a reflection of plasma norepinephrine levels in stress. Church found that warm water was as effective as glucagon at eliminating colonic spasm [40].

Other antispasmodics have been studied. Yoshikawa et al. compared scopolamine to glucagon in unsedated patients and demonstrated no difference in CIR, time to cecal intubation, pain score, systolic blood pressure, or oxygen saturation [41]. More patients receiving scopolamine had an increase in heart rate of 10 bpm than those given glucagon.

Hyoscyamine immediately before colonoscopy has been studied in various delivery forms—intravenous, sublingual, oral tablet, and oral spray [42]. Most have shown no benefit in patient comfort outcomes, ease of procedure, or speed of procedure. Sinus tachycardia has been a noted side effect in some studies.

Conclusion

Given the vast number of options available to the endoscopist and anesthesiologist, it is clear that sedation for colonoscopy is not a one-size-fits-all proposition. The trend toward increasing use of anesthesia personnel and specifically deep sedation with propofol seems unlikely to change in the near future. Financial pressures aside, the patient experience is superior with propofol, and patient satisfaction and the willingness to undergo future exams are important goals of insuring patient comfort. Additionally, the experience of the endoscopist favors propofol.

In settings in which the endoscopist wishes to maintain the role of providing sedation or in which the cost of anesthesia personnel is not feasible, the combination of a benzodiazepine and a narcotic remains an excellent combination. The addition of the other adjuncts mentioned above, such as water-aided colonoscopy, CO_2 insufflation, or a smaller diameter colonoscope, may allow for a decrease in the quantity of medication needed and thus allow for fewer cardiorespiratory side effects and faster recovery. However, in the hands of skilled experienced endoscopists, these adjuncts may not be necessary or even beneficial.

Unsedated colonoscopy is unlikely to achieve widespread acceptance in the USA but should be offered in appropriate cases. The adjuncts described above may be useful in this setting. This is with the understanding that there is no perfect predictor of which patients will have difficult colons to examine.

Pearls and Pitfalls

1. Monitored sedation for colonoscopy with propofol gives more predictable results than a benzodiazepine/opioid combination. The overall experience for the patient and endoscopist is better with propofol, patients are discharged home quicker, and return to baseline cognitive function within 1–2 h. However, there is an increased need for active airway management.
2. While adjuncts such as CO_2 insufflation and water-aided colonoscopy may decrease patient discomfort, there is no data indicating that their use will improve acceptance of unsedated colonoscopy.
3. The selective use of smaller diameter colonoscopes and or using the variable stiffness facilitates cecal intubation in difficult cases.

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VTE Prophylaxis: How to Optimize Patients on Anticoagulation and Avoid Infectious Complications

6

John R.T. Monson and Reza Arsalani Zadeh

Key Points

- Periprocedural management of anticoagulation is based on a balance between the procedure-related bleeding risk and the risk of thromboembolic complications.
- The risk of bleeding with colonoscopic procedures varies between very low in purely diagnostic tests to high in polypectomy. For low-risk procedures, no change in anticoagulation is necessary.
- The thromboembolic risk following discontinuation of anticoagulation or antiplatelet agents depends on the condition and other associated risks. Guidelines exist but are mainly based on low level evidence. Cardiology and neurology input should be obtained whenever in doubt about the periprocedural management.
- In patients undergoing procedures with high bleeding risks, warfarin should be stopped 5 days and new oral anticoagulation agents should be stopped 1–2 days prior to the procedure. Aspirin and NSAIDs can be safely continued. Other antiplatelet agents should be stopped prior to high-risk procedures (5 days for Clopidogrel, 3–5 days for ticagrelor, and 10–14 days for ticlodipine). Bridging therapy is only required for conditions with high risk of thromboembolic events.
- Antibiotic prophylaxis is generally not indicated in patients undergoing colonoscopy except those on continuous ambulatory peritoneal dialysis.

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Introduction

Colonoscopy is the gold standard diagnostic test for people with lower gastrointestinal symptoms. It is also the gold standard screening test for colorectal cancer. Approximately 2.8 million flexible sigmoidoscopies and 14.2 million colonoscopies were estimated to have been performed in 2002 in the USA [1]. These numbers certainly have increased over the last decade.

Anticoagulation is being increasingly used for treatment and prevention of both venous and arterial thromboembolic diseases. There has been a rapid evolution in the development of new anticoagulants over the last decade. An increasing number of patients on anticoagulation require endoscopic procedures. The risk of procedure-related bleeding vs. thromboembolic events during cessation of anticoagulation should be carefully considered in these patients.

Patients with prosthetic joints or heart valves may be at higher risk of prosthetic infection following colonoscopy.

In this chapter, we will review the current evidence about periprocedural anticoagulation management and antibiotic prophylaxis in people undergoing colonoscopic procedures.

Anticoagulation and Colonoscopy

Anticoagulation therapy is used for the treatment and primary or secondary prevention of thromboembolic events in various medical conditions such as atrial fibrillation, prosthetic heart valves, deep vein thrombosis, and pulmonary emboli. Anticoagulation is used for thromboembolic prevention in hypercoagulable conditions or after certain surgical procedures.

In order to provide appropriate advice regarding anticoagulation management prior to colonoscopy, one should consider two main factors; first the risk of bleeding which is related to the type of colonoscopic procedure and the class of anticoagulation medication. Second, the risk of thromboembolic events

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upon cessation of anticoagulation therapy. Interruption of anticoagulation will decrease the bleeding risk associated with the procedure. The occurrence of a thromboembolic event such as stroke or pulmonary embolus during the interruption period can have catastrophic effects for the patient. The risk assessment weighing these two factors should be the basis of decision-making with regard to anticoagulation management prior to any endoscopic procedure. The cooperation between cardiologists, hematologists, and endoscopists is essential for appropriate risk management.

Anticoagulants

Bleeding Risk

Bleeding risk is based on two factors of procedure type and the class of medication.

Procedure type: Purely diagnostic colonoscopies including those with simple mucosal biopsies are considered to be a low-risk procedure for bleeding.

High-risk procedures include polypectomy, tumor ablation and endoscopic mucosal dissection.

Risk of bleeding after colonoscopic polypectomy has been reported to be between 0.3 and 10.0%. There have been several studies to assess risk factors associated with post-polypectomy bleeding. Presence of cardiovascular disease, age more than 65 years, hypertension and polyps larger than 1 cm and anticoagulation are all shown to be associated with higher risk of post-procedure bleeding. In addition to polyp size, polyp morphology and location and resection technique influence the risk of bleeding. Polypectomy of right sided and sessile polyps is associated with increased risk of bleeding.

Endoscopic stent placement can also be associated with risk of bleeding. The incidence of bleeding associated with stent placement is reported to be between 0 and 5%. Bleeding is usually minor and does not require any intervention [2]. ASGE consider enteral stent placement to be a low-risk procedure with regard to bleeding.

Thromboembolic Risks

Atrial fibrillation: Chronic atrial fibrillation increases the risk of stroke and other thromboembolic events. The annual risk of stroke in atrial fibrillation is between 1.9 and 18.2%. Comorbidities such as heart failure, hypertension, or diabetes increase the risk of stroke in atrial fibrillation. $CHADS_2$ or CHA2DS2-VASc scoring system has been designed to quantify this risk (Tables 6.1, 6.2, 6.3, and 6.4) [3]. The overall risk of stroke is low in those patients whose anticoagulation is interrupted for the procedure. The risk increases almost tenfold in patients with increased age, hypertension, and history of stroke, diabetes, and congestive heart failure [3].

Table 6.1 CHADS2 scoring system for assessment of stroke risk in atrial fibrillation

Risk factors	Points
C: congestive heart failure	1
H: hypertension	1
A: age>75 years	1
D: diabetes	1
S: prior history of stroke	2

Table 6.2 Correlation between CHADS2 score and risk of stroke

CHADS2 score	Stroke rate per 100 patient-years
0	1.9
1	2.8
2	4.0
3	5.9
4	8.5
5	12.5
6	18.2

Table 6.3 CHA2DS2-VASc scoring system for assessment of stroke risk in atrial fibrillation

Risk factors	Points
C: congestive heart failure	1
H: hypertension	1
A2: age>75 years	2
D: diabetes	1
S2: prior history of stroke	2
V: vascular disease	1
A: age 65–74 years	1
Sc: sex category (female gender)	1

Table 6.4 Correlation between CHA2DS2-VASc score and risk of stroke

CHADS2 score	Stroke rate per 100 patient-years
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

Venous thromboembolism and pulmonary emboli: The risk of a second venous thromboembolic event after an episode of deep vein thrombosis or pulmonary emboli is dependent on the time passed from the initial event and comorbidities.

A high risk of more than 10% exists during the first 3 months after the thrombosis or if additional hypercoagulable conditions are present. These include malignancy, protein C or S deficiency, factor V Leiden mutation or other thrombophilic disorders. The risk is 5–10% between 3 and 12 months after the thrombosis and is low (<5%) 12 months after the primary event.

Valvular heart disease and prosthetic valves: The risk of thromboembolic events in patients with valvular heart disease or a prosthetic heart valve depends on the location and type of the prosthetic heart valve and also the presence of other risk factors such as atrial fibrillation, intra-cardiac thrombi or history of thromboembolic events. For example, the annual risk of a thromboembolic event in patients with bileaflet aortic valve and other risk factors is less than 5%. Patients with mitral or tricuspid mechanical valves or previous thromboembolic events will have more than 10% annual risk of thromboembolism.

A large meta-analysis demonstrated that the risk of all thromboembolic events when these patients are not on anticoagulation is only 8 per 100 patient years. This is equal to a risk of around 0.2% over a week. In one retrospective study of noncardiac surgery in patients with a prosthetic heart valve, short cessation of anticoagulation in the perioperative period (average 6.6 days) did not cause any thromboembolic events.

Ischemic heart disease and coronary artery stents: Patients with ischemic heart disease are generally treated with antiplatelet therapy. Coronary artery stents are being increasingly used as the primary management of ischemic heart disease. Bare metal stents require at least 1 month of dual antiplatelet treatment in order to decrease the risk of stent thrombosis. The recommendation for the duration of dual antiplatelet treatment for drug eluding stents is 1 year. The risk of stent thrombosis upon cessation of antiplatelet therapy during the first year increases after 5 days of interruption.

Classes of Medications

Aspirin

Pharmacology: Aspirin is a cyclooxygenase inhibitor and decreases the capacity of platelets to synthesize thromboxane. The half-life of aspirin is only 20 min; however its COX-inhibitory effect on platelets is permanent. Its clinical effect will therefore last for the life span of platelets, which is 7–10 days.

Clinical indications: The benefit of aspirin for protection against cardiovascular disease is well known. Aspirin given long-term can reduce the risk of both vascular events and vascular-related mortality. In addition, timely use of aspirin reduces the acute myocardial infarction-related mortality and also decreases the chances of myocardial infarction in patients with unstable coronary syndromes. Aspirin also has a proven role in the secondary prevention of stroke and reduction of mortality in patients with acute cerebrovascular ischemic events.

Risk of hemorrhage: Several studies have investigated the effect of aspirin on post-polypectomy bleeding. They are all retrospective case-control studies. A recent meta-analysis demonstrated that taking Aspirin or NSAIDs does not increase the risk of post-polypectomy bleeding. There is no need for interruption of these prior to the procedure [4]. This is in line with the current recommendation by ASGE [5].

Non-aspirin Antiplatelet Drugs

Pharmacology: In addition to aspirin, several new antiplatelet drugs have been in clinical use. Based on their mechanism of action, they are generally classified into three groups: inhibitors of ADP-induced platelet aggregation such as clopidogrel, ticlopidine; glycoprotein IIb/IIIa receptor blockers such as abciximab, tirofiban, and eptifibatide, other antiplatelet drugs such as dipyridamole and cilostazol (Fig. 6.1).

Inhibitors of ADP-induced platelet aggregation (clopidogrel and ticlopidine): These drugs are derivatives of thienopyridine and irreversibly block the ADP receptor on platelets. They are effective in the prevention of future vascular events in patients with transient ischemic event or strokes. They are also commonly used in patients after placement of coronary artery stents. Clopidogrel has a better side effect profile compared to ticlopidine. Antiplatelet effect of clopidogrel and ticlopidine takes several days to develop, reaching a maximum of 40–60% inhibition in 3–5 days. The duration of the antiplatelet affect lasts 7–10 days.

Glycoprotein IIb/IIIa receptor blockers (abciximab, tirofiban, and eptifibatide): Activation of platelet IIb/IIIa receptor complex is the final common pathway for platelet aggregation. The main clinical use of this class of antiplatelet agents is in patients with acute coronary syndrome. These drugs are administered parentally. Based on their molecular weight, they are classified into two groups. Abciximab is of larger size and is a monoclonal antibody. Its antiplatelet action lasts up to 24 h after stopping intravenous infusion. Tirofiban and eptifibatide are smaller in size and are non-peptide and peptide of GP IIb/IIIa receptor antagonists, respectively. They have a short duration of action and their effect lasts only 4 h after stopping the infusion.

The main clinical indication of GP IIb/IIIa inhibitors is in patients with acute coronary syndrome who are undergoing primary coronary intervention.

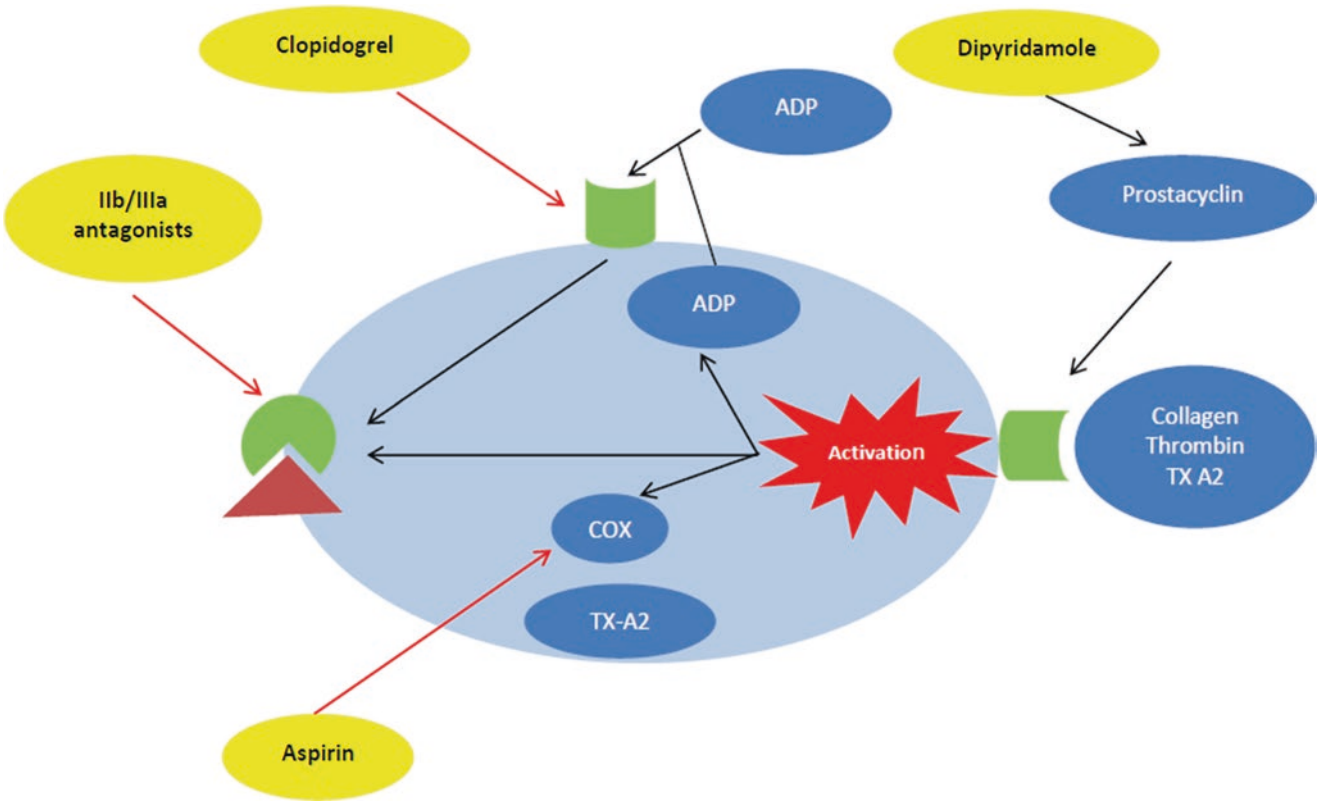

Fig. 6.1 Platelet action and the effect of antiplatelet drugs

Other antiplatelets (dipyridamole and cilostazol): Dipyridamole antiplatelet activity is by inhibition of adenosine uptake and cGMP phosphodiesterase activity. Its main clinical use is in the prevention of cerebrovascular events in combination with aspirin.

Cilostazol is another phosphodiesterase inhibitor that has both vasodilatory and antiplatelet effects. It is mainly used in patients with peripheral vascular disease to treat intermittent claudication.

Current Guidelines

Inhibitors of ADP-Induced Platelet Aggregation (Clopidogrel and Ticlopidine)

There is little data on the effect of antiplatelet drugs on post-polypectomy bleeding. Studies are restricted to case-control studies. A recent review showed that the risk of immediate and delayed post-polypectomy bleeding increases in patients taking clopidogrel alone or in combination with aspirin or NSAIDs [4].

Low-risk procedures: For low-risk procedures such as diagnostic colonoscopy and biopsy, there is no need for adjustment in the antiplatelet regimen.

High-risk procedures: There is very limited data to provide any evidence-based recommendation. In consideration of pharmacology and the bleeding risk associated with antiplatelet agents, it is recommended to discontinue non-aspirin antiplatelet agents 7–10 days prior to the procedure. As the onset of action of these medications is relatively slow, they can be restarted on the day after the procedure.

Glycoprotein IIb/IIIa Receptor Blockers (Abciximab, Tirofiban, and Eptifibatide)

It is very rare for patients undergoing colonoscopy to be on these medications. Nevertheless, GP IIb/IIIa infusion should be stopped in patients undergoing high-risk procedure or those with active GI bleeding. Platelet transfusion and/or use of DDAVP may have a role in reversing the effect of these medications.

Dipyridamole: Dipyridamole does not appear to increase the risk of bleeding when it is used alone or in combination with aspirin [6]. Low-risk procedures can be safely performed while taking dipyridamole. The safety of high-risk procedures in this group is unknown.

Although the evidence behind this guideline is limited, temporary cessation of antiplatelet agents and maintaining patients on aspirin as long as agreed by cardiologist is recommended.

Warfarin

Pharmacology: Warfarin is a coumadin derivative that inhibits the synthesis of vitamin K dependent factors, i.e., factors II, VII, IX, and X and also protein C and S. Its mechanism of action is through inhibition of intrahepatic activation of vitamin K. It has a rapid bioavailability with a half-life of 40 h. Its effect can be easily monitored using INR.

Clinical indication: Warfarin is one of the most used anticoagulants. It is effective in prevention and treatment of venous thromboembolic events. In addition, it protects against thromboembolism in the setting of atrial fibrillation and prosthetic heart valves. Increased risk of bleeding is an inherent side effect of warfarin.

Warfarin does not increase the risk of bleeding in patients undergoing low-risk procedures, as long as the INR is not beyond the therapeutic range. Simple mucosal biopsies can be safely performed in patients on warfarin; however, there is no trial data to fully support this.

Data on the risk of bleeding after high-risk procedures in patients on warfarin are very limited. One study of 1657 polypectomies showed that warfarin is an independent risk factor for bleeding [7]. It is also not entirely clear what level of anticoagulation is safe for high-risk procedures. It is accepted that the INR level below 1.5 is safe. There is very limited data for high-risk colonoscopic procedures; however, this level can be extrapolated from other procedures such as liver or renal biopsies. A randomized study of 70 patients on warfarin undergoing polypectomy for colonic polyps of less than 10 mm in size demonstrated a post-polypectomy bleeding rate of 23% and 6% for conventional and cold snare polypectomy, respectively [8]. This trial supports the use of cold snare for polypectomy pf small polyps in patients on warfarin.

If an elective endoscopic procedure with high risk of bleeding is being performed, warfarin should be stopped 5 days prior to the procedure. The INR decreases to less than 1.5 in more than 90% of cases 5 days after cessation [9]. When warfarin is stopped a complete risk assessment of thromboembolism should be performed to assess whether an interim substitution (bridging) of warfarin with other anticoagulants such as low molecular weight heparin (LMWH) is required. It is shown that bridging can increase the risk of overall and also major bleeding with no reduction in the risk of thromboembolic events [10]. Nevertheless, conditions with a high risk of thromboembolism should have bridging with LMWH (Table 6.5).

The risk of bleeding after high-risk procedures remains high for several days. The benefit of resuming antithrombotic therapy immediately after a procedure should therefore be carefully balanced against the risk of post-procedure bleeding. Data behind the risk of bleeding associated with immediate reinitiating of warfarin after endoscopic procedures is mixed and limited to case series or case-control studies. A retrospective study of 579 colonoscopies with polypectomy did not show any difference in the rate of bleeding and the timing of anticoagulation, post-procedure [11]. Other studies have also confirmed the safety of immediate anticoagulation, post-procedure [12]. On the contrary, another study found that resuming anticoagulation with either warfarin or heparin within the first week after polypectomy is associated with increased risk of severe delayed bleeding [13].

AHA/ACC guidelines recommend commencing warfarin within 24 h after the procedure in patients with valvular heart disease and low thromboembolic risks. Bridging with unfractionated or LMWH is recommended in patients with high risk of thromboembolism. Bridging should continue until INR is in the therapeutic range [14].

Table 6.5 Risk categorization of thromboembolic events in patients with atrial fibrillation or valvular heart disease

Low risk	High risk
AF	*AF*
– CHA2DS2-VASC score < 2	– Mechanical valves – History of CVA – CHA2DS2-VASc score ≥2
Valvular heart disease	*Vavular heart disease*
– Bileaflet mechanical aortic valve	– Mechanical AVR and any thromboembolic risk factors – Older generation mechanical AVR – Mechanical mitral valve

AF atrial fibrillation, *CVA* cerebrovascular accident, *AVR* aortic valve replacement

Novel Oral Anticoagulants (NOACs): Factor X and Thrombin Inhibitors

Pharmacology: Warfarin has been the drug of choice for thromboprophylaxis for many years. However, its use is limited by the need for continuous monitoring and wide drug interaction. There has been a recent advent in creating new oral anticoagulants to replace warfarin. The new oral anticoagulants are being increasingly used in the setting of nonvalvular atrial fibrillation and long-term treatment and prevention of venous thromboembolism [15]. Based on their mechanism of action, these drugs can be classified into two groups (Fig. 6.2).

Inhibitors of factor Xa (rivaroxaban, apixaban): Rivaroxaban directly inhibits factor Xa. It has a half-life of 5–13 h with more than 90% of plasma protein binding. Rivaroxaban is as effective as warfarin in the prevention of stroke with less risk of fatal bleeding [16]. Rivaroxaban is also used in the treatment and prevention of deep vein thrombosis.

Fig. 6.2 Coagulation cascade and the effect of anticoagulants

Apixaban is another direct factor Xa inhibitor. It has a half-life of 12 h with high binding to plasma proteins. Apixaban has shown to decrease the risk of stroke in the setting of atrial fibrillation with a significantly less risk of major bleeding in comparison to warfarin [17].

Direct thrombin inhibitors (dabigatran): Dabigatran reversibly inhibits thrombin. Its main mode of clearance is through the kidneys and renal function should be regularly monitored in patients on Dabigatran. Routine monitoring of coagulation is not necessary in patients on dabigatran. Thrombin clotting time and ecarin clotting time can be used to assess the effect of dabigatran. The activated partial thromboplastin time (aPTT) has a curvilinear dose–response relationship with dabigatran. However, the diluted thrombin time provides more direct assessment of thrombin activity and therefore is more accurate in the assessment of the effect of dabigatran. The half-life of dabigatran is 8–15 h.

Clinical indications: Rivaroxaban is approved for thromboprophylaxis after orthopedic surgery. It can also be used for the prevention of stroke or other systemic embolic events in patients with atrial fibrillation. Apixaban is also effective in the prevention of thromboembolic events in atrial fibrillation and post-orthopedic surgery thromboprophylaxis.

Risk of Hemorrhage

Current guidelines: There are no studies on the effect of NOACs in patients undergoing colonoscopy. The recommendation needs to be based on the extrapolated evidence of

Table 6.6 Periprocedural management of novel oral anticoagulants in high-risk endoscopic procedures

Creatinine clearance (mL/min)	Onset of action (h)	Timing of discontinuation (day)
Dabigatran		
>80	1.25–3	1–1.5
50–80	1.25–3	1–2
30–49	1.25–3	1.5–2
≤29	1.25–3	2–3
Apixaban		
>60	1–3	1 or 2
30–59	1–3	3
15–29	1–3	4
Rivaroxaban		
>90	2–4	≥1
60–90	2–4	2
30–59	2–4	3
15–29	2–4	4

Table 6.7 conditions associated with the worse outcome after infective endocarditis

Cardiac condition
Prosthetic cardiac valve
History of infective endocarditis
Patients with congenital heart disease (CHD)
Unrepaired cyanotic CHD
Completely repaired CHD with prosthetic material or device for the first 6 months after the procedure
Repaired CHD with residual defects at the site or adjacent to the site of prosthetic patch or device

bleeding risk with NOACs and also the pharmacokinetic of these new drugs.

The Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, compared the periprocedural use of dabigatran with warfarin. It is found that the risk of periprocedure bleeding is similar between both groups [18].

In procedures with low risk of bleeding, there is no need to stop any of the NOACs. In high-risk procedures, NOACs should be discontinued. The diminution effect of NOACs is predictable, and therefore a short-term cessation before procedure is adequate.

It is shown that diagnostic colonoscopy and simple biopsies can be performed in patients on warfarin and INR of therapeutic range, with no significant risk of procedure-related bleeding [19]. However there is currently no firm evidence that the same approach can be adopted in patients on NOACs.

The recommended time of cessation of NOACs is dependent on the renal function. European Heart Rhythm Association (EHRA) recommends 24 h. interruption of factor Xa inhibitors for low-risk procedures, in patients with GFR of more than 30 mL/min. The duration of cessation should be extended to 36 h if the GFR is less than 30 mL/h. At least 48 h of cessation is recommended for patients on factor Xa inhibitors who are undergoing high-risk procedures [20].

Elimination of Dabigatran is more dependent on renal function as it is 80% renally excreted. It has an estimated half-life of 13 h (range, 11–22 h); in those with a clearance of 51 to 80 mL/min, the half-life is 15 h; and in those with a clearance of 31 to 50 mL/min, the half-life is 18 h. The cessation recommendations of NOACs based on the ASGE guidelines are summarized in Table 6.6 [5, 20].

There are no data on optimal timing for restarting NOACs. In general, these agents have a much shorter onset of action than warfarin, and therefore if there are major concerns about post-procedure bleeding they should be withheld. In these cases, bridging with LMWH should be considered in patients at high risk for thromboembolism.

Antibiotic Prophylaxis After Colonoscopy

Bacteremia is a well-documented phenomenon after lower GI endoscopic procedures due to bacterial translocation of colonic microbial flora into the blood stream.

A prospective study of patients undergoing colonoscopy with or without polypectomy found the rate of transient bacteremia to be about 2–4% [21]. The observed bacteremia was short lived with no evidence of sepsis during 24 h post-procedure. Bacteremia is also relatively uncommon after endoscopic colonic stent placement (6.3%) with no evidence of post-procedure sepsis [22].

There have been reports of symptomatic sepsis or infective endocarditis with temporal association with endoscopic procedure. There is currently no evidence to support a cause–effect relationship between endoscopic procedures and these events. In addition, there is no data to support that antibiotic prophylaxis has any protective effect. Finally, the rate of bacteremia associated with daily activities such a brushing and flossing of teeth, exceeds that of associated with colonoscopy. There is therefore no need for routine use of preprocedure antibiotics.

Certain clinical conditions however require further discussion.

Prevention of Endocarditis

Routine use of prophylactic antibiotics is not recommended prior to colonoscopy [23].

AHA guidelines consider certain cardiac conditions to be associated with the worse outcome after endocarditis (Table 6.7). If patients with any of these conditions undergo endoscopic procedure in the setting of established infection of GI tract with enterococci, the AHA suggests consideration of prophylaxis against enterococci. There is no data to

support this recommendation. In addition, colonoscopic procedures are associated with low rate of bacteremia, and therefore routine use of antibiotics even with high-risk pre-existing heart conditions is not required.

Peritoneal Dialysis

Patients on peritoneal dialysis are susceptible to peritonitis. Colonoscopy can cause bacterial translocation and subsequently peritonitis in patients undergoing continuous ambulatory peritoneal dialysis (CAPD). There are several case reports of peritonitis following colonoscopy in patients on CAPD. The incidence of peritonitis following endoscopic procedures is about 6%. Peritonitis in patients on CAPD can cause increased morbidity and mortality and may lead to the need for alteration of dialysis modality [24]. In a retrospective study, 6.3% of the patients who underwent a colonoscopy developed peritonitis without prophylactic antibiotics. No patients who received prophylactic antibiotics developed peritonitis [25].

The ASGE guidelines suggest administration of antibiotic prophylaxis prior to lower GI endoscopy in patients on CPAD. The international Society of Peritoneal Dialysis (ISPD) recommends drainage of peritoneal fluid and intravenous antibiotic prophylaxis. Both of these recommendations are based on retrospective observational studies.

Other Conditions

Prosthetic joint infection and infection of non-valvular cardiovascular devices related to endoscopic procedures of lower GI tract is limited to isolated case reports [26, 27]. There is currently no recommendation for routine use of antibiotics in these patients [28].

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Endoscopic Equipment and Instrumentation

7

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Key Points

- Knowledge of the benefits of one piece of equipment over another is important not only based on reported efficacy but also with regard to the endoscopists level of comfort in performing the given technique.
- The theoretical efficacy of a given forceps simply based on larger size does not necessarily equate to improved acquisition of tissue and more accurate pathologic evaluation.
- Endoscopic mucosal resection and especially endoscopic submucosal resection are advanced techniques with a steep learning curve. One must be adequately trained and, as with all new advanced techniques, establish a proper, proctored, training pathway.
- Narrow band imaging and chromoendoscopy are effective and simple to perform techniques. The challenge is learning to identify the nuances in visualization offered by using these techniques.

Colonoscopes

The design of a flexible endoscope comprises of three parts: the control, the insertion tube, and the connector section (Figs. 7.1, 7.2, and 7.3). The control consists of two dials that move the tip of the scope up, down, and left or right, these dials can be locked in place. There are also separate buttons for suction, air or water insufflation, image freeze, and capture. Some endoscopes have additional buttons that can be programmed to perform other functions such as image printing, and other scopes can change the type of light that is seen for more specific identification of lesions. The control section also contains the working port for insertion of instruments through a channel that allows for use of these instruments through the tip of the endoscope.

The insertion tube is a flexible shaft attached to the control section. All the channels that pass from the control section to the tip pass through the insertion tube. Channel sizes vary from 2.8 to 4.2 mm. Some colonoscopes have two working channels that either allow for full suction while using the other working channel or allow for use of two instruments during a procedure. Some endoscopes also have an auxiliary water channel that allows for a foot-controlled water pump for extra flushing. The insertion tube also contains the cables that enable deflection of the tip. Additionally, all electronic parts that allow for image generation and illumination pass through the insertion tube. There are varying degrees of flexibility through the insertion tube. The distal portion is more flexible to allow negotiation through angulated areas of the colon and the proximal end is stiffer to reduce looping. Olympus (Olympus Medical Systems, Center Valley PA) also produces colonoscopes that can be further stiffened. These variable stiffness colonoscopes are said to reduce looping in more mobile sections of the bowel, with the ability to maintain flexibility in the more fixed sections.

Lastly, the connector section attaches the endoscope to the image processor, light, power source, air or CO_2 insufflator, and water.

Standard endoscopes magnify the images 30–35 times at baseline. Some endoscopes allow for a zoom feature that can magnify images up to 150 times. Endoscopes can be equipped with enhanced imaging such as narrow band imaging (NBI) (Olympus Medical Systems, Center Valley PA) and multiband imaging (MBI) (Fujinon, Wayne, NJ and Pentax, Montvale, NJ) [1]. These features will be discussed in more detail later in the chapter.

The optical resolution of a colonoscope affects the endoscopist's ability to distinguish between two closely approximated objects. Standard definition (SD) signals

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Fig. 7.1 Colonoscope control section

Fig. 7.2 Connector section

offer images in 4:3 (width: height) aspect ratio, with resolution of 640–700 horizontal pixels (width) X 480–525 vertical pixels (height). The chips used in current High Definition (HD) endoscopes produce signal images with resolutions that range from 850,000 pixels to more than one million pixels. HD scopes are available from all three colonoscope manufacturers, Olympus (Olympus Medical Systems, Center Valley PA), Pentax (Pentax, Montvale, NJ), and Fujinon (Fujinon, Wayne, NJ). HD imaging has been shown to improve the quality of colonoscopy [2].

Fig. 7.3 Insertion tube section

Fig. 7.4 Pediatric and adult colonoscopes

Colonoscopes have variable insertion tube lengths, 1330–1700 mm, and variable diameters, 9.7–13.8 mm. Pediatric colonoscopes (outer diameter in the 11 mm range or smaller) have been shown to be useful in completing a colonoscopy in patients with angulated sigmoid colons and benign sigmoid strictures (Fig. 7.4). There is evidence that a pediatric colonoscope should be used exclusively in women who have had a hysterectomy [3]. This smaller diameter and increased flexibility is at the expense of less stiffness, which can lead to more looping. The endoscopist should choose the appropriate patient for the scope used in order to increase the likelihood for cecal intubation.

Newer colonoscopy equipment that allows for wider angle of view is available. The Full Spectrum Endoscopy (FUSE) colonoscope has a 330-degree view of the colon, compared to the standard 140 or 170 for some endoscopes [1]. A study in Lancet Oncology compared colonoscopies performed with standard forward-viewing colonoscopes and FUSE. Adenoma

miss rate was significantly less in the FUSE group: 7% versus 41% [4]. The Third Eye Retroscope (Avantis Medical Systems Inc., Sunnyvale, CA) provides a retrograde view that compliments the colonoscope's forward view. This aides in detection of lesions located behind folds, where they are difficult to detect with standard forward-viewing colonoscopes. This technology has been shown to provide a greater than 23% increase in adenoma detection rate [5].

Biopsy Equipment

Many manufacturers produce hundreds of single use and reusable biopsy forceps, the following are the main types. There are two chief varieties of cold biopsy forceps, single bite and double bite. Double bite forceps are equipped with a needle spike between the opposing cups. This needle spike secures the first specimen on the needle during collection of a second (Fig. 7.5). Biopsy forceps with a needle also provide deeper biopsies than non-needle versions. Single bite cold biopsy forceps do not have a needle spike (Fig. 7.6). Biopsy cup jaws may be round, oval, or elongated, fenestrated or non-fenestrated, smooth, or serrated. Large capacity or "jumbo" biopsy forceps sample a larger volume of tissue, at least two times the surface area of standard size forceps, but they do not necessarily yield deeper specimens, and they require a larger diameter biopsy channel [6]. Multiple biopsy specimen forceps are also available. These are designed to obtain multiple specimens with a single pass. There is concern that the samples obtained with these forceps are too small for adequate diagnostic evaluation [7].

Polypectomy with hot biopsy forceps provides cautery via the two biopsy cups. There is concern regarding both adequate destruction of neoplastic tissue and also the possibility of transmural thermal injury [8]. Reports have shown that hot biopsy forceps may yield a deeper tissue injury than produced with a snare [9].

Polypectomy snares use a monopolar wire loop that is advanced through a plastic catheter with the intention of encircling the target tissue. The tissue is then transected by the means of mechanical and electrosurgical cutting as the loop is pulled back into the catheter. All snares can be used with electrocautery, but either hot or cold techniques can be employed. Snares are made of monofilament or braided wires of various gauges. Snares are made in loop sizes up to 60 mm and in a variety of shapes, designed to match the anatomic requirements for removing a given lesion (Fig. 7.7) [8].

Tattoo

Endoscopic tattooing is an essential practice in order to find a location in the bowel either at future endoscopy or during surgery. A tattoo is performed by injecting a solution submucosally using an endoscopic injection needle. Many injection needles are available; the most common are 22 or 25 gauge.

Many solutions including India ink, indocyanine green (ICG), methylene blue, indigo carmine, toluidine blue, isosulfan blue, hematoxylin, and eosin have been considered for endoscopic tattooing. Animal studies have shown that only India ink and ICG are seen at the injection site longer than 48 h [10].

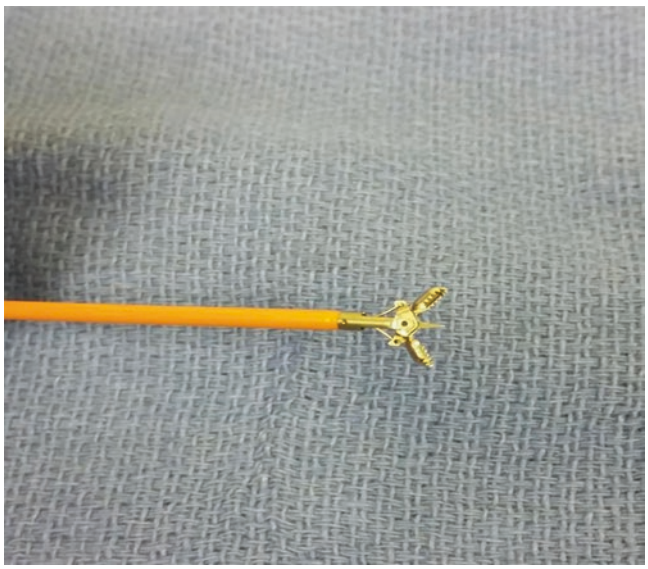

Fig. 7.5 Double bite biopsy forceps

Fig. 7.6 Olympus disposable EndoJaw biopsy forceps (single bite). Courtesy of Olympus

Fig. 7.7 Snares

India ink, used for writing in India since the fourth century BC, has been used for endoscopic tattooing since the 1970s. It is composed of a suspension of carbon particles in a solution of organic and inorganic substances. Various preparations exist which may contain numerous substances, which can cause local tissue reaction. Nonsterile India ink can be mixed with saline and made sterile by either autoclave or millipore filtration. A range of concentrations of India ink have been studied; undiluted and 1:10 dilution cause mucosal ulceration, a 1:100 produced no inflammation, and was seen at endoscopy and surgery for 5 months [11].

A sterile, biocompatible suspension, containing carbon particles known as Spot (GI Supply, Camp Hill, PA), was developed, and is specifically sold for endoscopic tattooing (Fig. 7.8). This product has been studied in 113 patients; it produced no signs or symptoms of inflammation. Ten of the patients underwent surgical resection; Spot was seen at the time of surgery in all cases; none of the specimens showed signs of necrosis or abscess formation. Forty-two of the patients underwent subsequent colonoscopy anywhere from 3 to 12 months from the time of tattooing; the Spot was seen in every case [12].

ICG is a dye originally used for in medical diagnostics. ICG is contraindicated in patients with allergy to iodine [13]. In a study of 39 patients, ICG was visible intraoperatively in all 29 patients having surgery within 8 days. However, in the remaining ten patients who underwent surgery more than 8 days after tattooing, staining was seen in only two patients [14].

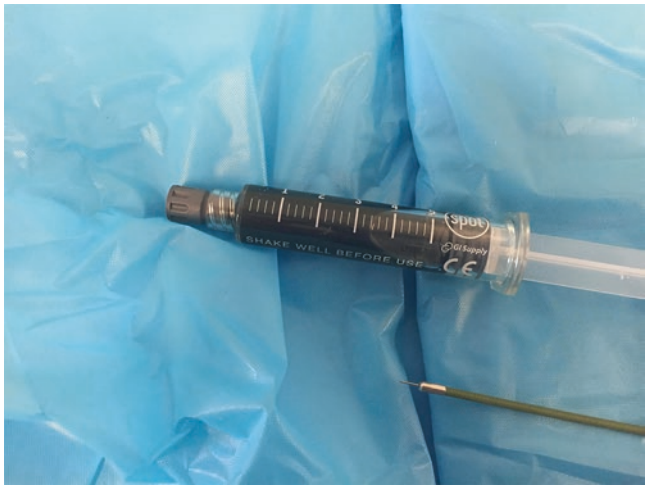

Fig. 7.8 Spot and injection needle

Endoscopic Mucosal Resection (EMR)

EMR is a procedure whereby a sessile polyp is removed; typically, lesions larger than 2 cm are removed piecemeal. The technology required for this procedure depends on the technique being used. Many endoscopists that perform EMR pre-inject liquid into the submucosal plane; this lifts the lesion to facilitate its removal, provide a cushion to prevent cautery injury to the deeper layers of the bowel, and in the event that a submucosal injection does not result in lifting of the lesion; this may indicate that the lesion is invasive and should not be resected in this fashion, but rather by surgical resection. For injection-assisted EMR one must have an injection needle (as discussed previously in this chapter) and the desired solution for pre-injection (Fig. 7.8). For EMR normal saline is typically used; however, other solutions are commonly used for submucosal injection, we will discuss these in more depth in the endoscopic submucosal dissection (ESD) section. If the endoscopist is performing the "Inject-and-Cut" technique, the next instrument required will likely be an electrocautery snare to resect the tissue desired. For the "Inject-Lift-and-Cut" technique one requires a colonoscope with two working channels and a grasping forceps as well. Grasping forceps are available as single use or reusable, and there are many different tips to choose from. Examples are: three-prong, five-prong, alligator jaw, rat tooth, rat tooth/alligator jaw, rubber tip, V shaped, and many more (Figs. 7.9, 7.10, 7.11, 7.12, 7.13, 7.14, 7.15, and 7.16). Additionally, many endoscopists perform what is known as cap-assisted EMR. This also uses submucosal injection and then dedicated mucosectomy devices that use a cap which is affixed to the tip of the colonoscope. A cap is a single use device, which also comes equipped with a specially designed crescent-shaped snare (Fig. 7.17). The mucosa is then retracted into

Fig. 7.9 Olympus injection needle. Courtesy of Olympus

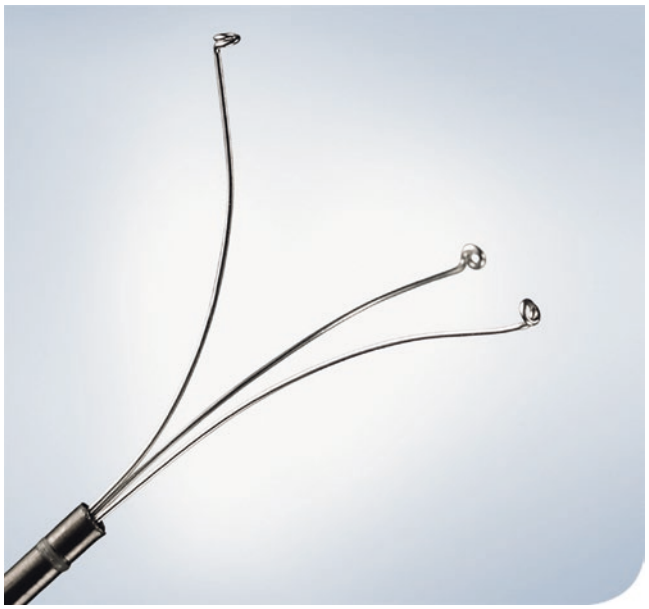

Fig. 7.11 Olympus three-prong grasper. Courtesy of Olympus

Fig. 7.10 Olympus alligator jaw grasper. Courtesy of Olympus

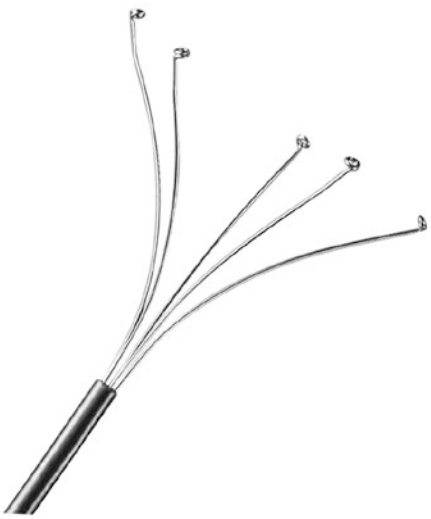

Fig. 7.12 Olympus five-prong grasper. Courtesy of Olympus

the cap, using suction, and the snare is closed to capture the lesion. The available cap-assisted mucosectomy devices vary based on the characteristics of the cap. There are flat (straight) or oblique tips, and soft or hard plastic tips (Figs. 7.18 and 7.19). Cap outer diameters come from 12.9 to 18 mm; different sizes are based on the size of the lesion being removed. Lastly, in ligation-assisted EMR, a standard variceal band ligation device is positioned over the target lesion, suction is then applied, and the band is deployed over the base of the lesion, and a standard electrocautery snare is used to resect the lesion beyond the band. A combination snare and multiband device is available from Cook Medical (Bloomington, IN) known as the Duette. This device is currently only approved for upper GI procedures. Once the tissue has been excised, it must now be removed, there are multiple tissue collection devices, examples are the US Endoscopy Roth Net and Poly-Pak, combination rotatable snare and Roth net, ConMed's Standard Nakao spider net, and Boston Scientific's Twister Plus, Rotatable Retrieval Device (Figs. 7.20, 7.21, and 7.22).

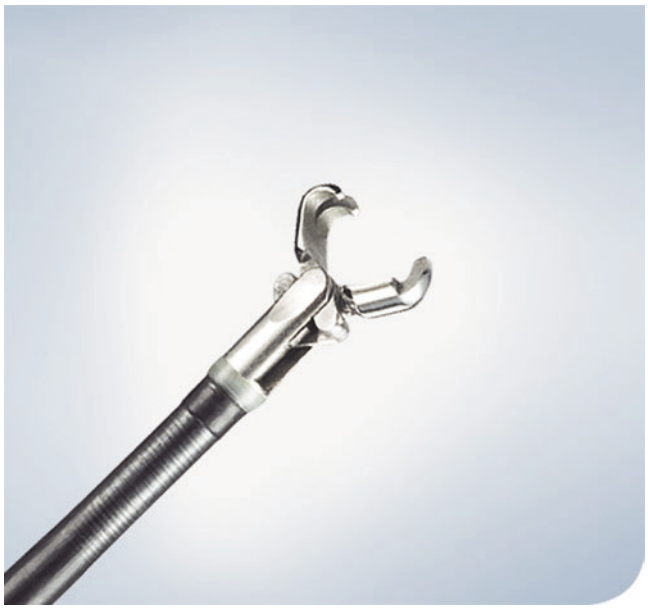

Fig. 7.13 Olympus rat tooth grasper. Courtesy of Olympus

Fig. 7.15 Olympus rubber tip grasper. Courtesy of Olympus

Fig. 7.14 Olympus V shape grasper. Courtesy of Olympus

Fig. 7.16 Olympus rat tooth alligator jaw grasper. Courtesy of Olympus

Endoscopic Submucosal Dissection (ESD)

ESD was developed for en block removal of large, flat lesions, usually more than 2 cm. There are many specialized instruments designed for this procedure's several steps. In ESD, the margins of the lesion are first marked by electrocautery; this can be done with any of the knife instruments that have cautery at the tip. The instrument that can be used for initial marking is the needle knife, which has a small contact area with high cutting power (Fig. 7.23). One can also use the hook knife (Fig. 7.24), similar to the needle knife, but bent at a right angle, this knife extends to 4.5 mm in length, with a 1.3 mm hook. Both the knife length and direction of the hook can be adjusted at the handle, extending it fully will lock the direction of the hook. The Triangle tip knife can also be used for initial marking; it has a non-insulated triangular electrode at the tip of a 4.5 mm knife (Fig. 7.25). The triangular electrode measures 1.6 mm on each side and maximally extends 0.7 mm away from the central knife. The DualKnife has a very small, non-insulated dome-shaped tip (Fig. 7.26). The maximum cutting length is 2 mm; however, it can be shortened and fixed at a 1.5 mm length, or one can fully retract the knife, so that only 0.3 mm

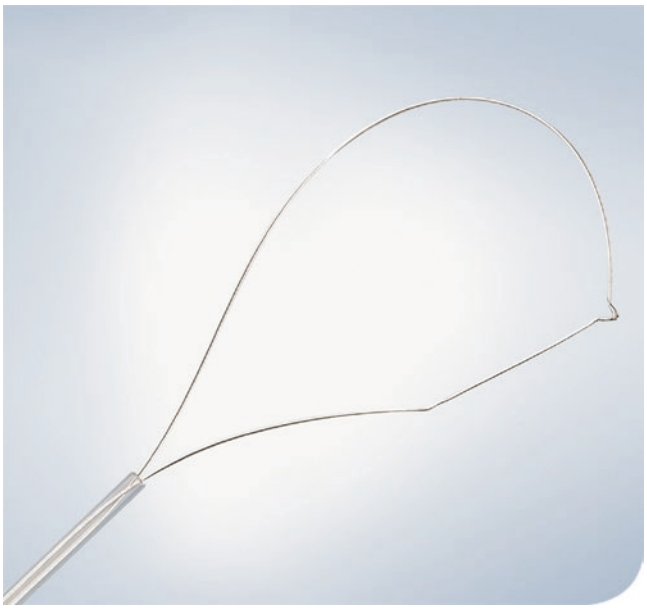

Fig. 7.17 Olympus crescent snare. Courtesy of Olympus

Fig. 7.19 Olympus EMR straight cap. Courtesy of Olympus

Fig. 7.18 Olympus EMR oblique cap. Courtesy of Olympus

Fig. 7.20 Roth Net

protrudes, which is ideal for the initial marking phase. The FlexKnife has a braided 0.8 mm cutting knife, with a looped tip at the end that can be adjusted to various lengths (Fig. 7.27). The HybridKnife has a central capillary within the cutting knife, which is 5 mm long, with 3 tip configurations: The I type is straight, with no added tip; the T type which features a non-insulated 1.6 mm in diameter disc shaped electrode, and the O type, which has an insulated dome-like tip (Fig. 7.28).

The next step of ESD is submucosal injection. An injection needle can be used for this. The ultrafine water-jet function of the HybridKnife can serve this function. There are many solutions used for this phase of ESD, and they all have their advantages and disadvantages. As in EMR, injection is used to bring the lesion forward to facilitate excision, and also to create a cushion to prevent perforation. In some ESD, solutions are also used to stain the deeper layers to aid in identification of the deep margin during the resection process. Normal saline is easy to inject and readily available, however is quickly absorbed, and therefore has a short duration of cushioning. Adding epinephrine theoretically will make the cushion last longer, as well as provide some hemostasis. This theory has not been substantiated in the literature [15, 16]. Hypertonic (3%) saline is easy to inject, readily available, and lasts longer, but can cause tissue damage and local inflammation. Hyaluronic acid is very long

Fig. 7.21 ConMed standard Nakao spider net

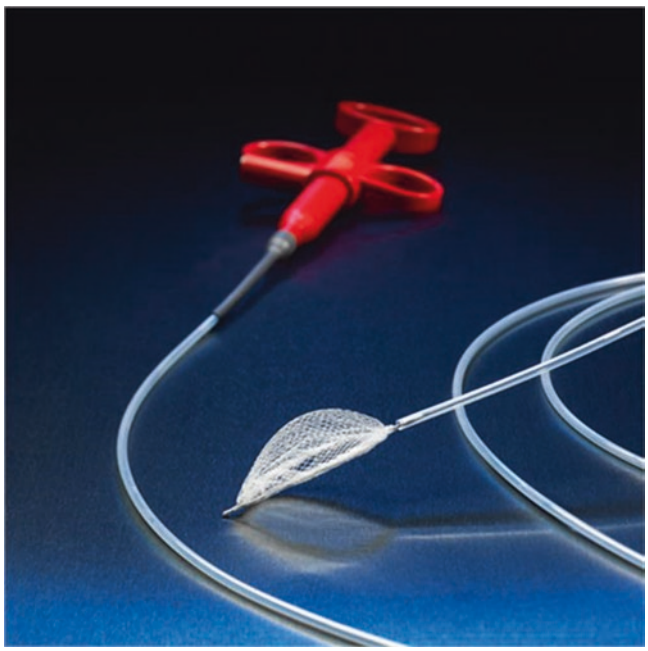

Fig. 7.22 Twister plus rotatable retrieval device. Courtesy of Boston Scientific

lasting, but not readily available, and is both very expensive and difficult to inject. Hydroxypropyl methylcellulose is long lasting as well, but again difficult to inject, and can cause tissue damage and a local inflammatory reaction. Indigo carmine or methylene blue is often added to the injection solution in order to clearly identify the limits of the submucosal layer.

Fig. 7.23 Olympus needle knife. Courtesy of Olympus

Fig. 7.24 Olympus hook knife. Courtesy of Olympus

The next step in this procedure is the circumferential incision into the submucosa. All of the knives previously mentioned can be used for this part of the procedure, as well as the IT (Insulated Tip) Knife. The ITKnife has a 4 mm long cutting knife and a 2.2 mm ceramic ball at the end to prevent cutting a deeper layer than desired (Fig. 7.29). The ITKnife 2 also has a triangular electrode under the electrode that aids in cutting (Fig. 7.30), and the ITKnife nano has a 3.5 mm long knife, and a 1.7 mm ceramic ball, a 0.9 mm circular electrode is recessed into the underside of the ceramic ball (Fig. 7.31). Any of the formerly listed knives can be used for the next segment: submucosal dissection.

Fig. 7.25 Olympus triangle tip knife. Courtesy of Olympus

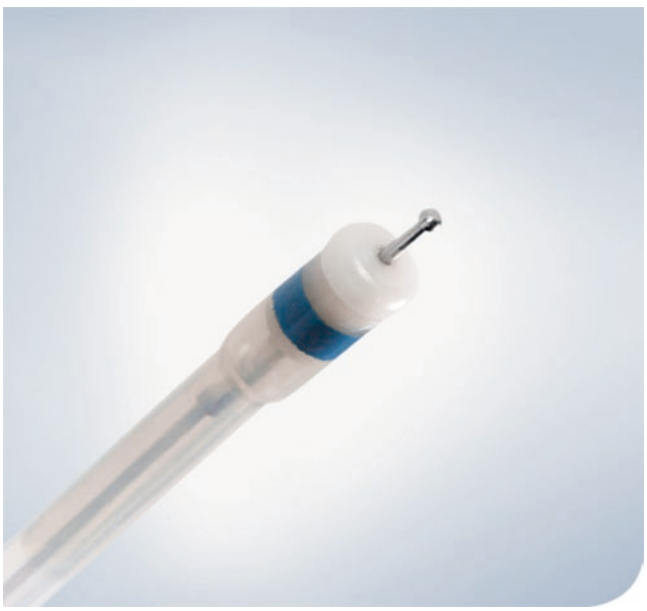

Fig. 7.26 Olympus dual knife. Courtesy of Olympus

Fig. 7.27 Olympus flex knife. Courtesy of Olympus

Fig. 7.28 ERBE hybrid knife. Courtesy of ERBE

For hemostasis, once the lesion is removed, any of the knives can be used, as well as the Coagrasper. The Coagrasper is a monopolar hemostatic forceps that features serrated jaws. This instrument has a 4 mm opening width to allow for more targeted coagulation, thus being effective for hemostasis without extensive thermal injury.

Caps are also available for ESD; they are particularly beneficial in maintaining visualization through the dissection phase of the procedure because it serves to keep the resected flap of mucosa off the endoscope lens. Some caps have drainage holes that allow water and blood to escape. Caps are available from many manufacturers in many sizes and have been discussed in the EMR section [17, 18].

Chromoendoscopy

Chromoendoscopy is the use of special dyes that are sprayed on the mucosal surface to enhance certain mucosal characteristics and facilitate identification of disease, more strategic biopsies, and complete removal of lesions. In order to perform chromoendoscopy, the endoscopist must have a spray catheter and appropriate stains. Spray catheters are available as single use and reusable from Olympus, Medivators, Cook Medical, Hobbs, and Nordson Medical, among others (Fig. 7.32). The use of high-resolution colo-

Fig. 7.29 Olympus IT knife. Courtesy of Olympus

Fig. 7.31 Olympus IT knife Nano. Courtesy of Olympus

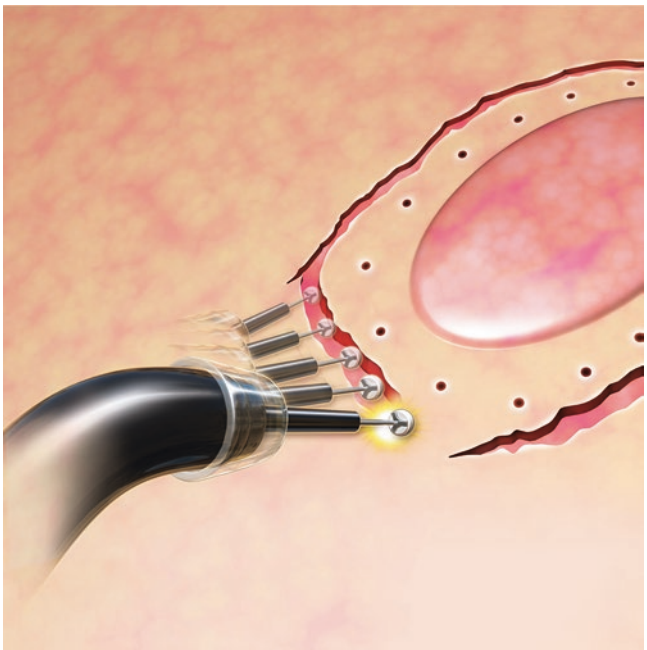

Fig. 7.30 Olympus IT knife 2. Courtesy of Olympus

Fig. 7.32 Olympus single use spray catheter. Courtesy of Olympus

noscopes with magnification increases the yield of the technique. The most common dye used in chromoendoscopy of the colon is indigo carmine. It is used to identify neoplastic lesions as well as the surveillance of chronic ulcerative colitis. The technique involves spraying the dye onto the mucosa and observing for pit patterns. Methylene blue staining involves the initial application of a mucolytic agent, 10% N-acetylcystine, followed by spraying of the dye, and then observation of the mucosa, flat lesions will be more easily visualized. Methylene blue can also aid in the ongoing surveillance of chronic ulcerative colitis [6].

Narrow Band Imaging (NBI) and Multiband Imaging (MBI)

The technology uses special endoscopes that are fitted with narrow bandpass filters in front of a conventional white-light source to produce the greatest contrast between vascular structures and the surrounding mucosa. NBI illuminates tissue at selected wavelengths of blue (415 nm) and green (540 nm), highlighting vascular detail. Blood vessels have a greater contrast to the surrounding mucosa, as the absorption

spectrum of hemoglobin matches the main peak and provides the vascular patterns that represent neoplastic lesions [1, 19]. A manufacturer of NBI capable endoscopes is Olympus, with the Elvis Extera (Olympus Medical Systems, Center Valley, PA). There is no additional technology necessary, the colonoscope is used in a standard fashion, and a button on the handle is depressed when NBI is desired. MBI is available in the Fujinon Intelligent Color Enhancement (Fujinon, Wayne, NJ) and the Pentax i-Scan (Pentax, Montvale, NJ). MBI processes the white-light image digitally, reconstructing it through software rather than a filter to enhance the appearance of the mucosa [1].

Confocal Laser Endomicroscopy (CLE)

CLE is a technology developed to obtain very high magnification and resolution images of the mucosal layer of the GI tract, termed "virtual histology." The goals for this technology are: to leave diminutive polyps in situ and reduce over treatment, to resect and discard small adenomas thus decreasing the cost of pathology, and to replace random UC biopsies with targeted biopsies primarily for inflammatory bowel disease. There are two FDA approved systems for CLE. Cellvizio confocal miniprobes (Mauna Kea Technologies, Paris, France) are probes that pass through the working channel of any endoscope; this requires a channel diameter of at least 2.8 mm (Fig. 7.33). This platform captures a video-like dynamic images at 9–12 frames per second. Endoscope-based CLE) uses an endoscope with a confocal microscope built into the tip (Pentax, Montvale, NJ), this system captures images at a rate of 1.6 frames per second. Endoscope-based CLE has a slightly higher resolution and a slightly larger field of view. At the present time, the Pentax Endoscope-based CLE is off the market and not available for purchase. A fluorescent contrast agent is needed for this study; intravenous fluorescein is most commonly used [20].

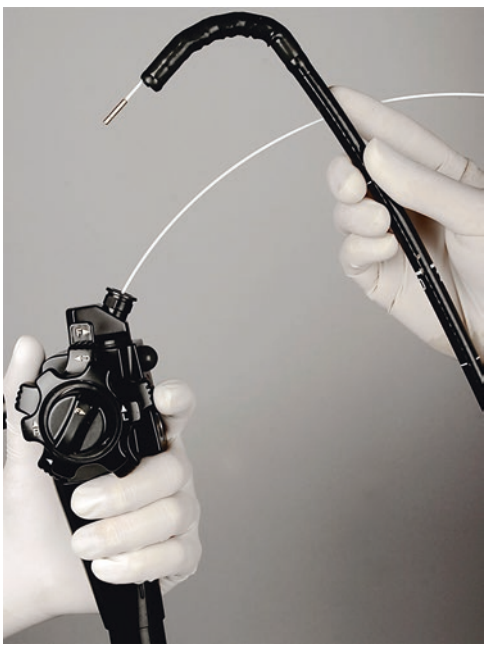

Fig. 7.33 Cellvizio. Courtesy of Mauna Kea Technologies

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Basic Colonoscopic Techniques to Reach the Cecum

8

W. Brian Sweeney

Key Points

- Anatomic variation is the norm—expect it and rely on landmarks and principles to safely complete colonoscopic examinations.
- Your preoperative preparation should focus on sedation, appropriate monitoring, and equipment check.
- Tip deflection, torque, and jiggle, hooking, slide-by, suction, and push/pull will help you navigate the twists and turns of the colon.
- Changing patient position, external compression, changing scopes, and the "elbow" trick are all adjuncts to achieving cecal intubation.

Introduction

One measure of a successful colonoscopy is the rate at which the endoscopist reaches the cecum. Cecal intubation rates of at least 90% for all colonoscopies and 95% for screening examinations are the expectation [1]. The goal of this chapter is to describe and illustrate techniques, maneuvers, and adjuncts that the endoscopist may find useful during the colonoscopic procedure. Colonoscopy is indeed an art and each endoscopist develops a style of their own using to some degree and at certain times the techniques and "tricks" reviewed.

Preprocedure Preparation

A complete colonoscopic examination to the cecum can be performed successfully with the patient receiving no, moderate, or deep sedation as well as a general anesthetic. The choice of level of sedation involves many factors but in general selecting some degree of sedation facilitates insertion of the colonoscope. The desire for no sedation by the patient tests the skills of the endoscopist and requires careful attention to maneuvers known to facilitate the exam. Deep sedation typically utilizing propofol has been shown to result in a 98% cecal intubation rate among experienced colonoscopists [2].

Currently, in most instances the patient receives a moderate level of sedation using a combination of a narcotic and a benzodiazepine. During moderate sedation (and certainly with no sedation), the patient will often feel some degree of cramping as the colonoscope is advanced as well as sense distention as air or CO_2 in insufflated. I find it helpful prior to sedating to invest a bit of time educating the patient about these sensations. Reassuring that these are normal and expected feelings, encouraging the passage of gas, and suggesting slow deep breathing during cramps versus breath holding and bearing down can be a simple way of facilitating a successful colonic examination.

The final preparation before even inserting the colonoscope through the anal canal and into the rectum involves proper instrument setup. Correct function of air/CO_2 insufflation, water irrigation, and suction should be demonstrated. Laying out, free of twists and loops, of both the insertion tube and the universal cord which connects to the light source ensures proper handling of the colonoscope during insertion (Figs. 8.1 and 8.2).

Technique of Insertion

Navigation of the large intestine from the anal canal to the cecum typically involves implementation of various maneuvers by the endoscopist. This section names these maneuvers and describes those situations where they may be of benefit. The following eight maneuvers will be discussed and illustrated: (1) tip deflection, (2) torque, (3) push/pull, (4) slide-by, (5) jiggle, (6) hooking, (7) suction, and (8) irrigation. Each of these skills are performed by the endoscopist with

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right hand holding the insertion tube and left hand holding the control section operating the deflection knobs, suction, air, and water.

Colonic anatomy is widely variable from patient to patient and is affected by inflammatory, neoplastic, functional (chronic constipation), congenital, and adhesive disease. Straight sections of the large intestine such as the rectum, descending and ascending colon may simply require insertion of the scope. The majority of the colon however consists of varying degrees of twists and turns necessitating colonoscope steerage. Tip deflection, torqueing, or a combination of the two allows steering of the colonoscope as it is advanced through these tortuous segments.

Tip Deflection

The control section held in the left hand has a large knob deflecting the tip vertically and a small knob deflecting laterally. Using these two knobs in combination permits tip deflection in all circumferential directions and at various angles of deflection up to slightly greater than 180° (Fig. 8.3). It is important to remember that depending on the particular endoscope in use, vigorous tip deflection may sweep quickly past the bowel lumen causing the tip to bounce from wall-to-wall making advancement difficult. Better to deflect the knobs in an unhurried and deliberate manner so as to not miss the lumen. Some endoscopists prefer to utilize the deflection knobs primarily rather than torqueing for steering the colonoscope. This requires periodic release of the insertion tube by the right hand in order to manipulate the deflection knobs with the right hand and the left thumb.

Fig. 8.1 Incorrect colonoscope set up

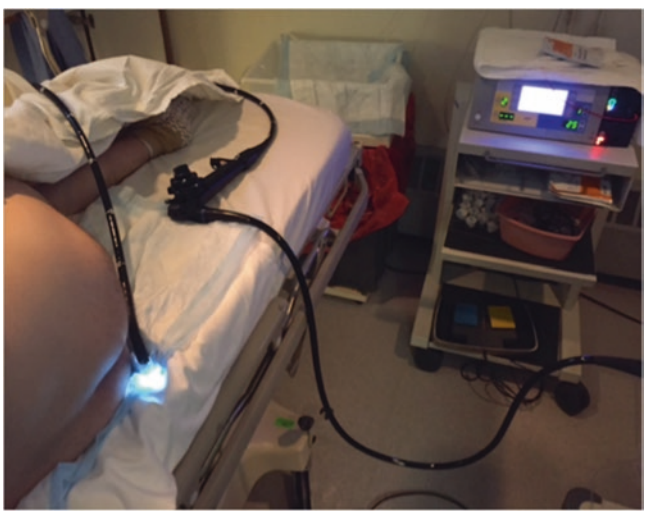


Fig. 8.2 Correct colonoscope set up

Torque

Torque is the application of a twisting force to the insertion tube of the colonoscope with the right hand. It is described as clockwise (twisting to the right) and counterclockwise (twisting to the left). When the tip is directed slightly upward or downward (using the left thumb), the application of torque has the effect of turning the colonoscope to the right or left without using the control knobs. Similarly, with slight right or left tip deflection, torque application steers up and down. Torque has the added benefit of adding a degree of "stiffness" to the insertion tube which may in turn minimize loop formation of the mobile colonic segments.

Push/Pull

Pushing forward or insertion of the colonoscope is ultimately the maneuver that produces advancement to the cecum. However, pushing forward also stretches the colon, especially in unfixed segments, namely, the sigmoid and transverse colon. Persistence in pushing causes further elongation or stretching and eventually a loop will form in the segment. The technique of push/pull involves pushing forward

Fig. 8.3 Tip deflection

followed by pulling back of the colonoscope. This has the effect of gathering or pleating of the colon over the colonoscope thereby shortening and straightening the colon (Fig. 8.4a–d).

Slide-by

The general rule when performing a colonoscopic procedure is to maintain visualization of the lumen at all times and to avoid the "red out" sign caused by the tip of the endoscope resting against the mucosal surface. At angulated locations or at the flexures, it may not always be possible to directly visualize the lumen despite attempts using tip deflection and torque. In these instances, the slide-by technique is utilized. The colonoscope is advanced slightly forward while steering in the anticipated direction of the lumen allowing the endoscope tip to gently slide along the mucosal surface (Fig. 8.5a). The key to this maneuver is deriving a strong impression as to which direction the lumen is truly located by visual clues. Demonstration of the site of proximal gas or liquid stool egress after suctioning provides a hint of lumen location. Anatomically, the inner circular smooth muscle of the colonic wall along with mucosal folds generates the appearance of a series of arcs visualized on the monitor (Fig. 8.5b). The imagined focal point of these arcs will point in the direction of the lumen. Slide-by is a skill that will be required and should always be performed with the utmost of caution and sensitivity for the amount of pressure exerted on the colonic wall. Any sensation of excessive force during insertion indicated by increasing resistance to insertion, stiffening of the deflection knobs, or white mucosal blanching demands withdrawal to avoid perforation.

Jiggle

Jiggle is produced by generating a series of rapid in and out movements with the right hand on the insertion tube. A clear lumen view is maintained at all times, and the distance of the

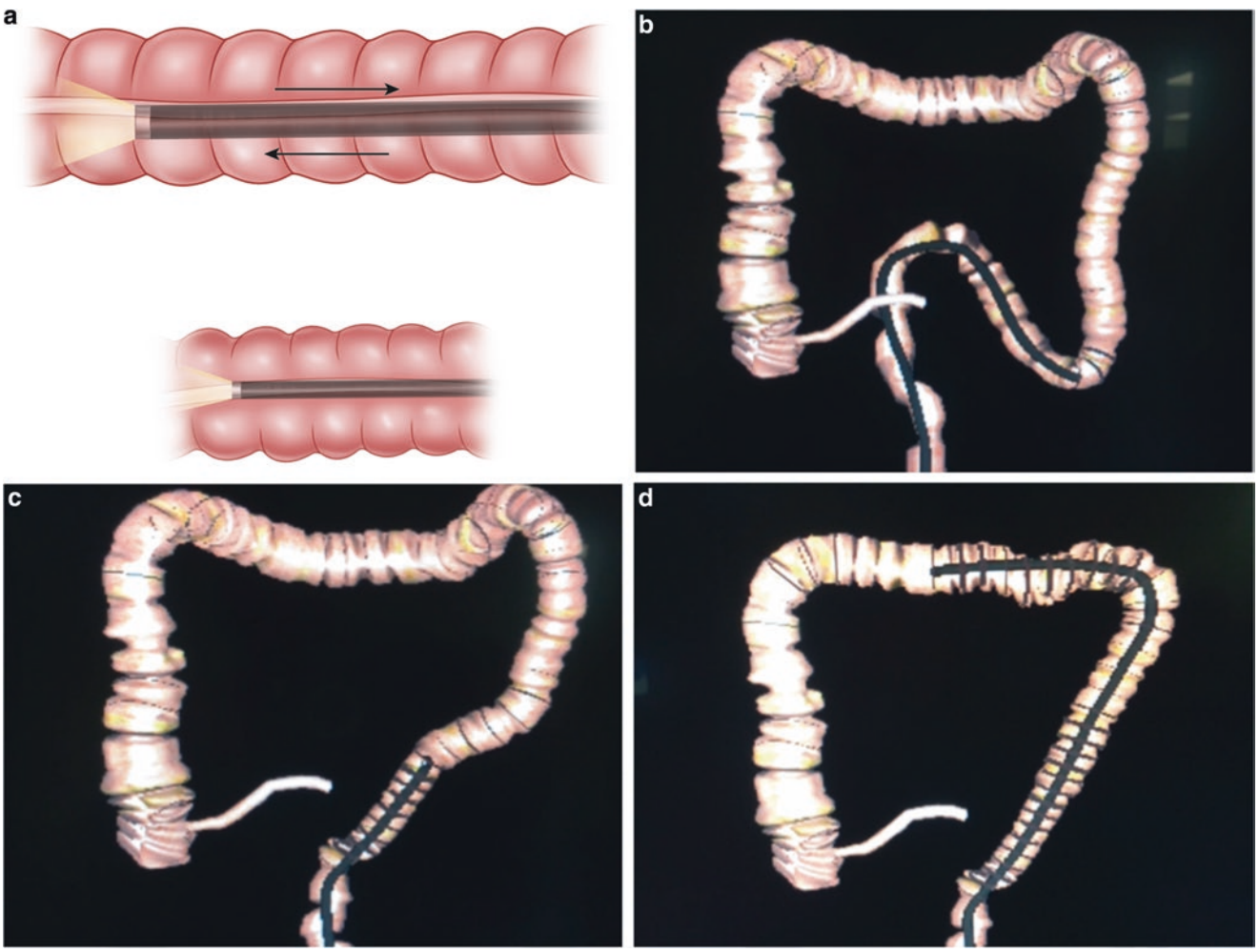


Fig. 8.4 (**a**–**d**) Push/pull

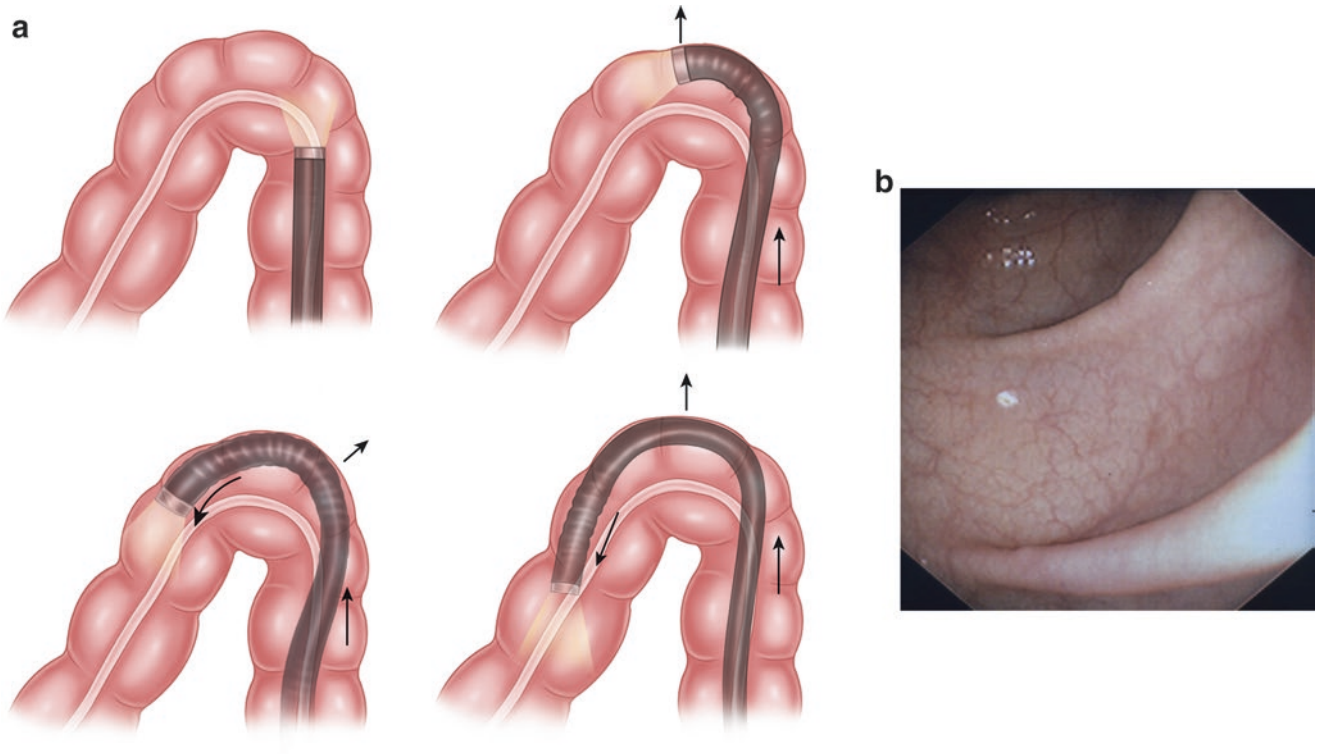


Fig. 8.5 (**a**, **b**) Slide-by

movement is short, ordinarily 5–10 cm. The effect of jiggling is to not only shorten the colon but also encourage the endoscope to "spring" forward when there is some degree of tension inherent to the insertion tube generated by some amount of loop formation. Jiggle is different from push/pull in that the latter is typically one event consisting of a longer distance of withdrawal. I have experienced that jiggle can also be an effective means to relax spasm or persistent peristalsis typically occurring in the sigmoid colon.

Hooking

Hooking is a technique designed to straighten a redundant or looped segment of colon without loss of progression of the tip of the colonoscope in the colon. As a flexure or angulation is approached, the tip of the colonoscope is deflected 90–120° to create a hook. With the "hook" held in position, the colonoscope is withdrawn a fair distance resulting in shortening the colon and loop reduction (Fig. 8.6a, b).

Suction

Insufflation using either air or CO_2 during a colonoscopic examination is essential for visualization. Because the colon is an elastic tube much like a slender balloon, continuous insufflation results in elongation—a greater anus to cecum length. Periodic suctioning in order to avoid unsuspected over distention is advised. The benefit of suction is often best seen when, after negotiating the hepatic flexure, the application of suction draws the cecum up to the tip of the colonoscope. This desired effect of suction can occur and I recommend should be applied routinely after negotiating each angulation and entering a new colonic segment.

Irrigation

Depression of the air/water button located on the control section held in the left hand causes water to stream across the "lens" and instill into the colon lumen. In addition, water or saline can be infused into the colon through the working channel by either syringe or a pump. Liquid infusion serves to lubricate the mucosa and facilitate tip passage, especially useful when the mucosa has a "sticky" appearance. The term water immersion colonoscopy refers to the procedure being performed during the injection of water or saline with a liquid infusion pump. In addition to lubrication, benefits include relief of spasm and straightening of the colon. The weight of the infused colon is said to "sink" to a dependent position and be less likely to elongate. Water immersion colonoscopy has

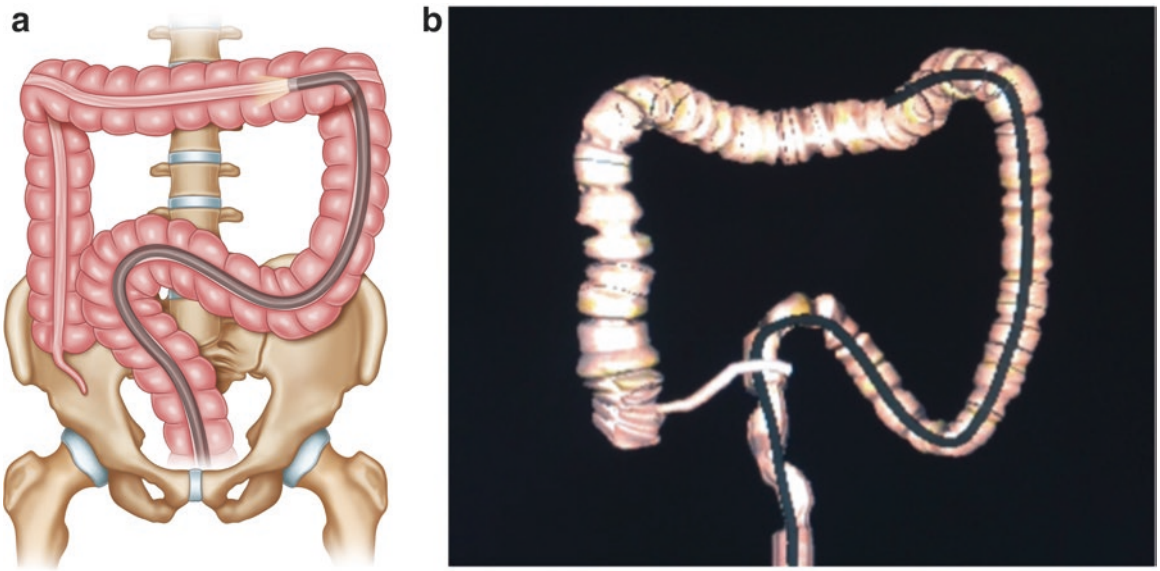


Fig. 8.6 (**a**, **b**) Hooking

been shown to decrease the time required to reach the cecum as well as reduce pain in patients receiving minimal or no sedation [3, 4].

Intubation of the Terminal Ileum

While insertion of the tip of the colonoscope through the ileocecal valve and into the terminal ileum is not mandatory for a complete and thorough examination, it may be desirable in patients with gastrointestinal bleeding and known or suspected inflammatory bowel disease. I recommend attempt at terminal ileal intubation in the majority of procedures so as to gain and maintain the necessary skill required in those cases where ileal visualization is desired. An added benefit from making the effort at ileal intubation is the thorough evaluation of the mucosa behind the valve in the cecum, a relative "blind spot."

The ileocecal valve is typically located 5 cm from the base of the cecum and appears as a prominent and sometimes bulbous fold. The actual orifice of the valve may not be obvious. Looking into the cecum and applying short bursts of suction often will pinpoint the valve orifice as gas or liquid stool will be seen squirting into the cecum. Intubating the valve requires passing the colonoscope tip beyond the valve into the cecum, flexing the tip 90° in the known direction of the valve and slowly withdrawing the scope (Fig. 8.7a–e). Once the tip has encountered the orifice, gentle puffs of air may help to open the valve and allow the tip to enter. More often than entering the ileum, the colonoscope tip slips off to one side or another. With skill practice, success rate will improve.

Challenges to Colonoscope Insertion

This section presents typical challenges that can make insertion of the colonoscope difficult. Angulated colons, redundant colons, hernias, looping, and extensive diverticulosis all can make for a tough examination. Adjuncts to the eight maneuvers previously discussed will then be described and illustrated as options for overcoming these challenges.

Every colon has a varying number of turns each at various degrees of angulation (Fig. 8.8). Some of these turns are at typical anatomic locations such as the rectosigmoid junction, the sigmoid-descending junction, and the splenic and hepatic flexures. Other angulations may be present secondary to adhesions from prior abdominal surgery, especially pelvic, or as a result of inflammatory processes notably diverticulitis. Redundant colons, often the result of chronic long-standing constipation, pose the challenge of numerous turns but also a length that may result in "running out" of scope (Fig. 8.9). It is in the patient with extreme redundancy that maneuvers to shorten the colon (push/pull, hooking) are imperative.

Unrecognized ventral and inguinal hernias, while not particularly common, can be a disaster if the colon is located in the hernia or made to enter the hernia by the procedure itself. Recognition of hernias through the history or by physical examination allows for manual reduction and support of the hernia site by an assistant during insertion (Fig. 8.10). If when inserting the colonoscope undue resistance is encountered without the sense that a loop has formed, consider the possibility of a hernia and palpate the groins (Fig. 8.11a, b).

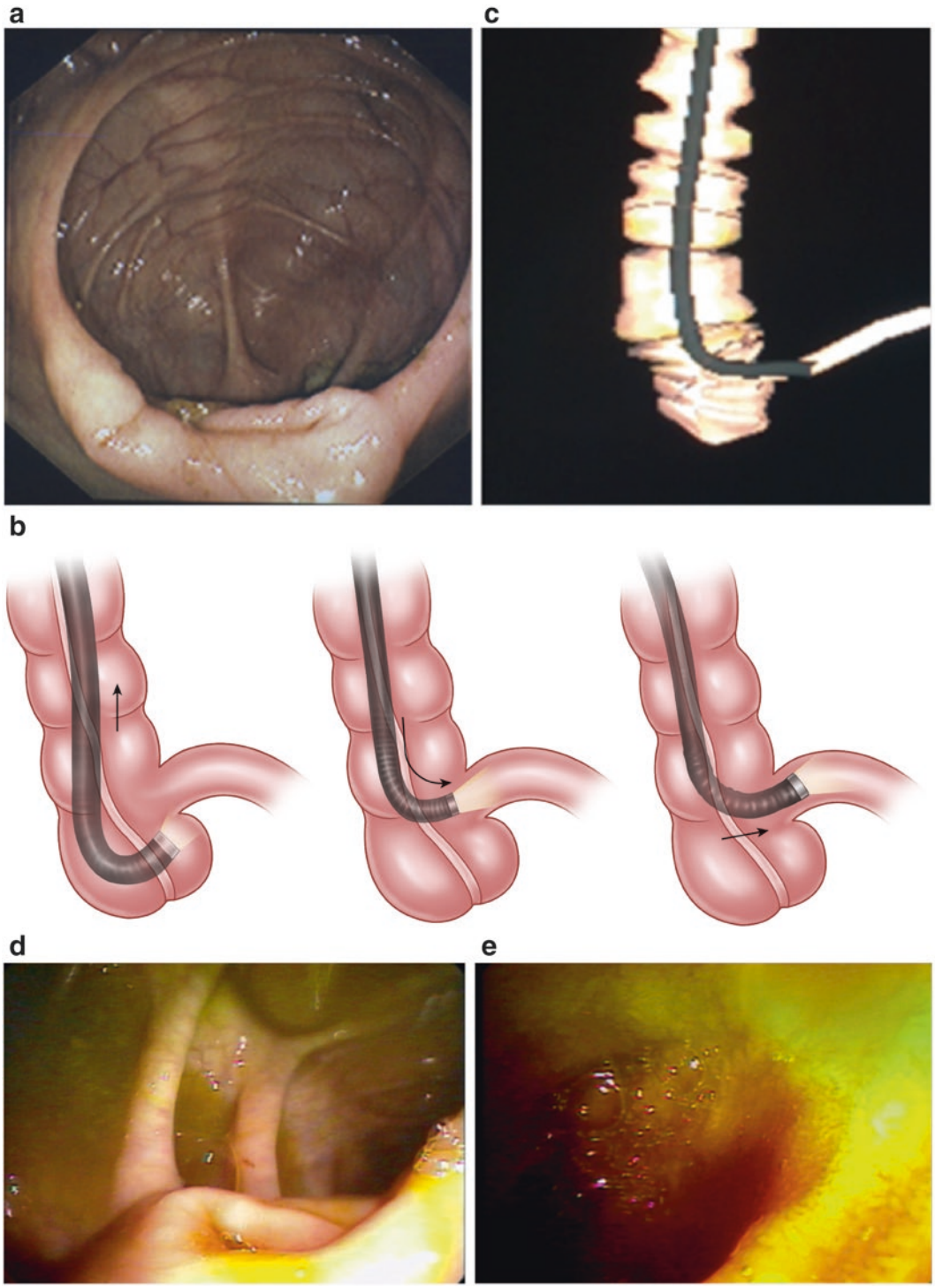


Fig. 8.7 (**a**–**e**) Terminal Ileum

"Looping" of the colonoscope, and by requisite the colon containing the scope, is a common challenge that occurs universally in varying degrees. Insertion of a floppy tube (the colonoscope) into a floppy tube (the colon) is a set up for loop formation. The floppier or more mobile the colonic segment, the more likely a loop will begin to form; hence, the sigmoid and transverse colon loops (Figs. 8.12 and 8.13). In most colonoscopic examinations, a complete 360° loop formation does not occur; rather, various degrees of stretching or bowing of the colonic segment ensues (Figs. 8.14 and 8.15). Looping is recognized by stiffening of the deflection knobs, failure of tip progression or even paradoxical backward

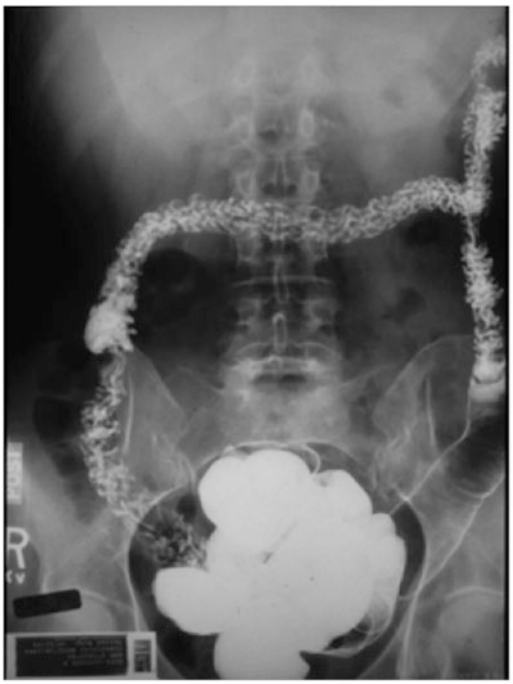


Fig. 8.8 Angulated colon

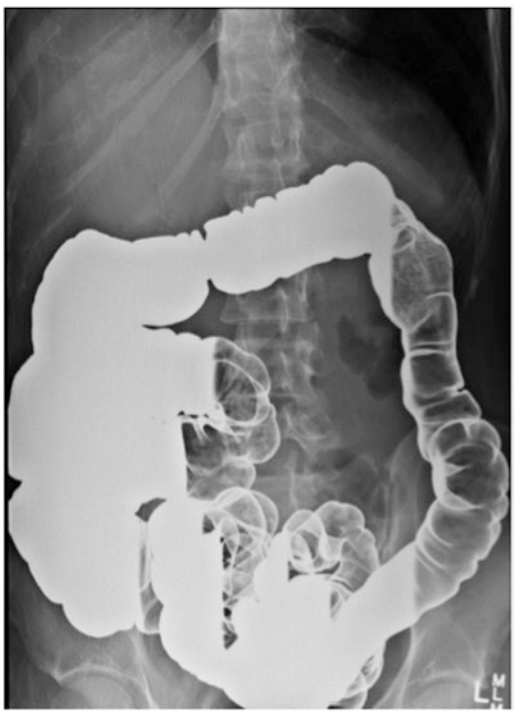


Fig. 8.9 Redundant colon

motion during attempted insertion, and finally, patient discomfort. Further insertion can indeed create the complete 360° loop and potentially damage the colonic wall. It is at this point that the endoscopist implements straightening and loop reduction maneuvers—jiggle, push/pull, hooking, and most

Fig. 8.10 Ventral hernia

effectively withdrawal combined with application of torque (typically in a clockwise direction). Reformation of the loop or bow after repeated attempts at insertion calls for the application of abdominal compression.

Diverticulosis is extremely prevalent during colonoscopic examinations, and it seems their presence is the rule rather than the exception. In most cases, the diverticular openings are few and scattered; however, they can be extensive and quite large making navigation and identification of the true lumen difficult (Fig. 8.16). It is important to traverse these segments slowly looking for clues such as gas and liquid intestinal contents passing distally from the true lumen. Additionally, the diameter of the opening may not be helpful as the true lumen may actually be smaller than the diverticular orifices.

Adjuncts to Colonoscope Insertion

Abdominal compression is the application of external force by the hand or hands of an assistant on a portion of the abdominal wall in order to splint a redundant segment of colon and prevent stretching and looping. In order for abdominal compression to be effective, the loop or bow needs to be completely reduced by endoscope withdrawal. A stretch of the sigmoid colon is typically palpated and thereby compressed by applying support in the left lower quadrant. With the patient in the left lateral decubitus position, the assistant "lifts" the left lower quadrant up and compresses toward the spine (Fig. 8.17). Compression of a transverse colon stretch or loop is best performed with the patient supine and the assistant applying pressure near the umbilicus and directing the force to the epigastrium (Fig. 8.18). These locations are a start and may need to be modified based on trial and error. In those situations where progress has been made to near the hepatic flexure but then stalled because of

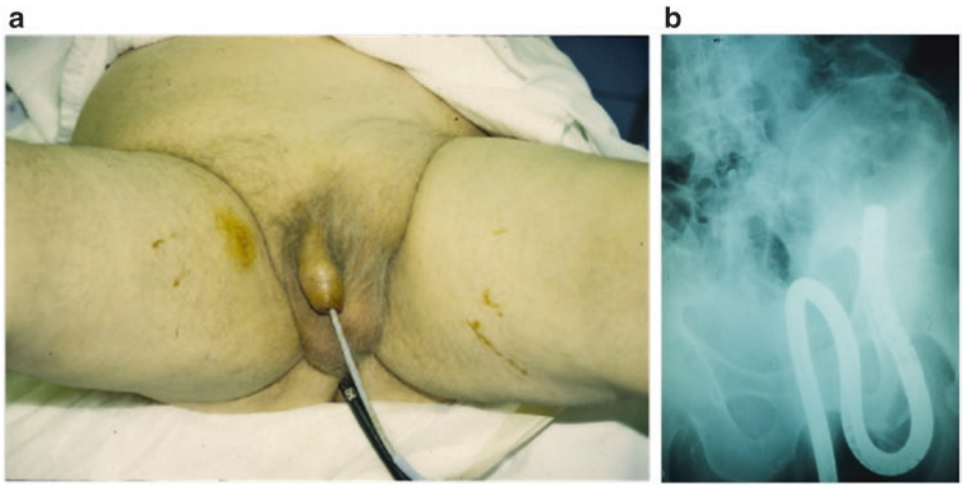


Fig. 8.11 (**a**, **b**) Inguinal hernia

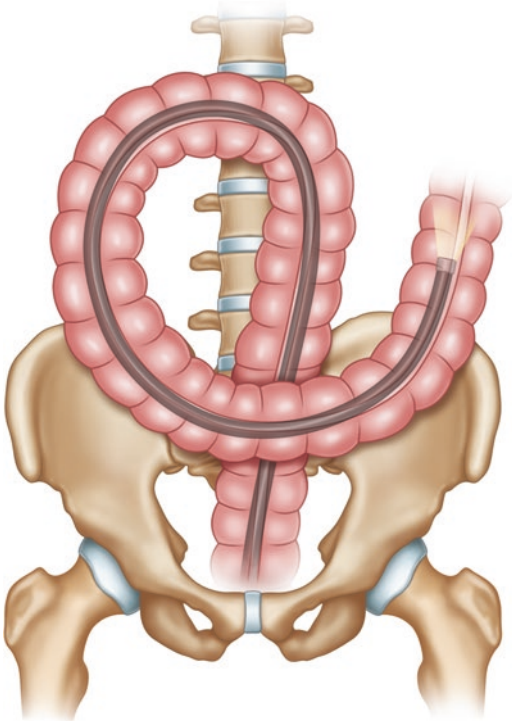


Fig. 8.12 Sigmoid colon loop

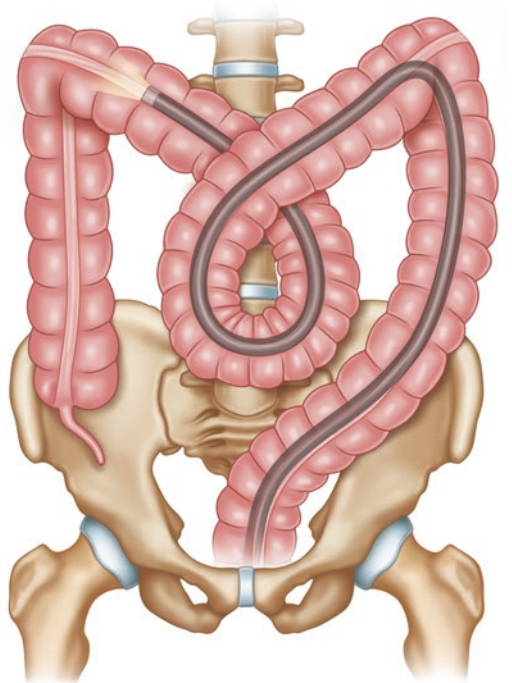


Fig. 8.13 Transverse colon loop

stretching or looping, I find the "elbow trick" to be of benefit. With the patient supine and all loops reduced by endoscope withdrawal, the endoscopist applies pressure in the region of the umbilicus with the left elbow (Fig. 8.19). The concept of this maneuver is that the elbow splints both the sigmoid and transverse colon allowing the endoscope to pass easily to the base of the cecum.

Newer colonoscopies are equipped with a stiffening system which when applied increases the stiffness of the insertion tube in hopes of preventing bowing and looping. Varying degrees of stiffness can be applied typically when there is difficulty navigating the transverse, hepatic flexure, and ascending colon (Fig. 8.20).

The use of patient breathing or breath holding is a simple adjunct tried when there is some difficulty negotiating the splenic or hepatic flexures. The rationale is that when a patient takes a deep breath and holds it, the diaphragm descends thereby pushing the flexures over the tip of the colonoscope. Its effectiveness is debatable but, since it is simple, it may be worth trying.

Having the patient change position in order to facilitate proximal passage of the colonoscope is another adjunct. This option is best utilized in exams performed under no or moderate sedation. Although not out of the question, moving patients under deep sedation is not always simple. Patients start in the left lateral decubitus position (Fig. 8.21). Rolling

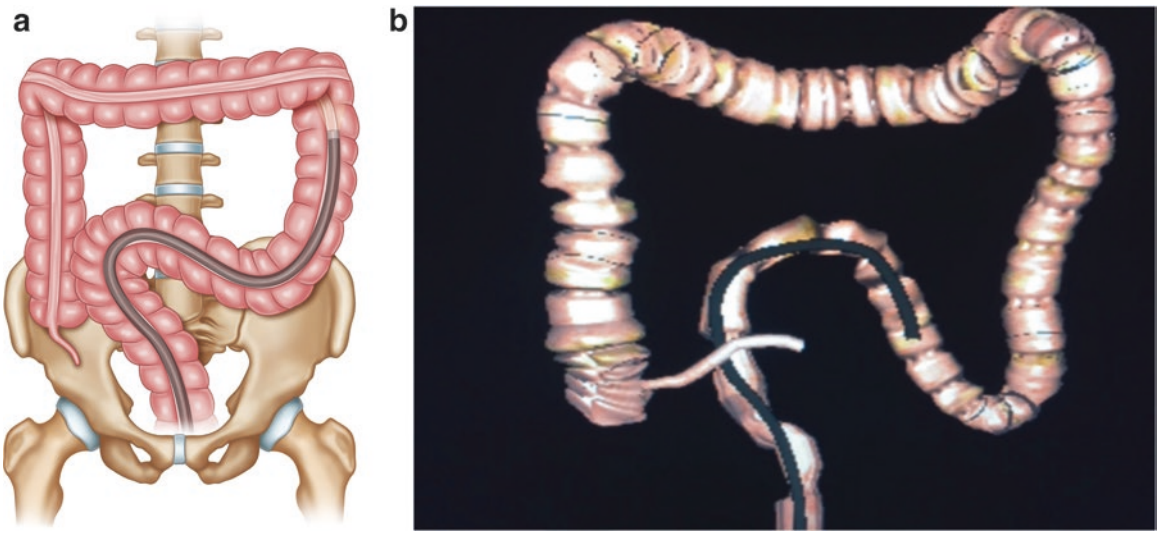


Fig. 8.14 (**a**, **b**) Sigmoid colon stretch

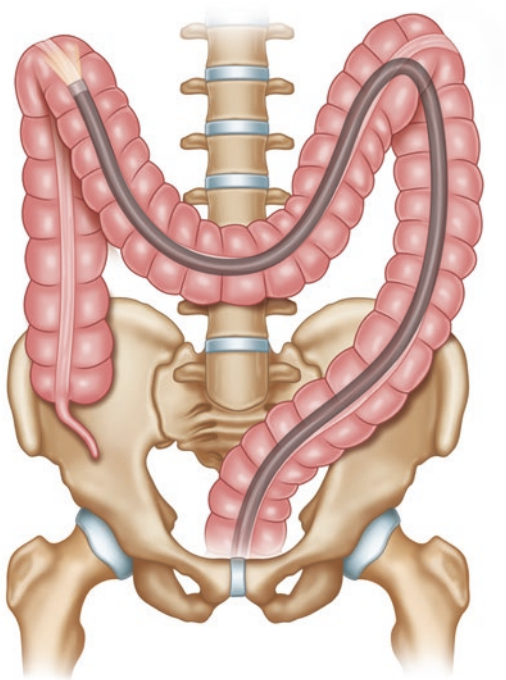


Fig. 8.15 Transverse colon stretch

supine often helps when difficulty is encountered inserting into the transverse and ascending colon. The supine position also affords the ability to perhaps more precisely locate and reduces loops. Having the patient roll onto the right side may possibly assist the tip of the scope to enter the base of the cecum in those procedures where only a few centimeters are required and all other maneuvers have failed. The prone position is a bit awkward, rarely if ever used, but has the possibility of splinting the entire colon by the patient's own body weight thereby preventing loops.

There has been a trend among endoscopists to routinely use the pediatric colonoscope because of its smaller diameter (11.3 mm) as compared to the standard adult colonoscope (13.3 mm) (Fig. 8.22). The pediatric colonoscope has proven value for not only traversing strictures but also for negotiating fixed angulations [5]. It has been well documented that this small diameter colonoscope is able to pass through the sigmoid colon in cases where expert endoscopists failed using the standard adult colonoscope [6]. The pediatric colonoscope is more flexible which indeed may desirable but also translates into a greater ease of loop formation. In addition, the therapeutic channel has a diameter of 2.8 mm as opposed to 3.2 mm in the standard adult colonoscope making suction perhaps less efficient and limiting the use of some instruments and devices. Because my style is to use less torque during insertion, I prefer the stiffer adult colonoscope and consider use of the pediatric colonoscope in cases of fixed angulation of the sigmoid colon often encountered in patients with extensive diverticular disease and women who have undergone pelvic surgery.

When All Else Fails

It is important to understand that even highly expert, well-seasoned endoscopists fail to reach the cecum in a small number of attempts [7, 8]. Although aborting the examination will be documented as a "failure" on the procedure report and by those gathering quality data, more often than not discontinuing further attempts demonstrates wisdom and good judgment.

Radiologic evaluation of the large intestine is recommended after failure of endoscopic exam by either air contrast barium enema or CT colonography. Performing the

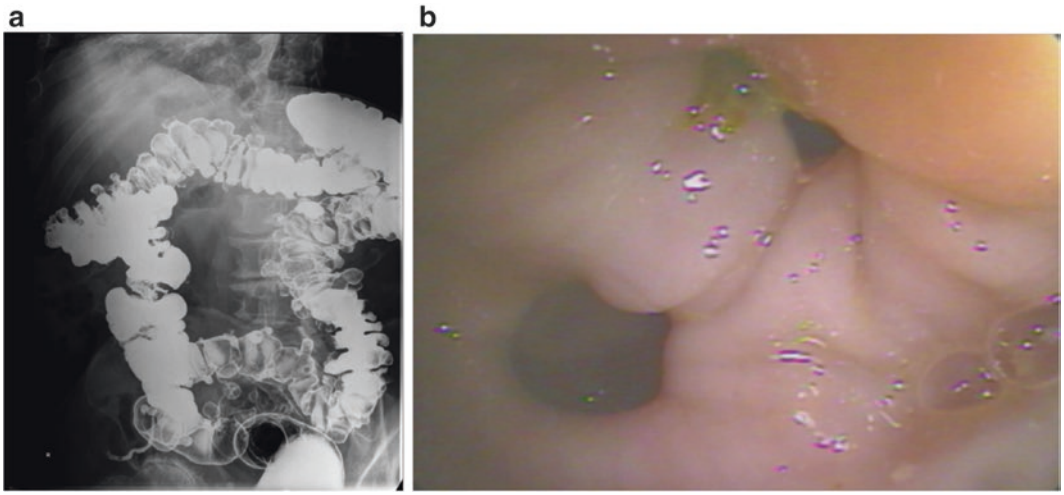
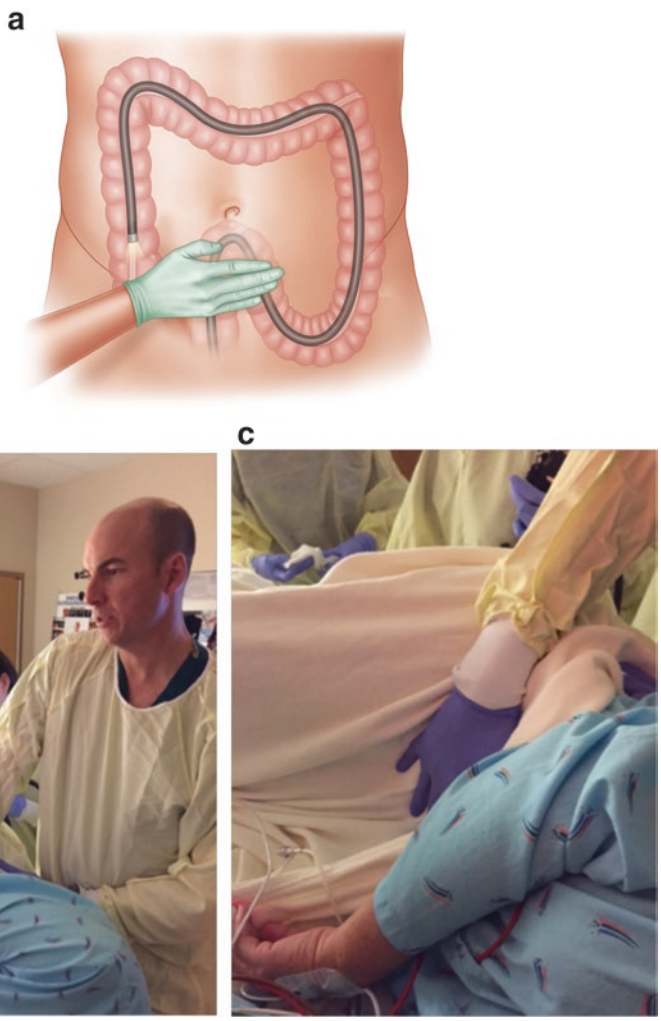


Fig. 8.16 (**a**, **b**) Extensive diverticulosis

Fig. 8.17 (**a**–**c**) Sigmoid support



exam in the operating room under general anesthesia, intraoperative colonoscopy, has been utilized for some time in cases where there was inability to fully colonoscope in the endoscopy suite [9, 10]. A recent version of intraoperative colonoscopy combining laparoscopic evaluation and mobilization of the colon has been termed CELS (Combined

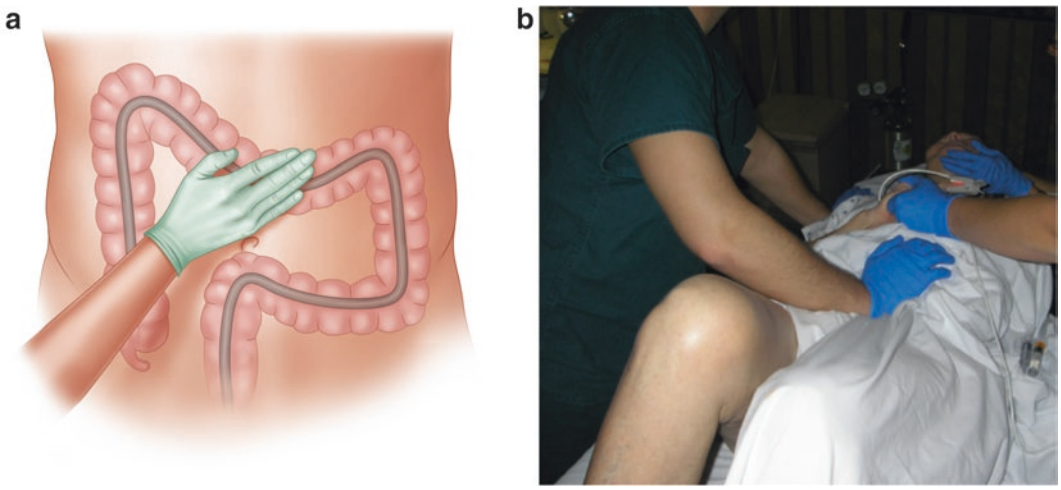


Fig. 8.18 (**a**, **b**) Transverse support

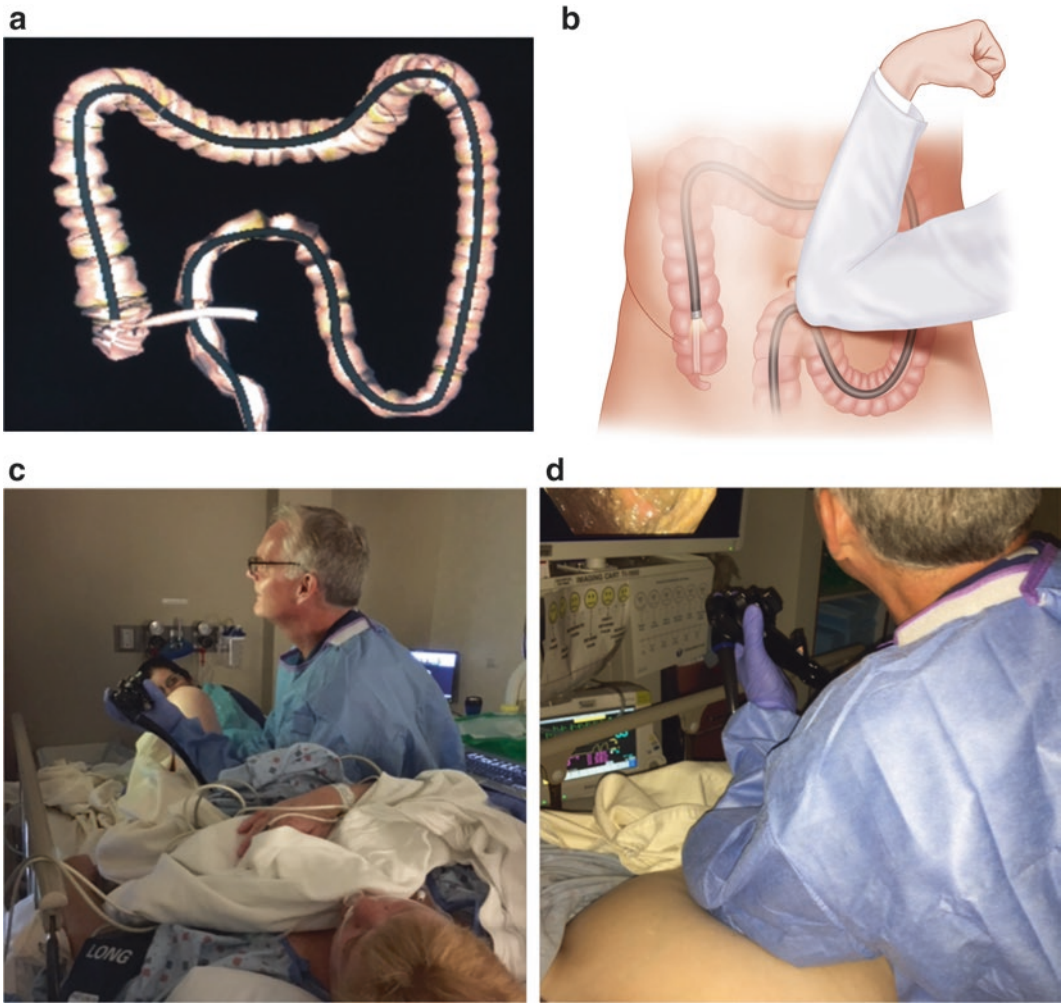


Fig. 8.19 (**a**–**d**) "Elbow trick"

endoscopic and laparoscopic surgery) [11]. CELS offers an alternative to bowel resection in select patients with polyps that are not amenable to or have failed standard colonoscopy. This technique could also be an option in a patient who has failed standard colonoscopy despite all maneuvers and has been demonstrated to have a worrisome radiologic finding.

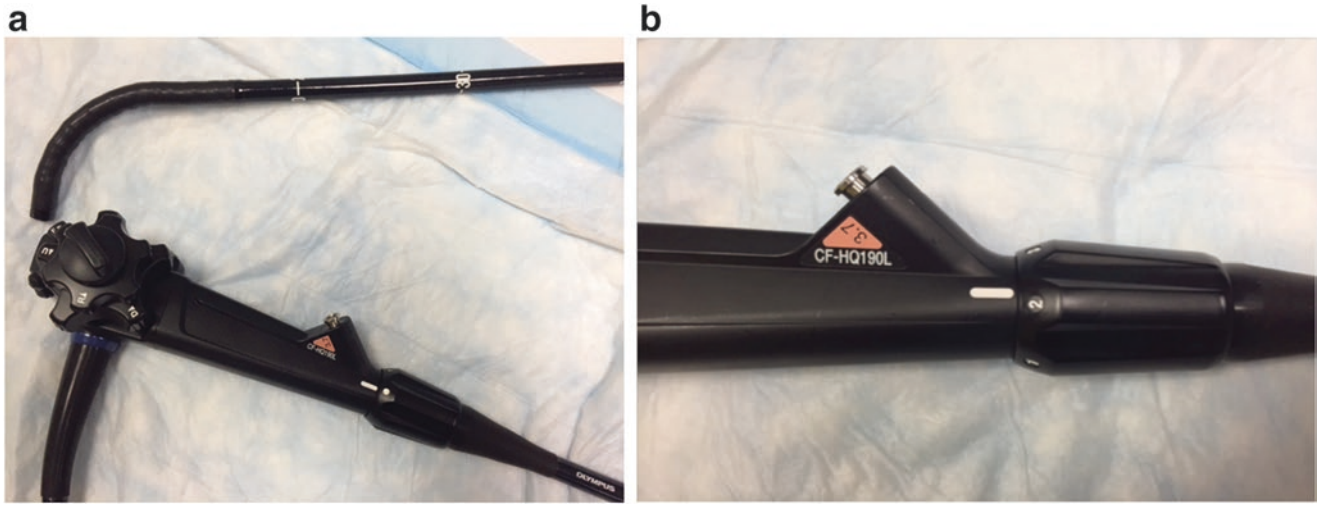
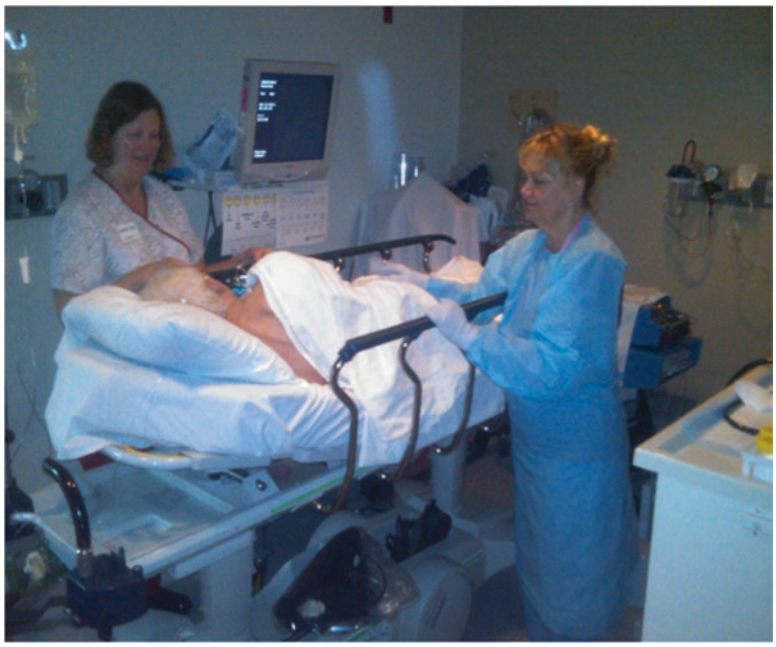


Fig. 8.20 (**a**, **b**) Stiffener

Fig. 8.21 Left lateral decubitus position



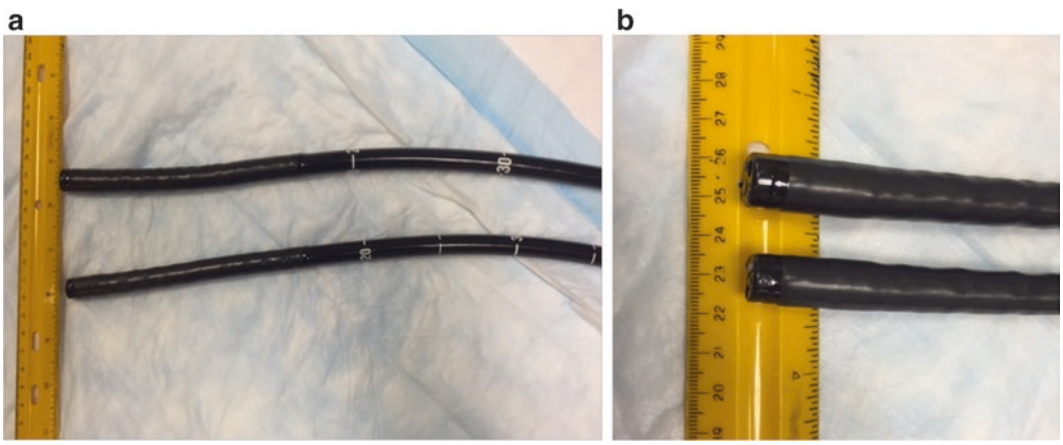


Fig. 8.22 (**a**, **b**) Adult and pediatric colonoscope diameters

Conclusion

The aim of this chapter was to offer, through description and illustration, maneuvers and adjuncts that may be of benefit to the endoscopist during colonoscope insertion with hope of achieving a high rate of cecal intubation. General principles of safe and effective insertion include: controlled tip deflection combined with torque application for steering, awareness of loop formation and mitigation, straightening and shortening the colon, optimal air insufflation, use of patient positioning and abdominal compression, and finally, knowing when to abort so as to do no harm. Familiarity and experience with the techniques reviewed is the path toward becoming expert in an often challenging procedure called colonoscopy.

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Basic Colonoscopic Interventions: Cold, Hot Biopsy Techniques, Submucosal Injection, Clip Application, Snare Biopsy

9

Steven A. Lee-Kong and Daniel L. Feingold

Abbreviations

EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
NCCN	National Comprehensive Cancer Network

Key Points

- Age-appropriate colorectal screening can reduce the risk of colorectal cancer by removal of premalignant adenomatous polyps.
- Polypectomy techniques must be tailored to the anatomy and location of the polyp.
- A variety of polypectomy or biopsy instruments (biopsy forceps, snares, nets, etc…) must be readily available at the time of colonoscopy as to avoid delays in treatment or need for repeat procedures.
- The endoscopist must be comfortable using instruments commonly used for removal of difficult polyps.
- Management of anticoagulants and antiplatelet agents are at the discretion of the endoscopist.
- Lesions concerning for malignancy should be endoscopically marked with permanent ink to facilitate identification of the site if future endoscopic or surgical treatment is contemplated.
- Incomplete polypectomy must be managed with a repeat attempt at endoscopic removal or surgical intervention for complete excision of the adenomatous tissue.

Introduction

The premise that colon and rectal cancers are preceded first by the development of benign adenomatous polyps was first proposed by Lockart-Mummary in 1927 [1]. Early clinicians posited that by removal of these premalignant lesions, one might prevent that polyp from developing into a cancer. Interest in removal of premalignant adenomatous polyps continued to grow as more physicians began advocating for endoscopic screening of the colorectum, with the intention of diagnosing and preventing the development of colon and rectal cancer.

Before the development of flexible endoscopes, rigid sigmoidoscopes were infrequently utilized for both colorectal cancer detection and prevention by polypectomy. A large population-based study at the University of Minnesota published early results with this method of screening [2]. This was repeated at the then Memorial Hospital in 1960, demonstrating a survival benefit for those patients screened by this method [3]. While effective, rigid sigmoidoscopy can be uncomfortable both for the patient and the physician. Expertise in its use was not widespread.

Wolff and Shinya first reported the use of a fiber optic colonoscope in 1960 for endoscopic screening of the colorectum and polypectomy, ushering in a new era in colorectal cancer diagnosis and prevention [4]. Multiple randomized controlled trials of screening colonoscopy in asymptomatic patients yielded significant reductions in colorectal cancer-related mortality [5–7]. In part due to the results of these and other studies, colonoscopy was included as a screening recommendation by the American Cancer Society and others [8].

The popularization of screening colonoscopy for the removal of precancerous adenomatous polyps, and the demonstrated reduction in the incidence of colorectal cancer, is

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one of the greatest examples of how widespread implementation of cancer-screening initiatives can have a meaningful public health impact [9].

Indications

National Comprehensive Cancer Network (NCCN) Guidelines Version 1.2015 suggests screening colonoscopy for all "average risk" individuals. Average risk is defined as all patients age 50 years or older who have no history of prior adenoma, sessile serrated polyp or colorectal cancer, no history of inflammatory bowel disease and no family history of colorectal cancer [10]. Patients with negative examinations should be rescreened 10 years after the index examination. Patients at increased risk of adenomatous polyps or colorectal cancer should be screened with increased frequency [10]. Any patient found to have an endoscopically resectable adenomatous polyp should undergo polypectomy by whichever technique available to ensure complete removal.

"Cold" Forceps Polypectomy/Biopsy

Perhaps the simplest method to remove small adenomatous polyps during colonoscopy is with a cold biopsy forceps. These flexible devices are usually less than 3 mm in diameter and are easily advanced via the working channel of the colonoscope. These are passed under direct vision and with an assistant operating the open/close mechanism. The jaws of the device are opened and closed over the polyp. With a quick "snap" of the wrist, the forceps are quickly withdrawn away from the mucosa, successfully removing the polyp without undue trauma to the remaining healthy surrounding mucosa. This can be performed a number of times, removing polyps "piecemeal" if needed. A needle at the end of the device keeps the excised tissue from falling out of the jaws of the forceps (Fig. 9.1 and Video 9.1). A number of companies specializing in endoscopic devices manufacture polypectomy/biopsy forceps with a variety of jaw sizes. The authors recommend that the endoscopist become familiar with the equipment available at his or her institution and ensure that commonly requested forceps be immediately available at the time of colonoscopy. Some studies suggest that the use of standard cold forceps is associated with significant rates of incomplete polypectomy (leaving residual adenomatous tissue in situ) [11, 12]. Forceps with small jaws may not be large enough to trap an entire polyp, and jumbo forceps may be required to ensure complete polyp removal. While standard size forceps may be able to remove a polyp of up to 3 mm in size in a single bite, a jumbo size forceps may be required to remove slightly larger lesions. The use of forceps may simplify polypectomy in difficult locations (behind folds, at the ileocecal valve and in the most distal rectum), where snare use may be hampered.

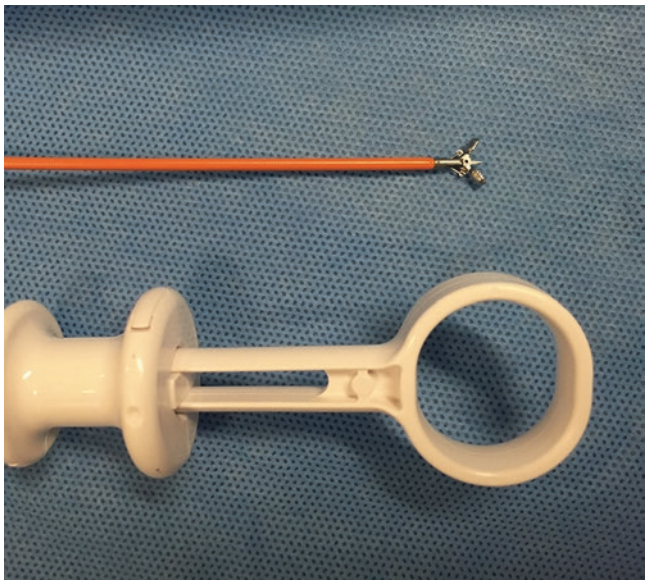

Fig. 9.1 Jumbo biopsy forceps

A recent meta-analysis investigated the role of cold forceps polypectomy during screening colonoscopy has been performed. Five randomized controlled trials, which included 668 patients in total, were analyzed. Use of a jumbo forceps or cold snare was associated with a lower rate of incomplete polypectomy when compared to "standard" cold forceps polypectomy [13].

"Hot" Forceps Polypectomy/Biopsy

Thermal energy can be applied to endoscopic forceps at the time of polypectomy or biopsy. Using the same principles and techniques described above for "cold" polypectomy/biopsy, monopolar electrocautery can be applied to enhance hemostasis and thermal destruction of the remaining margin of resected tissue. The theoretical benefit of this polypectomy technique has never been definitively proven. Additionally, the quality of the resected specimen can be degraded by cautery artifact, making histologic assessment by the pathologist difficult [14]. If polypectomy by forceps is thought to be appropriate given the size of the polyp, the authors recommend using a jumbo size forceps. Patients usually have a grounding pad applied to the mid-thigh before the procedure begins or when the decision is made to proceed with hot forceps polypectomy.

Submucosal Injection

The injection of liquid into the submucosal plane beneath a polyp may aide in adequate and complete endoscopic polyp excision and is essential to the techniques of endoscopic

mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Submucosal "lifting" of the target lesion off of the deep submucosa and muscularis propria is thought to minimize transmural damage to the bowel wall and thus perforation. Further, this may also allow for more complete adenomatous tissue removal and minimize local recurrence. The injectate is delivered endoscopically via a flexible needle, which is passed through the working channel of the colonoscope (Fig. 9.2 and Video 9.2).

Lesions that do not lift appropriately despite injection may indicate invasion of the submucosa or muscularis propria by an invasive cancer focus within the lesion. In the case of prior attempts at polypectomy, the resultant fibrosis and scarring within the adenomatous polyp may also prevent adequate lifting. Thought must be given to endoscopic attempts at polypectomy of lesions that do not lift appropriately after submucosal injection or lesions that have an ulcerated component. Various substances are currently used for submucosal injection. The cheapest and most readily available is normal saline. Other commercially available injectates are also used, including glycerol, hyaluronic acid, succinylated gelatin, and hydroxyethyl starch (Hetastarch). Colored compounds such as methylene blue, indigo carmine, or dilute India ink can also be used both for submucosal lifting of the lesion and tattooing (Video 9.3) for future site identification.

While normal saline is the cheapest and most readily available substance for this purpose, use is limited to procedures for which prolonged submucosal lift is not needed. Normal saline rapid clearance from the submucosal plane makes it unsuitable for procedures such as EMR or ESD. A recently presented meta-analysis demonstrated higher rates of en bloc resection and lower rates of residual tissue remaining using a viscous solution versus normal saline [15]. Another recent meta-analysis comparing various solutions to normal saline demonstrated equivocal results, likely due to a lack of standardized injectates between the individual randomized trials [16].

In summary, submucosal injection with normal saline or other solution should result in adequate lift of the adenomatous polyp to facilitate endoscopic polypectomy. Lesions that do not lift adequately with appropriate injection technique may be indicative of invasion from an occult cancer or excessive fibrosis from prior attempts at polypectomy or biopsy.

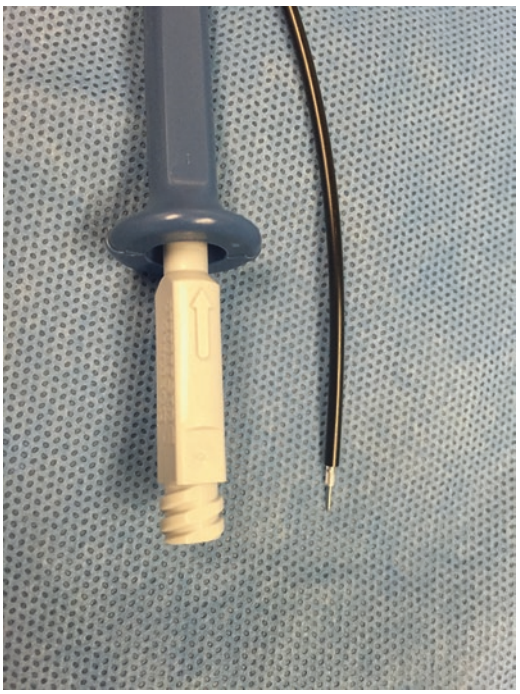

Fig. 9.2 Endoscopic injection needle

Clip Application

The availability of endoscopic clips has increased in recent years. Both through-the-scope and over-the-scope devices are commercially available to endoscopists for use during colonoscopy (Fig. 9.3, Video 9.4). Reported uses include rendering polypectomy sites hemostatic, closure of colonic perforations, and mucosal approximation after EMR or ESD [17]. Studying mucosal healing after advanced polypectomy, 28 patients were randomly assigned to clip closure of the polypectomy site versus leaving the wounds open. At 4 weeks, the patients who underwent clip closure had a significantly higher rate of mucosal healing than those who were not closed [17]. While the clinical significance of this is unclear, endoscopists should become facile at the use of endoscopic clip placement, should the need arise.

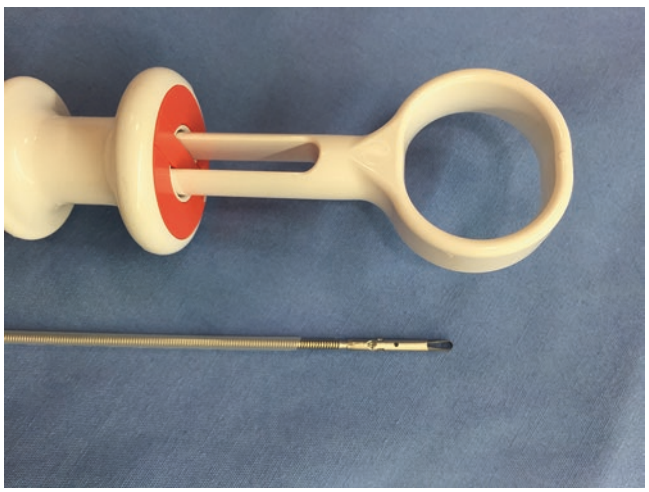

Fig. 9.3 Endoscopic clip

Snare Polypectomy/Biopsy

For lesions too large for endoscopic forceps, a snare may be useful for polypectomy (Fig. 9.4 and Video 9.5). Endoscopic snares are available in a variety of configurations and sizes, and one can be chosen based on the anatomy of the lesion to be removed. Shape, size, and morphology of the polyp often will influence which type of snare is best suited for the application. Given the size of the lesion, it may also be difficult to retrieve a polyp from the lumen of the bowel once it has been resected. Large lesions often cannot be suctioned through the colonoscope for fear they become trapped and lost. Simply grasping the lesion with the snare and removing it by withdrawing the colonoscope may not be feasible if the polyp is in the proximal colon. Additional endoscopic devices such as through-the-scope baskets and nets may be used for this purpose to secure the lesion as the colonoscope is withdrawn.

Snare polypectomy can be performed either "hot" or "cold," depending on preference by the endoscopist. Cold snare polypectomy can be associated with minor intraprocedural bleeding; however, this is rarely clinically significant and rarely needs further intervention. Snare polypectomy of sessile lesions can be aided by a saline lift technique, while pedunculated polyps can be amputated by applying the snare close to its base. To help facilitate application of the snare, the lesion to be removed should be positioned at the "5 o'clock" position relative to the tip of the colonoscope as this allows the snare to be deployed above the lesion. The snare is lowered around the lesion and slowly closed with the tip of the sheath just distal to it. Once the snare is snug around the polyp, it may be closed. If electrocautery is used, care should be taken to tent up the tissue as to avoid full thickness thermal injury to the bowel. If no electrocautery is used, this is not as important. Application of a snare is often facilitated by submucosal injection to lift the lesion, allowing more purchase for the snare and resection of the lesion with adequate margin.

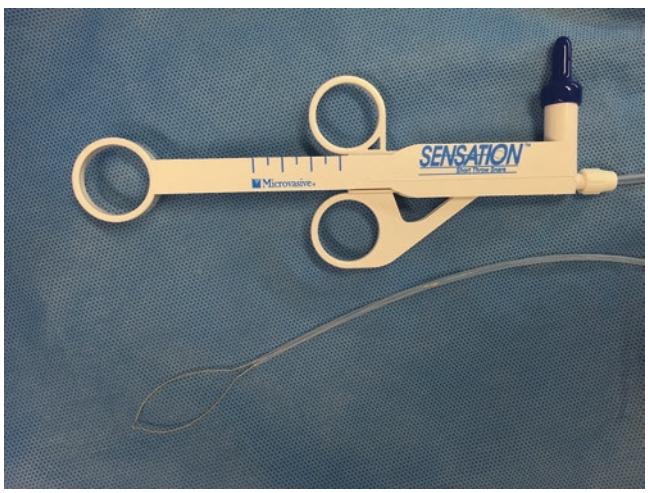

Fig. 9.4 Endoscopic snare

Larger polyps have a higher risk of post-polypectomy bleeding. Muniraj et al. reported on their series of cold snare polypectomy for large (>10 mm) adenomatous polyps [18]. They did not note an increased risk of post-polypectomy bleeding in their small cohort, advocating for consideration of cold snare polypectomy even for these larger lesions.

Pearls and Pitfalls

- The patient's prior endoscopy history should be carefully reviewed prior to your examination. Particular attention to quality of the last bowel preparation should be paid, as patients with a prior inadequate preparation should be considered for an alternative preparation or a 2-day preparation.
- Review of the location of prior adenomatous polyps should be noted, so that careful examination for local recurrence can be performed.
- The endoscopist should ensure the immediate availability of all potentially necessary endoscopic equipment, as various adenomatous polyp morphologies may require specialized instrumentation (snare, forceps, jumbo forceps, and injection needle).
- Adequate assistance should be available, particularly for difficult polypectomy (i.e., nurse and technician) and for administration of abdominal pressure.
- Should bleeding or a perforation occur, knowledge and experience in the use of endoscopic clip placement might avoid an unnecessary trip to the operating room.
- During attempts at submucosal injection, attention should be paid to the quality of the "lift" achieved. If the lesion does not lift appropriately, an occult malignancy or scarring from prior polypectomy attempts must be considered.
- For long procedures, carbon dioxide insufflation may be helpful to lessen post-procedural patient discomfort.
- Normal saline is often times sufficient as an injectate for submucosal injection.
- Difficulty using basic polypectomy techniques for polyp removal may require more specialized instrumentation and endoscopic expertise (EMR, ESD). Do not be afraid to call upon colleagues with more advanced endoscopic experience if you are having difficulty.

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Current Guidelines for Colonoscopy

10

Nallely Saldana-Ruiz and Andreas M. Kaiser

Abbreviations

ACS	American Cancer Society
ACG	American College of Gastroenterology
AGA	America Gastroenterology Association
ASCRS	American Society of Colon & Rectal Surgeons
ASGE	American Society of Gastrointestinal Endoscopy
CRC	Colorectal cancer
CRP	C-reactive protein
FIT	Fecal immunochemical testing
FOBT	Fecal occult blood testing
FAP/AFAP	Familial adenomatous polyposis/attenuated FAP
HNPCC	Lynch syndrome, hereditary nonpolyposis colon cancer
IBD	Inflammatory bowel disease
MAP	MUTYH-associated polyposis
WBC	White blood cells

Key Points

- Colorectal cancer (CRC) is the most common malignancy in the gastrointestinal tract and develops in 4.5% of the average risk US population. CRC can develop as sporadic cancer without any known gene mutation, result from known genetic mutations, or be superimposed on chronic inflammatory bowel disease.
- Cancer-specific survival at 5 years for all tumor stages is 65% with an indirect correlation between tumor stage and prognosis.
- Development of sporadic colorectal cancer is a slow process that takes 7–10 years to progress through a number of genetic steps from normal mucosa through precursor lesions (polyps) to an invasive and metastasizing cancer. This long interval provides us with an opportunity to intervene by screening for and eliminate precancerous lesions.
- Diagnostic colonoscopy is done as part of a workup for specific symptoms such as a positive fecal occult blood test, chronic anemia, or gross rectal bleeding.
- Screening programs aim at reducing the incidence of CRC by removing precursor lesions and to improve cancer survival by detecting cancer at an earlier stage

Introduction

Colorectal cancer (CRC) is the most common malignancy in the gastrointestinal tract. Over a lifetime, it affects 1 in 22 individuals (4.5%) of the general population in Western civilizations including the United States. Worldwide, however, there is a much larger geographical variation, with a crude incidence of 6.5/7.7 cases per 100,000 females/males in less developed areas as opposed to 48.3/36.6 in more developed regions. Since the mid-1980s, there has been a steady decrease in overall incidence in the United States, whereby some subgroups such as patients younger than 50 or African-American males in fact showed an increase or remained unchanged. According to the American Cancer Society despite the overall decline in incidence and mortality, CRC remains the third most frequently diagnosed cancer in both US men (lung/prostate) and women (breast/lung) and accounts for the third most common fraction of cancer death (behind lung, prostate/breast) [1]. In gender-neutral absolute numbers, colorectal cancer ranks fourth in annual cancer incidence (behind breast, lung, and prostate, respectively, excluding skin cancers) and second in cancer mortality (behind lung cancer) [1]. An estimate for 2016 of the incidence in the United States projects 95,270 new colon cancer

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and 39,220 new rectal cancer cases (total 134,490 cases); furthermore, 49,190 people are anticipated to succumb to colorectal cancer in 2016 [1].

The majorities of CRC cases are sporadic cancers and typically arise within a polyp. Adenomatous and serrated polyps are two subtypes that possess the potential to transform into a cancer through a series of gene mutations ("adenoma-carcinoma sequence"). The prevalence of polyps is an age-dependent phenomenon that increases from 11% at age 40–49 to 15% at age 50–59 [2]. In fact, up to 45–50% of asymptomatic average-risk individuals who undergo screening are found to have at least one polyp, of which about half shows an adenomatous (90–95%) or serrated (5–10%) pathology. This epidemiology translates into an estimated cancer risk of 1 in 5 polyps ultimately transforming into a cancer. Moreover, early detection is key as cancer-specific survival at 5 years is 65% for all tumor stages together, but it is directly correlated to the tumor stage with 90% for local (stages I/II), 71% for loco-regional (stage III), and 13% for distant metastatic disease (stage IV), respectively [1, 3].

Concept of CRC Screening and Surveillance vs. Diagnostic Workup

Since clinical symptoms are almost always late signs of colorectal cancer and hence not reliable for early risk or disease detection and since earlier tumor stages are associated with better cancer-specific outcomes, risk-adjusted screening programs have been developed and are supported by all major professional organizations (ACS, ACG, AGA, ASCRS, ASGE) with minor variations only [4–8]. The term screening in a strict sense is reserved to the testing of asymptomatic average-risk individuals.

If there is an underlying high-risk constellation or clinical symptoms are present (such as positive fecal occult blood test, noticeable bleeding, anemia, change in bowel habits, etc.), not screening but surveillance or appropriate age-adjusted diagnostic workup should be initiated [6]. Below the age of 40 without additional risk factors, a flexible sigmoidoscopy (or even less) may be sufficient, but a full colon evaluation is recommended for clinical symptoms above the age of 40, or if there are additional findings or suspicion to suggest more proximal pathology.

Screening efforts aim (a) at decreasing the burden of colorectal cancer by removing precancerous lesions, and (b) at reducing cancer mortality by detection of early rather than advanced disease [7, 9]. Effective screening is founded on the understanding that the multistep adenoma-carcinoma sequence may take up to 7–10 years from the first molecular change to a clinically manifest cancer; it should also take into consideration an individual's genetic and disease or age-dependent risk profile for the development of colorectal cancer.

Common screening tools fall into one of three categories: (a) complete or partial direct mucosal visualization (colonoscopy, flexible sigmoidoscopy), (b) indirect structural visualization by radiological imaging (surrogate tests), or (c) indirect nonstructural testing by stool analysis for fecal occult blood (guaiac-based FOBT versus immunochemical testing FIT) or fecal DNA (surrogate tests). For the procedural evaluations, most centers offer their patients to use conscious sedation or monitored anesthesia care (MAC). It is important to state that in order to optimize visualization and increase accuracy of the evaluation, all direct and indirect structural tests alike require a complete and thorough bowel preparation, which is among the most significant obstacles for patients to agree to screening. All circumstances taken together, these tests impose a relevant burden as the patients likely will miss 1–2 days of work and require the utilization of a chaperone for transportation after the intervention.

There is broad consensus among societies and organizations of medical professionals involved in developing screening guidelines that direct tests to detect cancer and adenomatous polyps should be preferred over the indirect tests where resources are available and if the individuals are amenable [7]. In populations where the required infrastructure is lacking, as well as in patients who are either unwilling and/or unable to undergo one of the structural tests or the necessary dietary and bowel cleansing preparation before, the use of stool-based colorectal cancer screening tests are an acceptable alternative.

In the United States, colonoscopy is recognized as the most effective screening tool and has become common practice with an estimated more than ten million procedures performed annually [9]. The advantages of the procedure are obvious as it allows for direct mucosal inspection of the entire colon and also provides opportunity for biopsy sampling for further evaluation as well as for definitive therapeutic interventions by polypectomy in the case of precancerous lesions or early stage cancers [9]. Data from the National Polyp Study, as well as other reports, have demonstrated that colonoscopy with polypectomy is able to reduce the incidence of polyps by 76–90% and the CRC mortality by 53% [10, 11].

Indications for Colonoscopy

In order to achieve good penetration of the target screening population while also remaining cost effective, it is of utmost importance to distinguish between screening of asymptomatic individuals and diagnostic workup for their appropriate use in regard to onset and duration of screening and frequency of repeat exams (Table 10.1).

Table 10.1 Distinction between and criteria for screening versus diagnostic colonoscopy

Setting	Parameters
Screening	Absence of symptoms
	Defined risk categories (Table 10.2)
	Establishing the time for the first screening (Table 10.3)
	Quality assessment parameters for each test in general and in individual patient (Table 10.4)
	Establishing the appropriate repeat intervals depending on (Table 10.5): • Basic risk profile • Quality of the test performance • Individual findings
Diagnostic workup	Symptom characterization
	Age
	Presence of age-independent risk factors
	Defining the appropriate role of other tests beyond colonoscopy

Table 10.2 Risk categories for the development of colorectal cancer

Category	Fraction of population (%)	Lifetime risk of CRC	Details
Average risk	65–75	4.5%	• No personal risk factors
			• Negative family history
Increased risk	20–30	10–20% (?)	• CRC or advanced adenoma in one first-degree relative with age ≤ 60 years or ≥ two first-degree relatives of any ages.
			• Personal history of curative resection of CRC.
			• Personal history of large adenomatous polyp (> 1 cm) or multiple colorectal polyps of any size.
			• Personal history of sessile serrated adenomas (proximal to sigmoid colon).
			• African-American ethnicity, Ashkenazi Jews
High risk	6–8	Nearly 100% by age 45	• FAP
		70%	• Attenuated FAP (AFAP)
		60–80%	• Lynch syndrome (HNPCC)
		Nearly 100% by age 65	• MUTYH-associated polyposis (MAP)
		10–20%	• IBD

CRC colorectal cancer, *FAP* familial adenomatous polyposis, *IBD* inflammatory bowel disease, *HNPCC* hereditary nonpolyposis colorectal cancer, *MUTYH* (*aka MYH*) MutY Homolog of E.coli gene

Risk Categories

Approximately, 65–75% of the population are considered to be low or average risk, i.e., there are no identifiable risk factors including, a lack of first-degree relatives with CRC or advanced adenomata (Table 10.2). Another 20–30% are at an increased risk of CRC, based on having one first-degree relative with an age of less than 60 years or two or more first-degree relatives of any age with CRC or advanced polyps, or a respective personal history; there are also a number of ethnicities who have been associated with an increased risk of CRC, including African-Americans and Ashkenazi Jews [4]. Additionally, 6–8% of the population are linked to a high-risk constellation for developing CRC based on the presence of genetic mutations/syndromes such as familial adenomatous polyposis (FAP) or its attenuated form (AFAP), Lynch syndrome (HNPCC), or MUTYH-associated polyposis (MAP), or based on the presence of chronic inflammatory bowel disease (IBD) [12].

Time for the First Screening

In the asymptomatic average-risk individual, it is recommended to start screening colonoscopy at age 50, and if negative to repeat it every 10 years (Table 10.3). Data from larger cohort studies suggest that the first colonoscopy was associated with the overall greatest benefit in risk reduction, and that an earlier start of general screening (e.g., at age 40) was of only limited value.

Table 10.3 Indications for screening based on risk constellation

	Start	Interval to subsequent colonoscopy (if no pathological findings)
Average risk		
• No personal/family risk factors	Age 50 years	Every 10 years
Increased risk		
• African-American ethnicity, Ashkenazi Jews, and other subgroups	Age 45 years	(5-) 10
• Personal history of CRC	Clearing colonoscopy within 6 months of surgical resection	1/3/5 years
• Personal history of large adenomatous polyp (>1 cm), multiple colorectal polyps of any size, or sessile serrated adenomas (proximal to sigmoid colon).	–	1/3/5 years
• Family history of CRC in FDR <60 years	Age 40 years or 10 years before the youngest affected immediate family member	Every 5 years
• Family history of CRC in any 2 or more family member(s) age <60 years	Age 40 years or 10 years before the youngest affected immediate family member	Every 5 years
• Family history of CRC in FDR(s) >60 years	Age 50 years	Every 10 years
High risk		
• FAP	Age 14	Annual with flexible sigmoidoscopy or colonoscopy until proctocolectomy @age 16–25
• FAP, status post IPAA/Kock pouch	1 year after surgery	Annual pouchoscopy and monitoring of ATZ
• Lynch syndrome / HNPCC	Age 20–25 years, or 10 years before youngest affected family member	Every 1–2 years
• Chronic IBD (UC, Crohn)	7–8 years post onset	Every 1–2 years
• IBD, status post IPAA/Kock pouch	1 year after surgery	Every 1–3 years

FDR first-degree relative, *ATZ* anal transitional zone, *FAP* familial adenomatous polyposis, *UC* ulcerative colitis, *IBD* inflammatory bowel disease, *IPAA* ileal pouch anal anastomosis, *ATZ* anal transition, *CRC* colorectal cancer

Table 10.4 Colonoscopy quality parameters

Accepted quality parameters	Benchmark
Withdrawal time (WT)	≥6 min
Cecal intubation rate (with photo documentation)	≥95%
Adenoma detection rate (ADR) in average risk screening colonoscopy	≥ 25% in men, ≥ 15% in women
Alternate or unquantified parameters	*Detail*
Polyp detection rate (PDR), including nonadenomatous polyps (hyperplastic polyps)	35%
Detection rate of proximal sessile serrated adenomata/polyps (SSA/SSP)	>4.5%
Miss rate	<6–12%
Quality of bowel cleansing	Scored by various instruments: (e.g., Boston bowel prep scale 0–9, based on sum of assessments in 3 segments, 0=unprepped, 3=perfect)
Incidence of interval cancer within 3–5 years	<2–9%

However, it has been postulated by some of the professional societies to start routine screening earlier in some subgroups and ethnicities that were associated with an overall increased risk or have shown no or an insufficient decrease of CRC incidence rates over the past decades. Among these groups are African-Americans who are recommended to start screening at the age of 45 years [4]. Moreover, if there is a positive family history involving, in particular, first-degree relatives, and no known genetic mutation is identifiable, the first screening colonoscopy should be recommended to start at age of 40 or 10–15 years before the age at diagnosis of the youngest family member with CRC or advanced adenoma (whichever comes first).

Table 10.5 Impact of pathological findings on subsequent surveillance intervals

Pertinent findings on index colonoscopy	Interval to subsequent colonoscopy
Small hyperplasic polyps in distal rectosigmoid	10 years
1–2 small tubular adenomas <1 cm with low-grade dysplasia	5–10 years
3–10 adenomas, or 1 adenoma >1 cm, or any adenoma with villous features/high-grade dysplasia	3 years
More than 10 adenomas completely removed in a single examination	1–2 years
Sessile adenomata removed in piecemeal	<6 months
Polyps in Lynch syndrome	1–2 years

Recommendations for high-risk categories include not only a much earlier start, but due to the accelerated adenoma-carcinoma sequence, much shorter intervals, more frequent repeat exams, and potentially screening for extra-colonic pathology. The specifics are also outlined in Table 10.3 and depend on the nature of the risk (e.g., genetic syndrome versus IBD) [12]. Preferably, the gene carrier status in families with known genetic syndromes (FAP, Lynch, MAP) should be established by genetic testing rather than "screening" for the presence of polyps. Patients with established clinical or genetic diagnosis of FAP have traditionally been recommended to start screening at age of 10–12 years with annual flexible sigmoidoscopy. In reality however, there is no non-surgical, pharmacological, or endoscopic intervention that could obviate the necessity for a prophylactic surgical resection (typically proctocolectomy) which should be planned for an appropriate time between ages 16 and 25. Particularly with wide availability of genetic testing, it is therefore our recommendation that these patients wait with "screening" until they reach the age of 14, as those 2–4 additional years allow these young patient to mature and get an opportunity to understand and participate in the process of screening rather than being traumatized. The risk of this delay is negligible as a proctocolectomy is almost never needed before the age of 14. The purpose of flexible sigmoidoscopy or colonoscopy in FAP is less to prevent CRC but to get a relative growth profile and establish the right timing for the inevitable surgery.

In contrast, Lynch syndrome (HNPCC) has a more variable phenotype. Patients with a clinical or genetic confirmation of a carrier status are recommended to begin colonoscopy screening at age 20–25 years or 10 years before the youngest family member with CRC or advanced polyps and to subsequently continue every 1 or 2 years.

Quality Assessment Parameters

The efficacy of colonoscopy as a screening tool has been linked to a number of quality parameters that involve (a) the endoscopist, (b) the patient and the bowel preparation, and (c) potentially some technological aspects (see Table 10.4) [13, 14]. The clinically most relevant though unpractical parameter would be the detection rate of interval cancers. Hence, the most important surrogate parameter appears to be the overall adenoma detection rate. Other similar parameters such as polyp detection rate (which includes hyperplastic polyps), the overall cecal intubation rate with photo documentation, and the average withdrawal time (typically greater than 6 min) have been used as quality benchmarks even though strong supportive evidence is lacking. Unquestionably, visibility is highly dependent on the completeness of the bowel cleansing. An adequate bowel preparation is critical for the accuracy and cost-effectiveness of colorectal cancer screening while inadequate cleansing should trigger an earlier reexamination [15].

Follow-up Surveillance and Repeat Intervals

After a previous polypectomy or colon resection for CRC, the aim of repeat colonoscopies is to detect and remove adenomata that were potentially missed on the initial exam as well as metachronous new adenomata with advanced pathologic features [16]. Defining the exact length of recommended interval depends on the number of factors to not only include the previously mentioned overall risk categories but also the individual findings (Table 10.5). In particular, the number of detected and removed adenomatous or serrated polyps, the completeness of the previous removal, the size of lesions, and the presence or absences of unfavorable features (e.g., high-grade dysplasia) have to be taken into account. Furthermore, the time interval may need to be shortened depending on the quality of the previous examination, e.g., if it was complete or the bowel cleansing and visibility were inadequate.

If there were only a limited number of small adenomata (tubular adenoma), a 5- to even 10-year interval is sufficient. A shorter interval of 3 years would be recommended if there were more advanced or multiple polyps ($\geq$ 3), including sessile serrated adenomata proximal to sigmoid colon. In patients who were found to have numerous adenomata (including serrated adenoma), a malignant adenomatous polyp with high-grade dysplasia or focal adenocarcinoma

(cancerous polyp), large sessile polyps including sessile serrated adenomata, incomplete removal of polyps, or whose colonoscopy was incomplete or otherwise unsatisfactory, an interval of a few months may have to be recommended (unless a surgical resection is carried out). No adjustment to the screening schedule of 10 years is needed if there were only hyperplastic polyps with typically distal distribution in the rectum and sigmoid colon. Patients with proximal serrated adenomata/polyps or with hyperplastic polyposis syndrome are exceptions from that.

For patients undergoing a curative resection for a colorectal cancer or advanced polyps, there should be a full colonic evaluation to rule out synchronous lesions. If the circumstances did not allow for preoperative clearance of the entire colon (e.g., emergency, obstruction), a full examination should be recommended within 6 months of the surgery. Subsequently, patients with sporadic cancers require surveillance of their colon to rule out true anastomotic recurrences (< 2% risk for colon, 5–20% for rectum); to detect and remove adenomata that have subsequently developed or were missed on the initial examination. Surveillance after CRC is to be planned after 1 year, then after 3 years, and subsequently every 5 years if everything looks normal. In case of pertinent findings as stated earlier, a tighter schedule would be entertained. CRC patients with high-risk constellations (particularly Lynch syndrome) who have only undergone segmental resections mandate continued annual surveillance of the residual.

Contraindications to Colonoscopy

Contraindications are defined by the factors related to either (a) the condition of the colon, (b) the patient's overall condition, or (c) denial of consent. In general, an intervention is contraindicated when the risks to the patient's health or life outweigh the potential benefits. Absolute contraindications to perform a colonoscopy include toxic megacolon, fulminant colitis, or a known free or concealed colonic perforation; furthermore, the list includes ASA IV/V, hemodynamic instability, or severe coagulopathy such as disseminated intravascular coagulation (DIC). Relative contraindications are situations in which the risk of the procedure (bleeding; perforation; extrinsic organ injury, e.g., to spleen or aortic aneurysm) or of the conscious sedation/anesthesia is substantially increased. Nonetheless, it may on occasion still be deemed appropriate to proceed with at least a limited evaluation if the information that may be acquired would have a crucial impact on further treatment and management decisions. Routine screening is never indicated in pregnancy. Specific situations in pregnancy or management of patients on medications (platelet inhibitors, anticoagulation) are being discussed later.

Effectiveness

Analysis of the effectiveness of colonoscopy is difficult and can be based on a number of different factors, including (a) the immediate procedural success and miss rates as well as accuracy and safety profile on an individual basis; (b) the population-based impact on CRC incidence and mortality; (c) the cost-effectiveness as measured, for example, by the number of gained patient years per invested direct and indirect dollar amount in comparison to other screening tools and interventions, or to no interventions at all.

Even if there are likely other contributing factors, the simple observation of decreasing CRC incidence and mortality since introduction of routine use of colonoscopies seems to provide convincing evidence for its effectiveness and justification of its broad use. It is not easy, however, to draft high-quality prospective, randomized controlled trials over several decades. The implementation of the National Polyp Study in the 1970s has, along with other large cohort studies, provided a flood of long-term data that demonstrate a lasting impact of interventions and polypectomies. Early reports of 76–90% reduction in colorectal cancer incidence have been recently supplemented with an observed long-term decrease of CRC mortality by 53% [10, 11, 17].

Undoubtedly, colonoscopy has remained and solidified its current role as the gold standard for detection and prevention of colorectal cancer. This remains true despite an imperfect score card. There is substantial inconvenience and the low, but not negligible, risk of side effects and complications associated with the procedure. Furthermore, colonoscopy has an estimated miss rate of approximately 6–12% for large adenomas (adenomas with a size greater than or equal to 10 mm) and a miss rate of 5% for colon cancer [9]. Lastly, while the population-wide screening rates have improved in the United States, 40% of Americans ages 50–75 years are still not being screened, and our set goals remain below the recommendations of our screening guidelines [18–20].

Complications

Problems and complications may result from the preparation, sedation, or occur during the actual procedure phase but signs and symptoms thereof may be delayed [21]. A high index of suspicion, early recognition, and prompt intervention are key to minimizing the morbidity and mortality associated with any major complication. Not surprisingly, pure screening procedures have the lowest risk of complications followed by diagnostic and interventional colonoscopies (e.g., polypectomy); both age and comorbid conditions increased the risk for adverse events [22].

Hemorrhage and Perforation

The two most serious complications are bleeding and perforation. The former is typically associated with endoscopic interventions, while the latter may be due to both, interventions or the mechanics of scope advancement and insufflation. The reported risk of colonic perforation increases with age and with the presence of diverticular disease and ranges from 0.01% to 0.2% of examined patients [21, 23]. In a random five-percent sample of Medicare beneficiaries with colonoscopies compared with a matched control group without colonoscopy, the unadjusted risk of perforation or bleeding increased from 0.1 to 0.6 and from 1.8 to 6.4 per 1000 procedures, respectively [22]. The unadjusted risk for gastrointestinal bleeding was more than four times higher in the polypectomy group than the screening alone group without polypectomy (8.7 vs. 2.1 per 1000 procedures, respectively) [22].

Mortality

The ultimate complication of death in relation to colonoscopy is rare but not negligible. It may be difficult to distinguish in larger databases whether the mortality was truly related to the intervention as such or more the result of a severe underlying disease and comorbidities. In a 2010 review of colonoscopy complications based on prospective studies and retrospective analyses of large clinical or administrative databases, there were 128 deaths reported among 371,099 colonoscopies, for an unweighted pooled death rate of 0.03% [21].

Abdominal Pain or Discomfort

Up to one-third of patients report at least one minor, transient gastrointestinal symptom after colonoscopy. The most commonly reported adverse effects of colonoscopy include bloating (25%) and abdominal pain or discomfort in 5% to 11% [24]. Avoidance of endoscope looping and minimized air insufflation help to reduce these symptoms during and after the procedure. Carbon dioxide compared with standard air insufflation accelerates the postinsufflation recovery [24].

Postpolypectomy Syndrome

After interventional colonoscopy with submucosal or transmural injection (e.g., endoscopic mucosal resection, tattooing) and/or application of electrocautery (e.g., hot-snare polypectomy), patients may develop localized abdominal pain and tenderness, occasionally associated with an increase in inflammatory parameters (WBC, CRP), but show no evidence for a perforation. Postpolypectomy electrocoagulation syndrome (PPES) is poorly quantitated with a wide range of reported incidences from 3 per 100,000 (0.003%) to 1 in 1000 (0.1%) [21]. It is thought to be the result of collateral transmural energy spread through the bowel wall which leads to a localized peritoneal reaction. Treatment is conservative and ranges from watch and wait to administration of antibiotics, which results in resolution of symptoms within a few days.

Gas Explosion

Explosive complications related to the use of cautery during colonoscopy are uncommon but can have dramatic consequences. A 2007 review reported 9 cases, each resulting in colonic perforation and, in one case, death [25]. The combination of hydrogen or methane gas at combustible levels, oxygen, and electrosurgical energy form the risk triangle for explosions. The lack of an adequate anterograde cleansing, use of nonabsorbable or incompletely absorbable carbohydrate preparations (such as mannitol, lactulose, or sorbitol), or the use of enemas-only cleansing (e.g., for flexible sigmoidoscopy) has been associated with an increased risk [26]. Electrocautery should not be performed during routine flexible sigmoidoscopy after enema preparation [26].

Management of Anticoagulants and Platelet Inhibitors

An increasing number of patients presenting for colonoscopy are being treated with antithrombotic agents (anticoagulants, platelet inhibitors) for a variety of conditions. The American Society of Gastrointestinal Endoscopy (ASGE) recently released extensive updated guidelines for the management of antithrombotic agents for patients undergoing endoscopy [27]. In essence, the individual circumstances have to be analyzed to determine (a) the indication, the urgency, and the bleeding risk of the procedure (screening only = low risk, intervention including polypectomy=high risk), (b) the type of antithrombotic treatment and medications, and (c) the risk of thromboembolic events if one or all of these medications were paused. For example, when the anticoagulation was interrupted in patients with atrial fibrillation, the risk of a periprocedural thromboembolic events and stroke within 30 days was low with 0.7% and 0.3% respectively [28]. On the other hand, the respective risk is very high if there is a mechanical heart valve or a recent status postpercutaneous coronary intervention. Careful interdisciplinary communication and discussion are critical to optimize outcomes.

Ideally, maintenance anticoagulation with warfarin or newer direct thrombin or factor Xa inhibitors (e.g., dabigatran, rivaroxaban) should be paused 5–7 days and 2–3 days before the colonoscopy, respectively, and bridged with subcutaneous injections of unfractionated heparin or low-molecular-weight heparin. Depending on the extent of procedural intervention, the baseline medications may be resumed after 0–5 days. Routine antiplatelet agents for general prophylaxis should be discontinued 7–10 days prior to the procedure and again depending on the degree of intervention can be resumed right away if no polypectomy was done, or after 3–5 days if one was performed. In case of a more critical need for single or dual antiplatelet agents or a nonelective procedure, it might be acceptable to proceed with continued medications for low-risk procedures, and to either postpone noncritical polypectomies or assure more careful hemostasis including application of clips to the polypectomy site. Dual antiplatelet therapy is common after cardiovascular interventions, particularly after placement of bare metal stents or drug-eluting stents; it is generally advisable to postpone elective procedures 1–12 months if clinically acceptable or to limit colonoscopy to diagnostic efforts only, even if some pathology were to be identified.

Colonoscopy During Pregnancy

There is never an indication for a pure colon screening during pregnancy. However, a need may arise for a diagnostic or therapeutic colonoscopy in that period. As with any intervention, the use of colonoscopy is contraindicated in situations where the risks to the patient or the fetus outweigh the expected benefits of the colonoscopy. While it is generally considered safe to perform a needed colonoscopy after the first trimester of pregnancy, it should be determined whether the indication is of such urgency that it cannot be postponed until after delivery [29]. Occasionally, however, a woman's condition is of such great concern that only the use of colonoscopy would have a reasonable chance to lead to an immediate resolution of the patient's ailment or establishing a needed diagnosis. Under such circumstances, the inherent procedural and sedation risks to the patient and the unborn fetus would be acceptable [29].

IBD—Screening and follow-up Pouchoscopies

Chronic inflammatory bowel disease poses a high risk for development of CRC. Routine surveillance with systematic biopsies is therefore recommended to start no later than 7–8 years after onset of the disease, in order to monitor for dysplasia—a cancer precursor. Restorative proctocolectomy eliminates the majority of the disease and the majority of the cancer risk [30]. However, there is a residual risk of cancer formation within the anal transitional zone cuff (even if a mucosectomy has been performed) and in any surgically constructed small bowel reservoir (ileo-anal pouch, Kock pouch) [31]. It is therefore recommended to perform surveillance of the pouch and the ATZ cuff every 1–3 years by means of a flexible pouchoscopy and random biopsies.

Colorectal Screening for Elderly

While there is a general broad consensus about the age of when to initiate CRC screening and surveillance, there remains significant controversy and silence about when to end it. As previously noted, this question does not or only to a lesser degree apply to the indications for a diagnostic workup for respective clinical symptoms, which are generally an accepted reason to perform a colonoscopy even in patients of advanced age and have been associated with a high yield of advanced neoplasms in 26–30% [32]. However, in absence of symptoms the potential screening benefits of prolonging cancer-free survival have to be weighed against the risks, the lower estimated gain in life expectancy (compared to younger individuals), and the cost of prophylactic screening for cancer in any patient subgroup. In the elderly population (as defined by an age above 75–80 years), the patient's overall performance status and non-CRC life expectancy have a much higher impact and should be taken into consideration [32–34]. A strict limitation based on a rigid age threshold would result in underuse of appropriate screening efforts in fit older individuals; at the same time, it would carry the potential of overusing it in otherwise less healthy younger individuals with limited life expectancy [35]. Unfortunately, elderly patients have been commonly excluded from participation in high-quality, randomized trials including colorectal cancer screening trials that aim at studying the efficacy of the screening colonoscopy. As such, the current screening colonoscopy recommendations have largely failed to address the impact of comorbidities, functional status, and life expectancy in general and particularly in the elderly [34].

Pearls and Pitfalls

- The start age and screening intervals recommended for the use of screening colonoscopies are patient dependent and rely largely on the patient population and associated underlying risk factors. Critical population characteristics and risk factors include:
  - Age (dependent on family history, race, and known genetic predisposition)

  - Family history (history of CRC and known genetic predispositions)
  - Personal medical history (including genetic predispositions, underlying inflammatory bowel disease, findings on prior screening colonoscopies).
- Appropriate preparation prior to the screening colonoscopy is critical for a clinically meaningful examination; this preparation includes the adoption of an appropriate diet and the completion of a recommended bowel-cleansing regimen.
- Colonoscopy guidelines for the purpose of identifying early disease in asymptomatic patients (screening), have no role in defining the appropriate use of colonoscopies with alternate roles (diagnostic or therapeutic colonoscopies) for identifying and treating pathology in the symptomatic patient.
- In the elderly, the role of screening colonoscopies has not been sufficiently defined but should be determined on an individual basis on criteria that include other factors than age only.
- In pregnant women, there is no role for screening colonoscopies. Inevitable diagnostic or therapeutic interventions must be undertaken with caution and clinical judgment of each individual patient case; evaluating the benefits and risks of the procedure for the mother and the unborn fetus.

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Difficult Colonoscopy: Tricks and New Techniques for Getting to the Cecum

11

Daniel L. Feingold and Steven A. Lee-Kong

Key Points

- Achieving a 95% cecal intubation rate for screening colonoscopy is an important quality benchmark that can maximize the efficacy of screening and decrease the incidence of interval colon cancers.
- The majority of colonoscopies performed after a failed prior attempt at colonoscopy can be successfully completed using readily available colonoscopes and utilizing proper insertion techniques.
- In cases where, despite adherence to proper insertion techniques, a colonoscopy fails to intubate the cecum, advanced endoscopic techniques using balloon technology or specialized endoscopes may be useful; alternative screening modalities like CT colonography should be considered as well.

Introduction

While there is no universally accepted definition, in general, a difficult colonoscopy is one where the colonoscopist struggles, requires a prolonged insertion time, or fails to intubate the cecum. An estimated 5 to 20% of all colonoscopies are considered "difficult" and failure to intubate the cecum occurs in the range of 2 to 15% of cases. Considering that Continuous Quality Improvement (CQI) guidelines recommend at least a 95% cecal intubation rate for screening colonoscopies, it is important to systematically analyze the causes of failed colonoscopy. Maximizing cecal intubation rates is important because failed exams typically lead to obtaining more studies and may contribute to the occurrence of interval colon cancers (colon cancers discovered within 3 years of a prior colonoscopy). In order to address the issue of difficult colonoscopy, it is helpful to consider the circumstances in which the colonoscopist fails to intubate the cecum.

Patient Factors

In terms of patient factors, the most common anatomic causes of incomplete colonoscopy are looping of the colonoscope due to a floppy sigmoid colon or redundancy of the transverse colon. Looping of the scope occurs when the tip of the scope does not advance to the degree that the scope shaft is inserted or when the tip of the scope moves distal along the colon upon scope insertion (i.e., paradoxical motion). Another common anatomic factor that can lead to incomplete colonoscopy is angulation or fixation of the colon, typically in the sigmoid or at sites of prior abdominopelvic surgery that can lead to tethering or angulation of the colon (Fig. 11.1a, b). Techniques to maximize cecal intubation rates in the setting of looping or fixation will be reviewed in detail in the following sections.

Potentially modifiable causes of a failed colonoscopy include poor bowel preparation and patient intolerance during the procedure. In terms of bowel preparation, there is no question that a poor preparation compromises the ability to successfully reach the cecum [1]. Using split dose preparations and individualizing bowel preps can be very helpful. Constipated patients, obese patients, and patients with a previous poor preparation or incomplete colonoscopy may benefit from more vigorous preparation including things like daily laxative use leading up to the bowel preparation, a prolonged period on a liquid diet, and more comprehensive patient education.

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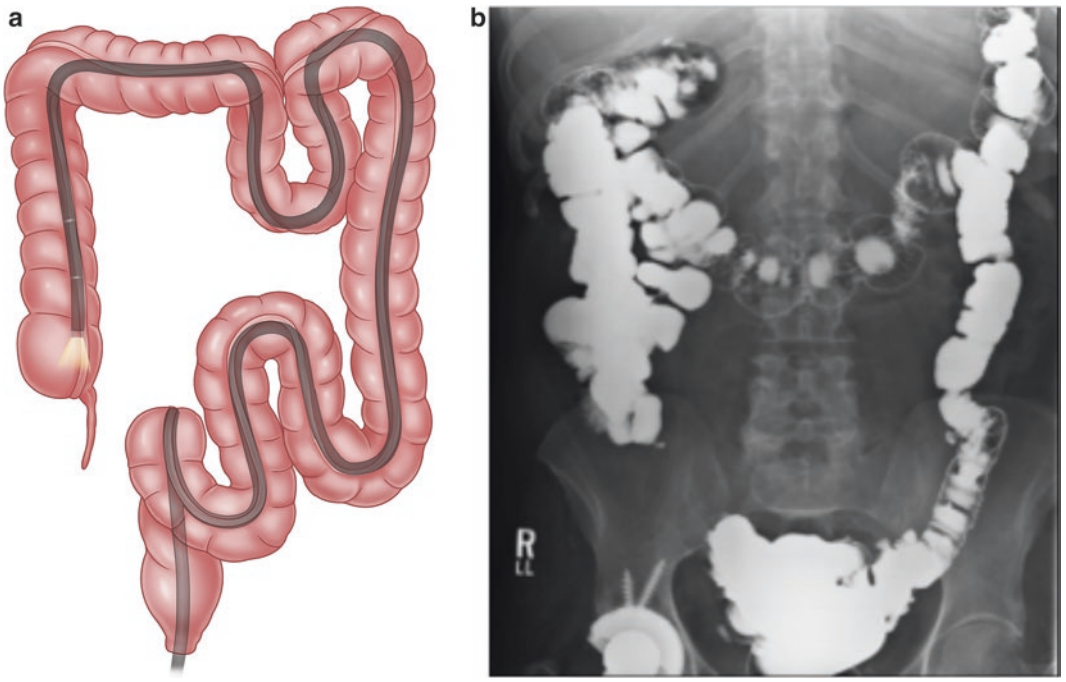

Fig. 11.1 (**a**) This is a schematic 3-dimensional map generated from a CT colonography in a patient with a difficult colonoscopy. Notice the acute angulation in the pelvic colon and the redundancy in the proximal sigmoid and in the transverse colon. (**b**) A contrast enema from a patient with a difficult colonoscopy due to tortuosity in the pelvic colon and proximal redundancy

Patient intolerance due to attempting to negotiate an angulated colon or due to bowing of the colonoscope in the setting of looping can jeopardize the colonoscopist's ability to complete the procedure. Tolerability can be improved by reducing and minimizing looping of the instrument using techniques described in the following sections and by incorporating monitored anesthesia care into the endoscopy suite. Having a dedicated team member responsible for adequate and safe sedation of the patient also allows the colonoscopist to focus entirely on the difficult colonoscopy being performed and facilitates successful completion of the procedure.

Nonmodifiable risk factors for an incomplete colonoscopy include female gender, low body mass index, prior surgery (including hysterectomy), and age over 60 [2]. The presence of advanced or complicated pathology (e.g., obstructing cancer, active colitis, severe diverticulosis, stricturing disease) can also limit the extent of scope insertion either from a technical standpoint or due to safety concerns. It is important to consider that factors that make a particular colonoscopy difficult can also increase the risk of perforation during the procedure. For instance, the risks of perforating the colon by mistakenly intubating a large diverticulum or bowing the shaft of the instrument causing the wall of the colon to split or tear can be reduced by staying in the actual lumen of the colon to avoid pushing through a false diverticulum and by reducing and limiting loops that are formed during the procedure, as reviewed in the following sections.

Colonoscopist Factors

Cecal intubation rates can also be influenced by colonoscopist-related factors like individual practitioner experience. A landmark population-based study evaluated over 330,000 patients undergoing index screening colonoscopy in Canada and showed that the endoscopists in the lowest volume quintile had a 29% colonoscopy failure rate [3]. This puts into perspective the impact of individual practitioner experience as it relates to the success of colonoscopy. Other clinician factors relating to cecal intubation rate include skill, manual dexterity, and technique.

Many of the potential problems related to completing a colonoscopy can be avoided by using sound insertion techniques including repeatedly shortening the colon and reducing loops along the shaft of the scope. Hooking a mucosal fold by deflecting the tip of the colonoscope anchors the position of the tip of the scope and then withdrawing the scope with a clockwise torque reduces loops and shortens the colon by telescoping the colon up onto the shaft of the scope. In situations where attempts at clockwise loop reduction are not effective, withdrawing the scope using counterclockwise torque may facilitate scope advancement. This maneuver can be especially helpful in negotiating the proximal transverse colon. As the colonoscopist attempts to pleat the colon over the scope, it is common to first lose some

ground as the colon slides off of the scope. With continued efforts to shorten the colon, the colonoscopist should be reassured that this ground will be regained and the scope will advance.

Failing to repeatedly withdraw sufficiently and reinsert is thought to be the most common error made when attempting colonoscopy through a redundant or floppy colon. In a difficult colonoscopy with looping or redundancy, repeated efforts to pleat the colon onto the scope are often required in order to advance the colonoscope. The goal is to achieve at least "one-to-one" transmission of shaft movement to the tip of the device. Deliberate to-and-fro movement of the scope (jiggling) or gentle shaking of the colonoscope (dithering) can also pull the colon onto the shaft of the instrument. In situations where the lumen proximal to the tip of the scope is not well visualized, these movements can also help the colonoscopist find the lumen. The importance of proper technique cannot be overemphasized, especially when you consider that the majority of repeat colonoscopies after a failed colonoscopy are completed using routine colonoscopes and proper technique [4].

Hooking the colon and withdrawing scope, as described earlier to reduce looping, can also be helpful when negotiating an angulated area where the view is limited and the proximal lumen is not seen well. Blind insertion ("slide by") in this situation should be avoided as this could be traumatic. Recognizing that the colon, to some degree, is mobile; this maneuver manipulates the anatomy and may allow better visualization of the lumen and safe scope advancement. This manipulation is also helpful for finding the lumen along a segment of severe diverticulosis.

Right-handed torqueing of the shaft of the instrument adds additional degrees of freedom of motion to the colonoscope and affords the colonoscopist finer control of the tip of the device rather than relying solely on the control dials to navigate in the "X" and "Y" axes. This is especially useful when negotiating through the rectosigmoid junction or through an area of diverticulosis or tortuosity. This right-handed maneuvering, together with the torqueing used to reduce loop formation, can, over the course of a difficult insertion, cause the colonoscope shaft to assume a contorted shape. The more convoluted the instrument, the more rigid the shaft becomes and the harder it is to control the tip of the instrument and to advance the scope through the colon. Gently rotating the shaft counterclockwise to allow the scope to assume a more neutral configuration relieves the rigidity associated with a misshaped instrument and permits further scope advancement.

Controlling and correcting the degree of gaseous distension is also helpful during insertion. It is important to avoid overinsufflation, as this tends to elongate the colon and make insertion more difficult and may lead to barotrauma. An overly distended colon can be difficult to telescope over the colonoscope while suctioning out excess gas facilitates insertion particularly when coming across the transverse colon.

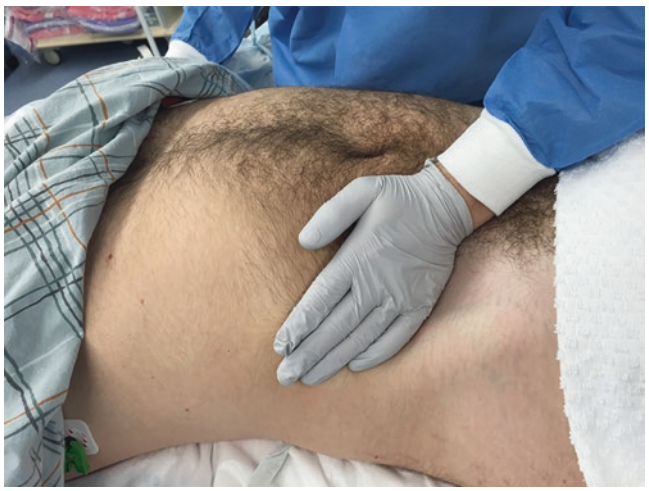

Fig. 11.2 An assistant applying gentle abdominal pressure in the right lower quadrant can help deliver the cecum to the tip of the colonoscope ("cecal lift"). Two-handed pressure over the distribution of the sigmoid or transverse colon is routinely utilized to fix the colon in place and allow advancement of the colonoscope with minimal looping. On occasion, four-handed pressure may be required

Liberal use of external pressure can limit loop formation and facilitate cecal intubation and changing out of the left lateral position can expedite advancement of the scope (Fig. 11.2). The benefit of an experienced assistant applying appropriate external pressure cannot be overstated. Supination can help negotiate a difficult hepatic flexure and right lateral positioning, an underutilized maneuver, can help move from the ascending colon into the cecum. Rarely, pronation may permit further advancement of the colonoscope by using the weight of the patient to fix the colon in place.

Another readily available way to potentially increase the success of cecal intubation is changing out the colonoscope. To overcome the looping problem during colonoscopy, variable stiffness colonoscopes have become widely available even though these scopes have not been shown to reliably improve cecal intubation rates. In theory, increasing shaft rigidity transmits the force of insertion to the tip of the scope by reducing bowing and loop formation. In terms of using thinner, more flexible colonoscopes, the literature supports the idea that in patients who fail colonoscopy due to angulation, especially women who have had a hysterectomy, a thinner scope may improve the chances of successful colonoscopy. A pediatric scope with decreased cross-sectional surface area as compared with an adult scope can overcome angulation, fixation, or tortuosity and should be available for use in the setting of a difficult colonoscopy. In cases of severe angulation, a thinner, more flexible upper endoscope may be useful. The shorter length of these upper scopes,

however, can limit the extent of insertion. Changing out the upper scope for a longer pediatric colonoscope using a guidewire exchange technique, after traversing the angulation, may be helpful.

In the midst of a difficult colonoscopy, confirming cecal intubation is essential to avoid mistakenly concluding that a complete colonoscopy has been performed. This may be confidently accomplished by inspecting the cecal strap (crow's foot), appendiceal orifice, and ileocecal valve. Intubating the ileum, while not required for a complete colonoscopy, can further confirm the anatomy and the true extent of the examination performed. Due to the ptosis of a redundant transverse colon, transillumination in the right lower quadrant is not sufficient evidence that the scope has reached the cecum. The colonoscopist should be wary of relying only on pattern recognition of a thickened mucosal fold as evidence of reaching the ileocecal valve as a bend near the hepatic flexure colon can mimic the appearance of the valve and spiraling of the colon due to prior abdominal surgery can cause the wall of the colon to appear like the confluence of the tenia in the caput (the fool's cecum).

Antispasmodics and using CO_2 insufflation instead of ambient air have also been evaluated and have not been shown to reliably improve cecal intubation rates or scope insertion times during a difficult colonoscopy.

Water Immersion

Another consideration that may prove helpful when performing a difficult colonoscopy includes using warm water instead of ambient air insufflation during insertion ("submarine" colonoscopy). Water immersion techniques have been studied to possibly improve colonoscopy success rates and to decrease the discomfort of the exam. In theory, instilling water into the sigmoid colon, with a patient in the left lateral position, uses gravity to straighten the colon and reduce angulation, facilitating insertion with less looping. This method may also minimize the degree of colon elongation associated with conventional air insufflation allowing the colonoscopist to use less length of the colonoscope and, in theory, reduces the spasm associated with air insufflation. Water immersion has been studied mostly in the setting of unsedated colonoscopy. Residual material mixed with the infused water can impair visualization and cause this method to fail. It is important that the immersion is instituted from the onset, as water use once the scope is well underway may not prove to be as effective.

A modification of the water immersion method is the "water exchange" technique whereby the endoscopist uses air insufflation and suction to evacuate the residual material encountered in the colon and then resumes the water immersion method. The literature studying this technique was reviewed in a meta-analysis including 18 randomized controlled trials with almost 2800 patients who underwent either water immersion with water exchange or standard air insufflation colonoscopy [5]. This paper demonstrated a statistically higher cecal intubation rate with an odds ratio of 1.9. This study also showed better patient tolerance with water infusion in terms of decreased pain during the procedure and increased willingness to repeat the same procedure in the future. The aggregate of the literature supports water exchange as being particularly useful in unsedated patients and in patients with prior pelvic surgery.

Fig. 11.3 The Spirus Endo-Ease system

Overtubes and Other Devices

Other potential methods to improve cecal intubation rates during a difficult colonoscopy utilize a variety of devices like overtubes, caps, balloons, and advanced imaging platforms. Standard rigid overtubes emerged in the early 1980s as a method of splinting the sigmoid colon to minimize looping and facilitate insertion. These were often combined with fluoroscopy in order to guide insertion and were associated with mucosal trauma and an increased rate of perforation. More recently available overtubes appear to be safer and do not require fluoroscopic imaging [6].

The ShapeLock (USGI Medical, San Clemente, CA), a next-generation "smart" overtube, allows the operator to control its rigidity. This device can assume 2 forms–the first is extremely floppy and readily conforms to the configuration of the colon. The device is left flexible during insertion and when the handle is snapped into place, the tube's configuration locks and becomes rigid to prevent looping. This interesting device received positive reviews when it was first launched but is presently not commercially available.

The Spirus Endo-Ease system (Spirus Medical, Stoughton, MA) was originally used for enteroscopy and was subsequently modified for use in colonoscopy in conjunction with a pediatric colonoscope (Fig. 11.3). This device is a semi-flexible threaded overtube with a raised spiral grip that shortens and stabilizes the redundant colon without requiring

fluoroscopy. Clockwise rotation of the overtube mimics the motion of a corkscrew and pleats the colon back onto the tube. This device may prove to be particularly helpful in patients who failed standard colonoscopy because of a redundant colon and early reports show high cecal intubation rates in this group of patients [7]. The benefits of this device are its ease of use and its compatibility with colonoscopes routinely available in the endoscopy suite.

Attaching a small, transparent cap or "hood" to the tip of the colonoscope has been studied extensively as a possible method for increasing the adenoma detection rate by depressing mucosal folds. To evaluate whether caps improve cecal intubation rates and shorten colonoscope insertion times, Ng and colleagues performed a meta-analysis of 16 randomized controlled trials comparing standard colonoscopy to cap-assisted colonoscopy and included almost 9000 patients [8]. The cap-assisted group had a statistically significant mean difference in intubation times of only 38 s which was not clinically meaningful. The cecal intubation rates between the two groups were both 96%. The literature, in aggregate, does not support use of caps for the purpose of improving cecal intubation rates or shortening scope insertion times.

Fig. 11.4 An example of a disposable balloon system

Balloon technology, first introduced as an anterograde method of evaluating the small intestine, has been applied in retrograde fashion in the setting of colonoscopy. This technique requires dedicated equipment including a thin, extremely flexible therapeutic endoscope; a disposable sliding overtube with a balloon; and a balloon control unit (Fig. 11.4). The inflated balloon stabilizes the colon and allows further insertion. When the scope cannot advance any further the tip of the scope is deflected down hooking the colon and then the scope together with the overtube is pulled back pleating the colon over the tube. This cycle is then repeated until the cecum is reached (Fig. 11.5). There are many reports in the literature specifically looking at double- or single-balloon colonoscopy after failed conventional colonoscopy that consistently show high cecal intubation rates of 93% or greater [9]. This versatile technology can overcome a severely redundant colon as well as a sharply angulated colon. In terms of double- versus single-balloon platforms, the success rates seem to be comparable but the single-balloon method may be easier to learn and is more intuitive to perform as compared with the double-balloon approach.

Another potentially useful method for overcoming looping during colonoscopy is to provide real-time views of the shaft of the scope during the procedure to facilitate straightening of the colon. This was originally accomplished using fluoroscopy but this was essentially abandoned over time due to the inconvenience, cost, and radiation exposure.

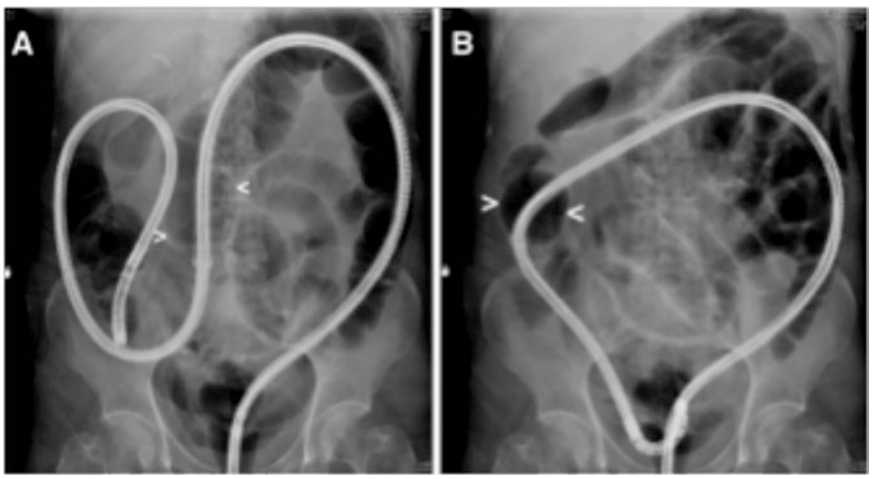

Fig. 11.5 An example of a balloon system straightening a redundant colon. Panel A shows a single-balloon colonoscopy with a loop in the transverse colon. Panel B shows the device after the transverse colon has been straightened. The arrows show the position of the inflated balloon at the tip of the overtube [6]. With permission from Moreels TG, Macken EJ, Pelckmans PA. Renewed attention for overtube-assisted colonoscopy to prevent incomplete endoscopic examination of the colon. Dis Colon Rectum 2013; 56: 1013–1018. © Wolters Kluwer

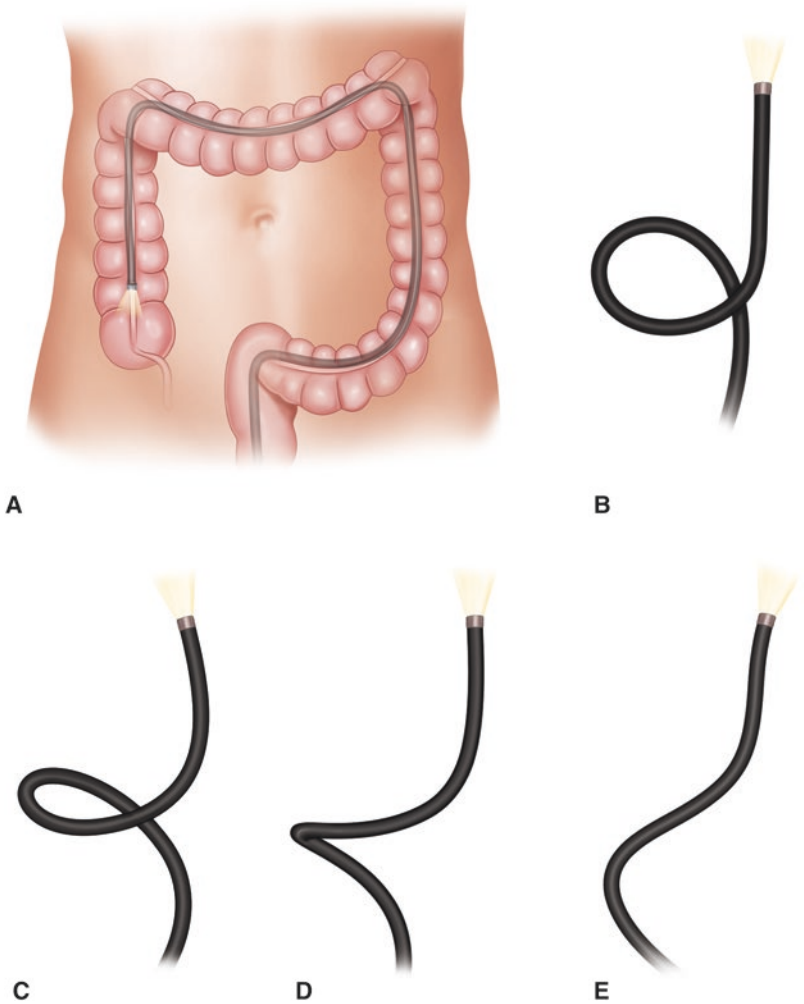

Fig. 11.6 Using MEI technology an alpha loop is reduced with clockwise motion of the scope

Magnetic Endoscopic Imaging (MEI) technology uses a series of electromagnetic generator coils within a catheter that is passed through the working channel of a conventional colonoscope. External sensors detect the magnetic pulses and these are converted into a 3-dimensional image of the colonoscope (Fig. 11.6). The literature evaluating this device generally supports that it helps endoscopists-in-training to recognize and reduce loops and to perform a technically proper insertion. The question is whether or not this technology offers any advantage among experienced clinicians. To answer this question, Szura and colleagues conducted a randomized controlled trial with experienced colonoscopists in the setting of unsedated colonoscopy [10]. They compared 100 patients undergoing conventional colonoscopy with 100 patients undergoing colonoscopy assisted by MEI technology. The cecal intubation rate was 98% in each group. The insertion time in the MEI group was shorter by an average of only 35 s but, interestingly, the subjective pain scores were also lower in the MEI group. A more recent randomized controlled trial was designed similarly to the first trial but these patients were sedated during their procedures [11]. Again, no difference was found in the cecal intubation rates between the two arms. Interestingly, in the 24% of cases that were subjectively described as "difficult," the insertion times of the MEI cases were shorter by an average of 3.3 min. These are encouraging results and the role of this technology in the setting of unsedated or difficult colonoscopy deserves further study.

Advanced Technologies and Novel Concepts

There are a number of emerging technologies that offer alternative platforms for endoscopic imaging of the colon. These novel approaches generally decrease looping in an effort to improve tolerability in unsedated patients and utilize advanced propulsion systems, next-generation optics, and/or computer-aided insertion. Three unique "out-of-the-box" concepts that are being developed for possible implementation in the colonoscopy suite that have been tested in patients at least in terms of proof of principle are reviewed in the following.

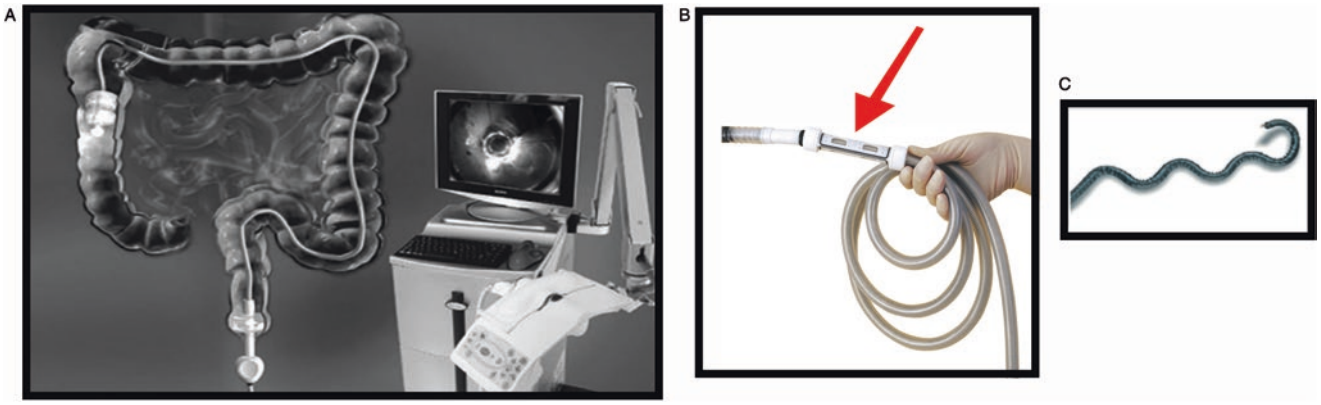

Fig. 11.7 (**a**) The Aer-O-Scope self-propelling system. (**b**) The Invendo system. The arrow shows where the driving motor attaches to control insertion and withdrawal. (**c**) The NeoGuide system

The Aer-O-Scope (GI View, Ramat Gan, Israel) is a pneumatic, self-propelled device that carries an endoscope through the colon (Fig. 11.7a). The propulsion system consists of two balloons the first of which rests at the anorectal ring and occludes the rectum. Carbon dioxide is then insufflated into the lumen and the pressure gradient advances the second balloon through the colon. This is a "self-navigating" system. The benefits of this technology are that it is disposable and that little technical skill is required to perform the colonoscopy. The downside of this device is that it has no therapeutic capabilities.

Another alternative endoscopic platform is a computer-assisted colonoscope that also uses a novel propulsion mechanism. The Invendo SC20 (Invendo Medical, Kissing, Germany) is a single-use, self-propelled colonoscope that relies on a drive mechanism described as an "inverted sleeve" (Fig. 11.7b). The operator uses a handheld unit to control the drive wheels causing the scope to elongate or shorten. Theoretically, the device minimizes forces across the colon wall and transmits the force of insertion to the tip of the device. A postmarketing study using this device evaluating the cecal intubation rate was closed early and, at this time, the future of this technology is not clear.

The NeoGuide endoscopy system (Los Gatos, CA) uses a computer to control the shape of the colonoscope during insertion in order to limit patient discomfort and avoid looping. The scope is made of 16 jointed segments or "vertebrae" that are each 8 cm in length (Fig. 11.7c). When the scope is manually advanced, the computer algorithm changes the configuration of the scope so that each segment follows the track of the segment in front of it (a "follow the leader" algorithm). This, in theory, reduces the lateral forces required for advancement of the scope. The monitor in this system displays the endoscopic image as well as a 3-dimensional map of the device similar to magnetic endoscopic imaging technology.

Summary

The main issue with difficult colonoscopy is safely maximizing the cecal intubation rate. The available evidence is not strong enough to recommend a rigid practice algorithm for these patients, but there are a few key concepts to keep in mind. Most importantly, using proper insertion techniques will permit cecal intubation in the majority of cases. It is also helpful to recognize that one colonoscope does not fit all patients. Patients with angulated or tortuous colons may best be approached with more flexible scopes and patients with redundant or floppy colons may require a stiffer scope like a standard adult colonoscope. In cases with a particularly difficult sigmoid, water immersion may be helpful. Ultimately, some patients will require more advanced techniques like overtubes and balloons in order to complete their colonoscopy. Finally, after an incomplete colonoscopy and depending on the clinical situation, it is important to consider alternative imaging modalities like virtual colonoscopy.

Pearls and Pitfalls

- Prior to performing a colonoscopy for a patient after a failed prior attempt at colonoscopy, it is helpful to assess why the prior attempted colonoscopy failed and address possible factors that may increase the likelihood of successful subsequent colonoscopy. For instance, improving the bowel preparation in a patient with an inadequate prior preparation or having a pediatric colonoscope available for a patient with known colon angulation or severe diverticulosis may be very helpful.
- Patience, relying on proper technique, and not allowing the frustration of the situation to negatively impact the

procedure (similar to surgeons' approach to a difficult operation in the operating theatre) are critical to the successful completion of a difficult colonoscopy.

- Given the availability of CT colonography, it is important to weigh the risks and benefits of proceeding with repeat colonoscopy after a failed prior colonoscopy. Similarly, in a situation where the cecum is not reached despite utilizing proper techniques and an appropriate colonoscope, aborting a difficult colonoscopy in anticipation of subsequent colonography may be prudent to decrease the risk of perforation.
- Failing to repeatedly withdraw sufficiently and reinsert is thought to be the most common error made when attempting colonoscopy through a redundant or floppy colon.
- When the colonoscope is at the level of the proximal ascending colon and will not pass into the caput of the cecum easily, maneuvers to facilitate insertion include applying a cecal lift, repositioning the patient, aspirating gas to pull the cecum onto the scope, and repeatedly withdrawing the scope to shorten the colon and reinserting.
- In a situation where the scope is fully inserted such that no length of the shaft remains outside of the patient but the cecum has not yet been reached (the colonoscopist has run out of scope) repeatedly withdrawing and reinserting the scope is required to pull the redundant colon onto the scope in an accordion fashion.
- New technology including balloon assistance and computer guidance is on the horizon and may be available to facilitate cecal intubation for the difficult colonoscopy.

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How to Recognize, Characterize, and Manage Premalignant and Malignant Colorectal Polyps

12

Jeong-Sik Byeon

Abbreviations

CI	Confidence interval
CIMP	CpG island methylation phenotype
CIN	Chromosomal instability
CRC	Colorectal cancer
EMR	Endoscopic mucosal resection
EPMR	Endoscopic piecemeal mucosal resection
ESD	Endoscopic submucosal dissection
HP	Hyperplastic polyp
LST	Laterally spreading tumor
LST-G	Granular laterally spreading tumor
LST-NG	Nongranular laterally spreading tumor
MMR	Mismatch repair
MSI	Microsatellite instability
NBI	Narrow band imaging
NICE	NBI International Colorectal Endoscopic
SSA/P	Sessile serrated adenoma/polyp
TSA	Traditional serrated adenoma
WASP	Workgroup serrAted polypS & Polyposis

Key Points

- White light endoscopy is the basic, but most important, imaging technique in the differential diagnosis of colorectal polyps. Hardness, expansile growth, fold convergence, and depression and/or ulcer are suggestive of deep submucosal colorectal cancers (CRCs).
- Pit pattern correlates well with histological diagnosis of colorectal polyps. Although chromoscopy with or without magnification is ideal for pit pattern analysis, current high definition colonoscopy can also be used to evaluate pit patterns without chromoscopy. Type V_N pit pattern indicates the risk of deep submucosal CRCs.
- Equipment-based image-enhanced endoscopy, such as narrow band imaging (NBI), is helpful in the real-time histological diagnosis of colorectal polyps. NBI International Colorectal Endoscopic (NICE) type II is indicative of benign adenomas, which should be resected endoscopically. NICE type III suggests the risk of deep submucosal CRCs.
- Real-time diagnosis of sessile serrated adenoma/polyps (SSA/Ps) is based on their clinical and endoscopic features. Most SSA/Ps are located in the proximal colon and are > 5 mm in diameter. Workgroup serrAted polypS & Polyposis (WASP) classification is useful for the diagnosis of SSA/P. SSA/Ps should be resected endoscopically.
- Early CRCs should be resected *en bloc*. Deep submucosal CRCs with poor prognostic histological features should be managed surgically.
- Most benign adenomas can be safely and effectively resected piecemeal. Although endoscopic piecemeal mucosal resection (EPMR) is associated with a high local recurrence rate, most recurrences can be managed by repeat endoscopic resection. The main indication for EPMR is homogenous granular laterally spreading tumor (LST).
- Endoscopic submucosal dissection (ESD) can achieve a high *en bloc* resection rate. As its perforation rate is high, ESD should be reserved for *en bloc* resection of large superficial submucosal CRCs. Nodular mixed granular and nongranular LSTs are the main indications for colorectal ESD.

Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide. As most CRCs develop from adenomatous polyps, early detection of premalignant colorectal polyps and/or early CRC is pivotal in preventing the development of

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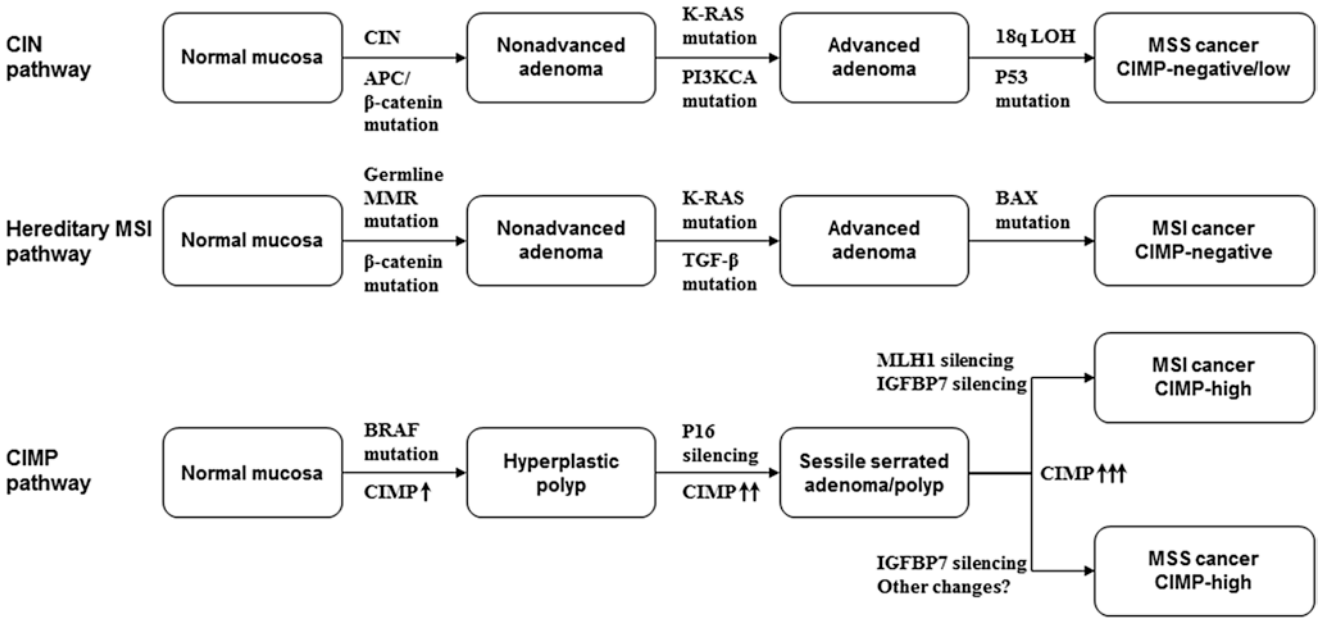


Fig. 12.1 Molecular pathways of colorectal cancer (CRC) carcinogenesis. CIN and hereditary MSI pathways are genomic instability pathways and CIMP is an epigenomic instability pathway. *CIMP* CpG island methylation phenotype, *CIN* chromosomal instability, *MMR* mismatch repair, *MSI* microsatellite instable, *MSS* microsatellite stable

advanced CRC, thereby reducing CRC-associated mortality. Colonoscopy is the most important tool for management of colorectal neoplasia, as it can not only detect colorectal lesions, but also remove premalignant polyps and some early CRCs by endoscopic resection. Despite its usefulness, colonoscopy is not completely safe because of complications such as bleeding and perforation. These complications occur more frequently during therapeutic colonoscopy, including endoscopic resection of colorectal lesions, than during diagnostic colonoscopy. Because some colorectal polyps, such as inflammatory polyps and small hyperplastic polyps (HPs) of the rectosigmoid colon, do not have malignant potential, they can be left in situ without endoscopic resection. Thus, accurate recognition and characterization of colorectal polyps are crucial in determining whether these polyps should be resected. This chapter will address the recognition, characterization, and management of premalignant and malignant colorectal polyps.

Molecular Pathways of Colorectal Neoplasia

CRC develops through multistep carcinogenic pathways, including alterations of function in multiple signal transduction pathways. Functional alterations are associated with changes in the cellular environment, which can lead to genetic mutations and epigenetic changes, alterations termed genomic and epigenomic instability, respectively. Chromosomal instability (CIN) and microsatellite instability (MSI) are two types of genomic instability (Fig. 12.1), whereas CpG island methylation phenotype (CIMP) is a representative pathway of epigenomic instability [1]. Although CRC carcinogenesis may occur via any of these pathways, these molecular pathways are not completely separate. Some CRCs may develop through mixed routes, such as crossover or even overlap between pathways.

Chromosomal Instability

CIN refers to structural alterations or numerical gain or loss of chromosomes, leading to aneuploidy and the loss of heterozygosity. About 70% of CRCs may develop through the CIN pathway [2]. The gatekeeper mutation for adenoma development through the CIN pathway occurs in the *APC* tumor suppressor gene. Because *APC* plays a pivotal role in the Wnt signal transduction pathway, mutations in this gene can increase the proliferation of colorectal epithelial cells, thereby initiating adenoma development. Mutations in the *K-RAS* oncogene are also frequent genetic alterations in the CIN pathway. As the K-RAS protein is involved in the receptor tyrosine kinase cascade, *K-RAS* mutations affect cell proliferation and apoptosis. Mutations in the *p53* tumor suppressor gene are involved in the progression of early adenomas to late advanced adenomas. Loss of heterozygosity of chromosome 18q also contributes to CRC development as a late event in the CIN pathway. Tumor suppressor genes located on chromosome 18q include *DCC*, *SMAD2*, and *SMAD4*, which are important in regulating cell proliferation and apoptosis. The development of CRC may require

10–15 years, from normal colorectal mucosa to conventional adenoma to CRC, via these multistep genetic changes in the CIN pathway.

Microsatellite Instability

DNA mismatch repair (MMR) systems, such as MLH1, MSH2, MSH6, and PMS2, repair errors that occur during DNA replication. If MMR dysfunction occurs, mutations in other genes cannot be repaired and multiple mutations may accumulate, accelerating the CRC carcinogenic process. Microsatellites are simple repeat nucleotide sequences of DNA that are subject to mutations and base-pair substitutions during DNA replication in the presence of MMR dysfunction. The MSI pathway refers to the carcinogenic pathway stemming from MMR dysfunction. About 10–15% of CRCs show MSI. Of these, around 20% have a germline mutation in one of four MMR genes (MLH1, MSH2, MSH6, and PMS2), a condition called the Lynch syndrome. The remaining 80% of CRCs with MSI may arise from the hypermethylation of the promoter of MLH1 [1]. The latter is an important example of epigenomic alteration and gives rise to sporadic CRCs with MSI.

CRCs that arise through hereditary MSI pathways, such as the Lynch syndrome, frequently show mutations in *TGF-β* and *BAX*, the exons of which contain microsatellites. *K-RAS* mutations may also occur, but *p53* mutations are rare in the MSI pathway. Because MMR dysfunction increases mutation rates 100-fold, CRCs that arise through the hereditary MSI pathway may develop very rapidly, with only 3–5 years required for progression from normal mucosa to conventional adenoma to hereditary MSI CRC.

CpG Island Methylation Phenotype

Expression of a specific gene is suppressed when CpG sequences in the promoter of that gene are methylated. The CIMP pathway of colorectal carcinogenesis involves the methylation of CpG sequences of tumor suppressor genes. The CIMP pathway is also called the serrated neoplasia pathway, because this route is the main pathway through which serrated polyps progress to CRC.

Serrated polyps can be classified as HPs, sessile serrated adenoma/polyps (SSA/Ps), and traditional serrated adenomas (TSAs) [3]. Histologically, serrated polyps have a saw-tooth appearance, resulting from the proliferation and hyperplasia of crypt epithelium and the resultant saw-tooth infolding of the crypt. HPs can be subdivided into microvesicular type, goblet cell-rich type, and mucin-poor type HPs. SSA/Ps are thought to arise from microvesicular-type HPs and are the main precursors of CRC through the CIMP pathway. TSAs are also believed to be premalignant polyps. However, the molecular pathway from TSA to CRC is largely unknown because TSAs are very rare.

The CIMP pathway involves the hypermethylation of the promoter regions of tumor suppressor genes and/or MLH1, a specific DNA MMR gene. Hypermethylation of the MLH1 promoter can lead to MMR dysfunction followed by MSI. This pathway constitutes the carcinogenic mechanism by which SSA/Ps develop into sporadic MSI CRCs (Fig. 12.1). Tumor suppressor genes frequently silenced by the CIMP pathway include *p16* and *IGFBP7*. *BRAF* oncogene mutation is another important feature in the serrated neoplasia pathway. *BRAF* mutations have been detected in 50–72% of microvesicular-type HPs, 70–80% of SSA/Ps, and 77% of CIMP-high CRCs, but in only 1% of conventional adenomas, supporting the hypothesis that the CIMP pathway involves the transformation of SSA/Ps to CIMP-high, *BRAF*-mutant CRCs [1].

Endoscopic Features of Colorectal Polyps

Colorectal polyps have a variety of histological subtypes, with conventional adenomas, including tubular/tubulovillous/villous adenomas, SSA/Ps, and TSAs being the main types of premalignant polyp. Although some hamartomatous polyps can progress to CRCs, they are rare. Endoscopic characterization of these polyps is important for histological diagnosis, thereby determining the treatment plan.

The Paris Classification

The Paris classification, formulated in 2002 and updated in 2003, was established to categorize superficial neoplastic lesions of the gastrointestinal tract (Table 12.1, Fig. 12.2) [4]. Superficial neoplastic lesions are lesions that are considered on endoscopy to be benign adenomas, mucosal cancers, and/or submucosal cancers. The Paris classification has categorized these lesions into three morphological groups: protruding lesions (type I), nonprotruding and nonexcavated lesions (type II), and excavated lesions (type III). Type I lesions can be further subdivided into pedunculated (type Ip) and sessile (type Is) lesions, whereas type II lesions can be subdivided into slightly elevated (type IIa), completely flat (type IIb), and slightly depressed (type IIc) lesions. Types Is and IIa can be differentiated by placing a biopsy forceps next to the lesion as a calibrating gauge. A lesion protruding beyond the level of the closed jaws of the biopsy forceps (approximately 2.5 mm) is classified as type Is, whereas a lesion protruding less than this level is classified as type IIa.

Chromoscopy and Pit Patterns

Chromoscopy refers to the endoscopy technique, in which dye is sprayed on the colorectal mucosal surface to observe lesions in greater detail. Indigo carmine and crystal violet are the two most commonly used dyes. The former is a contrast agent that is not absorbed by colonic epithelial cells but enhances the contrast between a lesion and adjacent mucosa. As it exaggerates the unevenness of the polyp surface, indigo carmine spray can also assess the surface pit patterns of a polyp in greater detail. Crystal violet is an absorbable dye that can assist in the detailed assessment of surface pit patterns, especially minute pit patterns such as Kudo types III_S, V_I, and V_N (Fig. 12.3).

Table 12.1 The Paris classification of superficial neoplastic lesions in the gastrointestinal tract [4]

Protruding	**I**
Pedunculated	Ip
Sessile	Is
Nonprotruding and nonexcavated	**II**
Slightly elevated	IIa
Completely flat	IIb
Slightly depressed	IIc
Elevated and depressed types	IIa+IIc, IIc+IIa
Excavated[a]	**III**[a]
Ulcer	III
Excavated and depressed type	IIc+III, III+IIc

[a]Paris type III lesions are rarely observed in the colorectum

A pit is a structure formed by the opening of several crypts. The pit appearances of a polyp surface have been classified into several types [5]. Pit patterns were originally assessed by magnifying chromoendoscopy. However, current high definition colonoscopes may be used to evaluate pit patterns without chromoendoscopy and/or magnification, although the accuracy of this approach should be further investigated. Pit patterns correlate well with the histopathology of colorectal polyps (Table 12.2, Fig. 12.4). The overall accuracy of pit patterns for the histological diagnosis of colorectal polyps has been estimated at approximately 70–80%, with accuracy depending on the expertise of the operator. Classification of pit patterns may

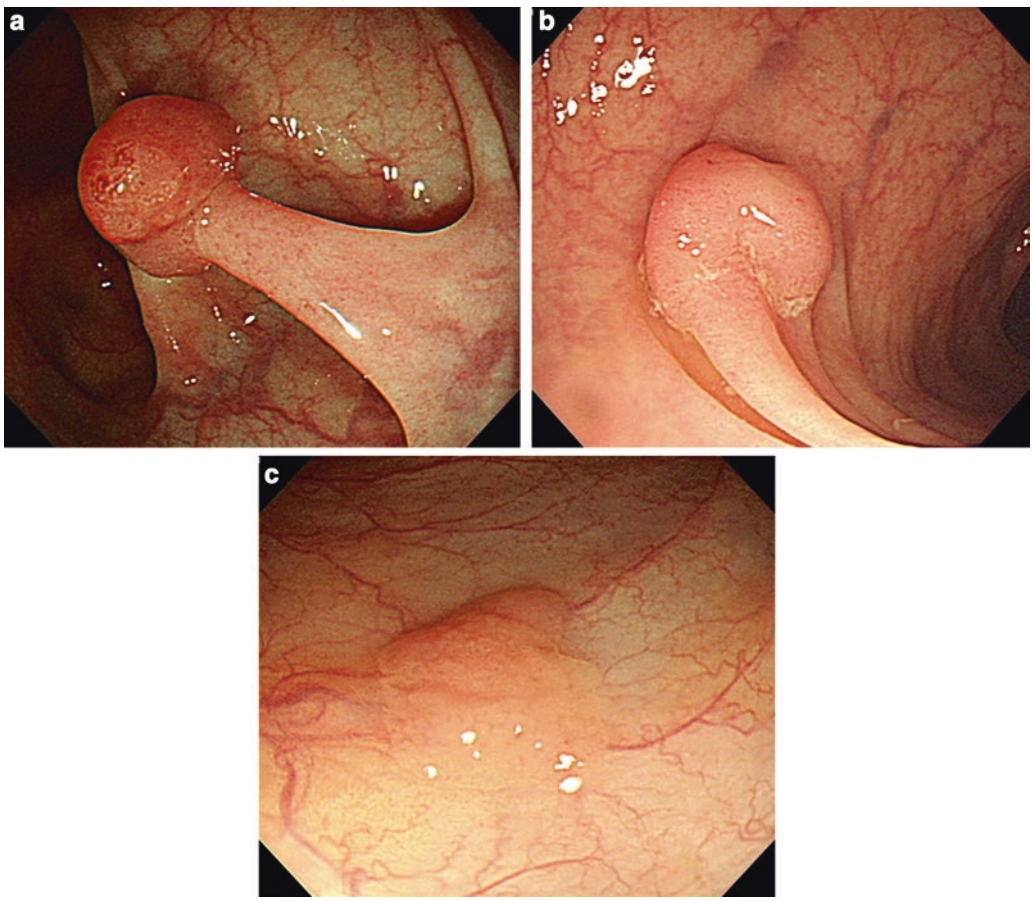


Fig. 12.2 The Paris classification of colorectal polyps. (**a**) Type Ip polyp with head diameter 8 mm and a stalk, (**b**) Type Is polyp 8 mm in diameter, (**c**) Type IIa polyp 10 mm in diameter

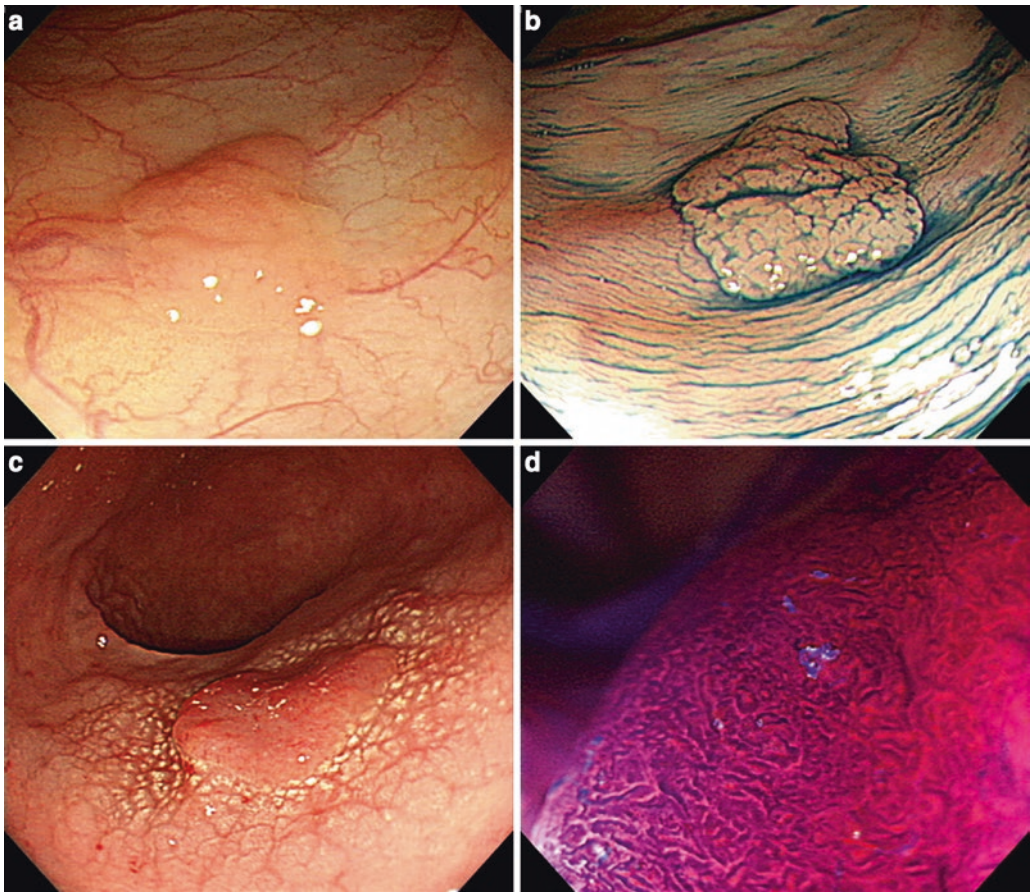


Fig. 12.3 Chromoscopy results. (**a**) A type IIa polyp. (**b**) Chromoscopy with indigo carmine, a contrast agent makes flat polyps look more prominent. Delineation of the polyp and assessment of the surface pattern are easier with indigo carmine chromoscopy. (**c**) Another type IIa polyp. (**d**) Chromoscopy with crystal violet, an absorbable dye making assessment of fine surface pit patterns easier. Irregular type V_I pit patterns are clearly delineated

Table 12.2 Pit patterns and their correlation with histopathology of colorectal polyps

Type	Description	Most common histopathology	Management
I	Normal round pits	Normal colorectal mucosa	Observation
II	Stellate or papillary pits	Hyperplastic polyp	Observation
			If SSA/P is suspected, endoscopic resection
III_S	Small round or short tubular pits	Conventional adenoma	Endoscopic resection
III_L	Large round or long tubular pits	Conventional adenoma	Endoscopic resection
IV	Branch-like or gyrus-like pits	Conventional adenoma	Endoscopic resection
V_I	Irregular pits	Mucosal cancer	Endoscopic resection
V_N	Nonstructural pits	Submucosal cancer, especially deep submucosal cancer	Surgical resection

help choose a treatment plan. For example, polyps with a type III_L pit pattern are usually benign conventional adenomas and can therefore be resected endoscopically. By contrast, polyps with a type V_N pit pattern are indicative of deep submucosal cancers with lymph node metastasis and should be managed by surgical resection plus lymph node dissection.

Equipment-Based Image-Enhanced Endoscopy

Narrow band imaging (NBI) was developed to more clearly visualize surface microvessels. NBI uses an optical filter that selects specific ranges of wavelengths of visible light, allowing the vessels to be enhanced and visualized more prominently. Other techniques such as FICE and iScan use a

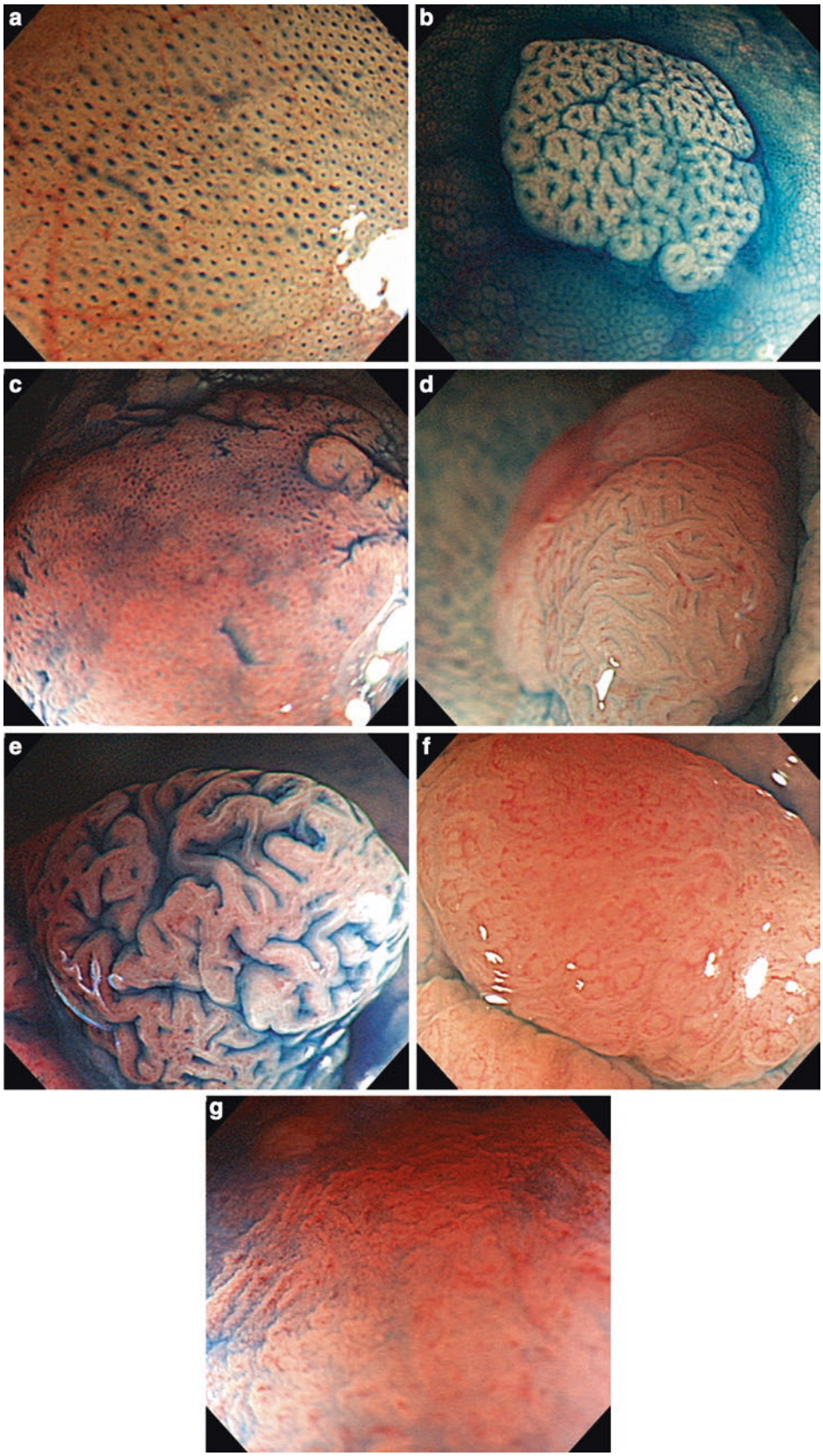


Fig. 12.4 Pit patterns of types (**a**) I, (**b**) II, (**c**) III_S, (**d**) III_L, (**e**) IV, (**f**) V_I, and (**g**) V_N

software program that can modify the white light images, enhancing the microvasculature and surface structures and allowing them to be visualized more clearly. All these image-enhanced endoscopy techniques have been shown useful in the histological diagnosis of colorectal polyps.

The NBI International Colorectal Endoscopic (NICE) classification was established to categorize colorectal polyps according to the NBI features of polyp surfaces [6]. NICE classification addresses three features: color, vessels, and surface pattern of colorectal polyps (Table 12.3). Similar to pit patterns on chromoscopy, NICE classifications correlate well with the histological diagnosis of colorectal polyps. Most polyps classified as NICE type 1 are hyperplastic. Most conventional adenomas are NICE type 2, as are some early cancers of depth limited to the mucosa or superficial submucosa. NICE type 3 is indicative of deep submucosal cancers with lymph node metastases (Fig. 12.5).

Many studies have evaluated the performance of NBI in the differential diagnosis of colorectal polyps. A meta-analysis showed that the pooled negative predictive value of NBI for adenomatous polyp histology was 91% (95% confidence interval [CI], 88–94%) [7]. Moreover, the agreement in assignment of postpolypectomy surveillance intervals based on optical biopsy with NBI of colorectal polyps < 5 mm in size was 91% (95% CI, 86–95%) in academic settings and 92% (95% CI, 88–96%) when performed by experienced endoscopists [7]. However, when performed by inexperienced endoscopists and/or trainees, the performance of NBI was <90%, limiting its usefulness. In addition, NBI was less accurate in differentiating between types 2 and 3 (i.e., differentiating mucosal/superficial submucosal cancers and deep submucosal cancers) than for differentiating between types 1 and 2.

The WASP Classification

Although the NICE classification is very useful, it cannot differentiate SSA/Ps accurately, as some SSA/Ps show features of NICE type 1 and others show features of NICE type 2. This led to the development of the Workgroup serrAted polypS & Polyposis (WASP) classification [8]. The WASP classification is based on four NBI features that favor SSA/P: clouded surface, indistinctive borders, irregular shape, and dark spots inside crypts (Fig. 12.6). The presence of at least two of these features is considered diagnostic of an SSA/P (Fig. 12.7). After training on the WASP classification, the accuracy of optical diagnosis for SSA/P was 0.79 (95% CI, 0.72–0.86), and the accuracy for polyps diagnosed with high confidence was 0.87 (95% CI, 0.80–0.95).

Treatment Strategies for Colorectal Polyps

Premalignant polyps should be completely resected to prevent the progression to CRCs. Some early cancers can be also cured by endoscopic resection. Thus, accurate histological diagnosis and a proper treatment plan based on this diagnosis are vital in managing patients with colorectal polyps.

Indications for Endoscopic Resection

Inflammatory colorectal polyps and small hyperplastic polyps at the rectosigmoid colon do not have malignant potential and therefore do not require treatment. By contrast, premalignant polyps, such as conventional adenomas, SSA/Ps, TSAs, and some hamartomas such as Peutz–Jeghers polyps, must be endoscopically resected. Malignant polyps (early CRCs) can be resected endoscopically or surgically, with the latter accompanied by lymph node dissection. The decision to resect endoscopically or surgically is based on the absence or presence, respectively, of metastases at regional lymph nodes. As mucosal CRCs are never accompanied by lymph node metastases, they can be managed by endoscopic resection. The risk of metastases of submucosal CRCs to regional lymph nodes is about 10% and is associated with the histopathological features of the primary tumor. Poorly differentiated adenocarcinomas, cancer invasion of the lymphatic or vascular channels in the submucosa,

Table 12.3 NBI International Colorectal Endoscopic (NICE) classification[a]

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels may be present coursing across the lesion	Thick brown vessels surrounding white structures	Has area(s) with markedly distorted or missing vessels
Surface pattern	Dark or white spots of uniform size, or homogenous absence of pattern	Oval, tubular, or branched white structures surrounded by brown vessels	Areas of distortion or absence of pattern
Most likely pathology	Hyperplastic polyp	Adenoma	Deep submucosal cancer

[a]NICE classification can be applied using colonoscopy with or without magnification

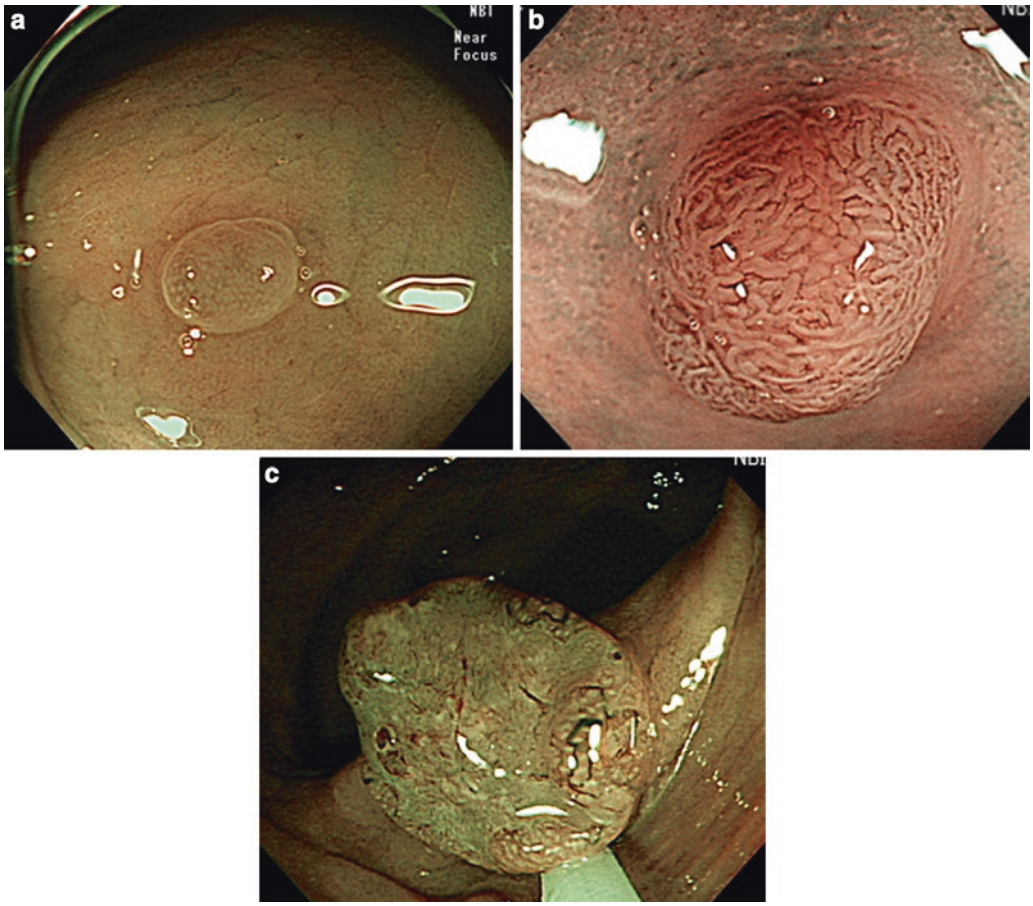
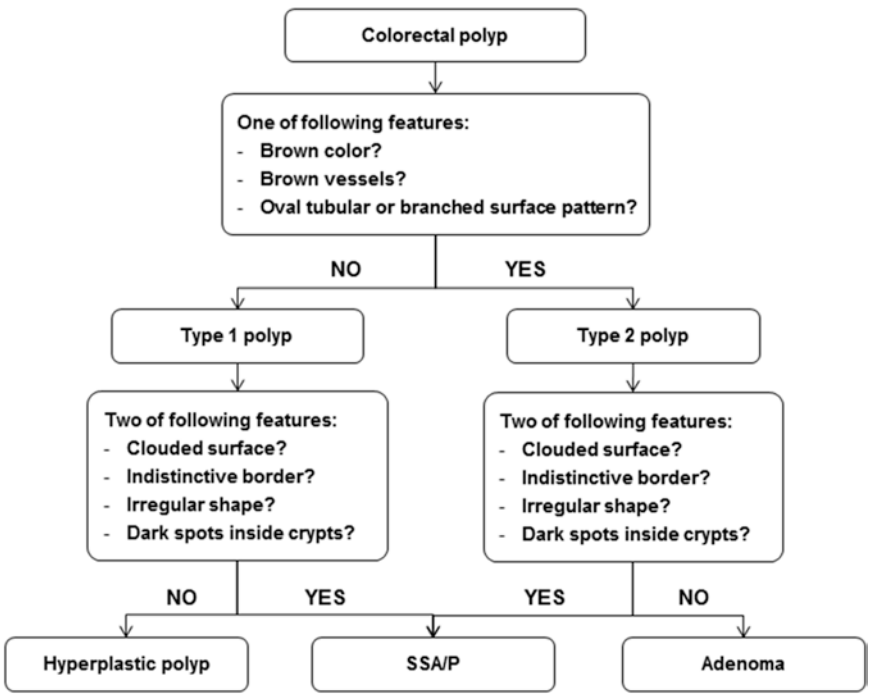


Fig. 12.5 NBI International Colorectal Endoscopic (NICE) classification of colorectal polyps. (**a**) A diminutive polyp of NICE type 1, which was a hyperplastic polyp. (**b**) Small type Is polyp with NICE type 2, which was a tubular adenoma. (**c**) An approximately 12-mm sized NICE type 3 polyp, with final pathology of a submucosal cancer with invasion depth of 2500 μm

Fig. 12.6 The WASP classification



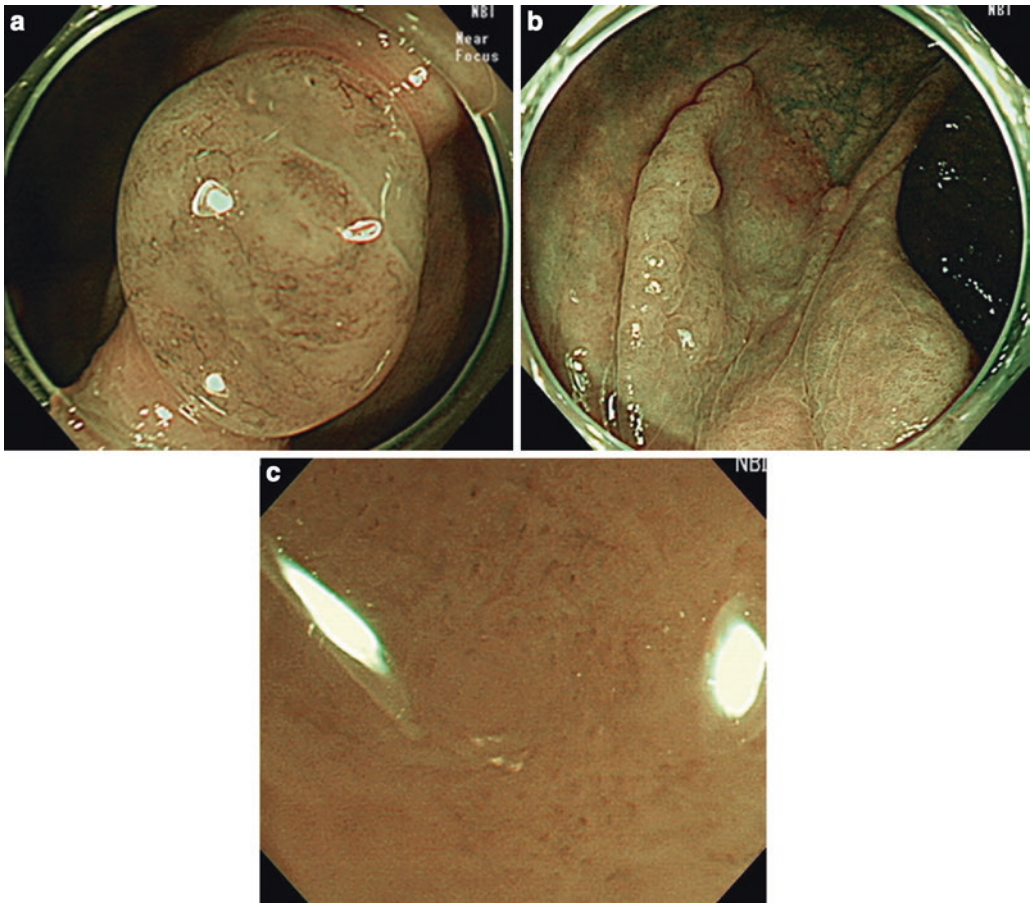


Fig. 12.7 NBI features of SSA/P. (**a**) Clouded surface, (**b**) indistinctive borders and irregular shape, and (**c**) dark spots inside crypts

submucosal cancer invasion depth ≥ 1000 μm, and tumor budding are thought to increase the risk of regional lymph node metastasis. Therefore, submucosal CRCs without these histological features indicative of poor prognosis can be managed by endoscopic resection alone. By contrast, submucosal CRCs with any of these features should be managed surgically. These findings have led the American College of Gastroenterology and the Japanese Society for Cancer of the Colon and Rectum to formulate guidelines for the management of endoscopically resected submucosal CRCs (Tables 12.4 and 12.5) [9, 10]. Indications for endoscopic resection are summarized in Table 12.6.

Real-Time Histological Diagnosis of Colorectal Polyps

Real-time histological diagnosis of colorectal polyps during colonoscopy is crucial to determine whether the polyp can be resected endoscopically. Techniques used for real-time histological diagnosis include assessment of gross morphology by white light endoscopy, pit pattern analysis by high definition endoscopy with or without chromoscopy, and vascular pattern analysis by equipment-based image-enhanced endoscopy such as NBI. HPs usually present with a type II pit pattern and a NICE type I NBI pattern. They are usually small and more frequently located in the rectosigmoid than in the proximal colon. Conventional adenomas, including tubular, tubulovillous, and villous adenomas, may have types III_S, III_L, and/or IV pit patterns and a NICE type II NBI pattern. Conventional adenomas, which can be located throughout the entire colorectum, vary in size from < 5 mm to > 20–30 mm. Mucosal and/or superficial submucosal CRCs with invasion depth < 1000 μm usually show a type V_I pit pattern and a NICE type II NBI pattern, but their vascularity may be more irregular than the typical NICE type II observed in tubular adenomas. Deep submucosal CRCs with invasion depth ≥ 1000 μm usually have a type V_N pit pattern and a NICE type III NBI pattern.

The differential diagnosis of diminutive polyps, defined as those < 5 mm in diameter, is necessary in planning treatment. Because white light endoscopy alone cannot differentiate between diminutive HPs and diminutive adenomas, NBI is commonly used for real-time histological diagnosis. As NBI performs well in the real-time histological diagnosis of diminutive polyps, these polyps may be

Table 12.4 The American College of Gastroenterology recommendations for management of endoscopically resected submucosal colorectal cancers

Consider additional surgery with lymph node dissection	Poorly differentiated adenocarcinoma
	Vascular or lymphatic involvement of cancer
	Involvement of cancer at the endoscopic excision margin
Consider follow-up without additional surgery	Absence of the earlier three conditions

Table 12.5 The Japanese Society for Cancer of the Colon and Rectum recommendations for management of endoscopically resected submucosal colorectal cancers

Consider additional surgery with lymph node dissection	Submucosal invasion depth ≥ 1000 μm
	Vascular invasion of cancer
	Poorly differentiated adenocarcinoma/signet-ring cell carcinoma/mucinous carcinoma
	Tumor budding at the site of deepest invasion
	Involvement of cancer at the vertical resection margin
Consider follow-up without additional surgery	Absence of the earlier five conditions

Table 12.6 Colorectal polyps indicated for endoscopic resection

Colorectal polyps not requiring treatment	Colorectal polyps requiring endoscopic resection	Colorectal polyps requiring surgical resection
Inflammatory polyp	Conventional adenomas (tubular, tubulovillous, and villous adenomas)	Submucosal CRC with poor prognostic histological features[a]
Hyperplastic polyp		
Others (muco-submucosal elongated polyp, lymphoid polyp, etc.)	Sessile serrated adenoma/polyp	
	Traditional serrated adenoma	
	Some hamartomas (Peutz–Jeghers polyp, juvenile polyp in juvenile polyposis)	
	Mucosal CRC[b]	
	Submucosal CRC without poor prognostic histological features[c]	

CRC colorectal cancer

[a]Submucosal CRCs with any of the earlier poor prognostic features may recur or metastasize if managed only by endoscopic resection. Therefore, they should be managed by surgical resection with lymph node dissection

[b]Mucosal CRC, also described as high-grade dysplasia, indicates CRCs whose depth is limited to the epithelium, lamina propria, or muscularis mucosa

[c]Poor prognostic histological features include deep submucosal invasion (≥ 1000 μm depth of submucosal invasion from the muscularis mucosa), poorly differentiated carcinoma, lymphovascular tumor invasion, tumor budding, and cancer involvement at the endoscopic resection margins. Patients with submucosal CRCs lacking these features may be at little risk of lymph node metastasis and recurrence after endoscopic resection

managed clinically by a resect-and-discard or a diagnose-and-leave strategy. In a resect-and-discard strategy, endoscopists do not send the endoscopically resected specimens to pathologists for histological diagnosis when they have high confidence in the real-time histologic evaluation of diminutive polyps. In a diagnose-and-leave strategy, endoscopists do not resect but leave rectosigmoid diminutive polyps in situ when they have high confidence that the polyp is an HP histologically. These two strategies, which may improve the cost-effectiveness of endoscopic diagnosis and treatment of colorectal polyps, should be performed cautiously and only by experts in image-enhanced endoscopy such as NBI.

The differential diagnosis of HPs and SSA/Ps is also important for determining treatment. Although the WASP classification is highly accurate in the differential diagnosis of SSA/Ps, it is not perfect. Whereas HPs are usually < 5 mm in diameter and located in the rectosigmoid colon, SSA/Ps are usually > 5 mm in diameter and located in the proximal colon. These findings suggest that all serrated polyps proximal to the sigmoid colon should be fully resected, as should all serrated polyps in the rectosigmoid colon > 5 mm in diameter [11].

Treatment Strategy of Submucosal CRCs

Improvements in endoscopy have expanded the indications for endoscopic management of colorectal neoplasms. Early CRCs can now be removed by endoscopic resection. Mucosal CRCs do not metastasize and can be managed by endoscopic resection. By contrast, submucosal CRCs have about a 10% risk of lymph node metastasis. Therefore, the first step in the management of submucosal CRCs is the assessment of risk of lymph node metastasis.

As presented in Tables 12.4 and 12.5, histological features are optimal in predicting the risk of lymph node metastasis. However, endoscopists should assess the risk of metastasis of submucosal CRCs before resecting the primary tumor. The risk of lymph node metastasis has been found to correlate with the depth of submucosal cancer invasion. Superficial submucosal invasion < 1000 μm is associated with little risk of metastasis, whereas deep submucosal invasion ≥ 1000 μm has a risk of lymph node metastasis. Therefore, endoscopic features suggesting deep submucosal cancer invasion should be carefully investigated to determine whether endoscopic resection is indicated. Table 12.7 and Fig. 12.8 summarize the endoscopic features suggesting deep submucosal cancer invasion and the associated risk of lymph node metastasis. Suspected submucosal CRCs with any of these endoscopic features should be managed surgically, whereas those CRCs without these features may be managed endoscopically.

Table 12.7 Endoscopic features suggesting deep submucosal cancer invasion and probable lymph node metastasis

White light endoscopy features	Pit pattern	Image-enhanced endoscopy features
Hardness	Kudo type V_N	NICE type III
Fold convergence		
Expansile growth		
Definite depression or ulcer		
Nonlifting sign		

If possible, endoscopic resection of early CRC should be *en bloc*, with tumor-free resection margins. Endoscopic piecemeal mucosal resection (EPMR) may result in residual cancer at the resection site, with a risk of recurrence. In addition, EPMR specimens are not suitable for histopathological evaluation, making it difficult to determine the occurrence of poor prognostic histological features, such as involvement of resection margins. Suspected early CRCs should therefore be resected *en bloc*.

The nonlifting sign is regarded as indicative of a tumor with deep submucosal cancer invasion (Fig. 12.9). Normally, colorectal tumors are lifted following the submucosal injection of saline. However, submucosal saline cannot lift tumors with deep submucosal cancer invasion. The presence of this nonlifting sign suggests that these tumors may be deep submucosal or more advanced cancers and indicate the need for surgical resection without a trial of endoscopic resection.

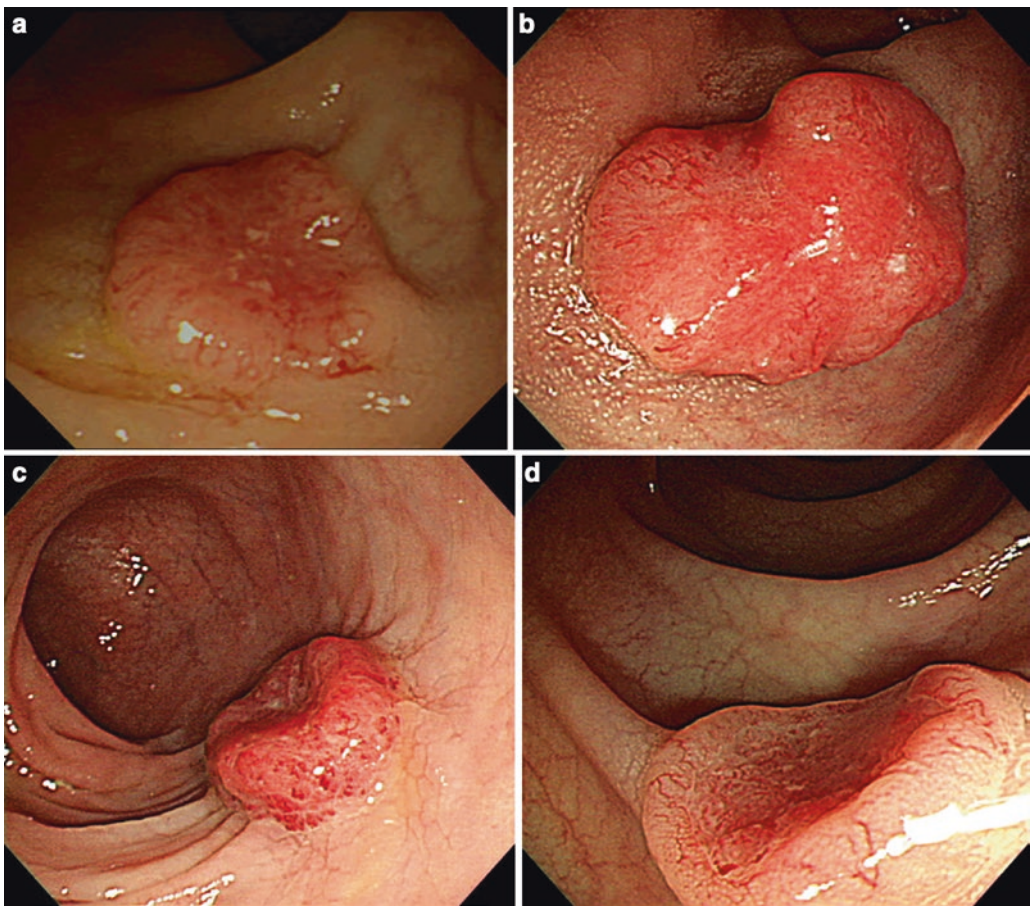


Fig. 12.8 Endoscopic features of deep submucosal cancer invasion. (**a**) Hardness, (**b**) expansile growth, (**c**) fold convergence, and (**d**) depression or ulcer

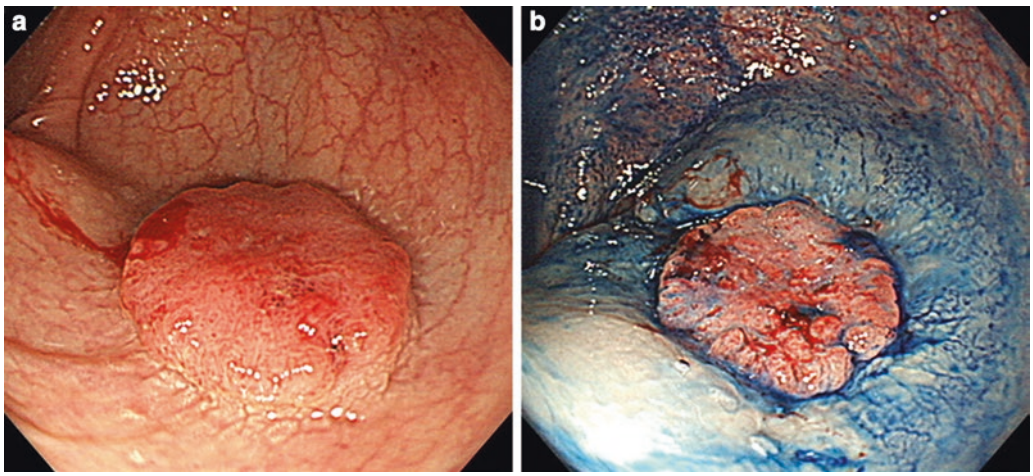


Fig. 12.9 Nonlifting sign. (**a**) An approximately 14-mm sized, hard polyp. (**b**) Submucosal injection of saline lifted the area surrounding the tumor, but not the tumor itself. The patient underwent surgical resection, with the resected specimen showing deep submucosal cancer

The nonlifting sign may be present in benign adenomas with severe submucosal fibrosis caused by previous multiple biopsies.

Treatment Strategy for Laterally Spreading Tumors (LSTs)

LSTs are colorectal tumors > 20 mm in diameter that mainly grow laterally without vertical growth. According to the Paris classification, LSTs are classified as large IIa lesions. LSTs may be subclassified as granular (LST-G) and nongranular (LST-NG) types. LST-Gs can be subdivided into homogenous and nodular mixed types and LST-NG into elevated and pseudodepressed types (Fig. 12.10). The risk of submucosal cancer differs among the subtypes of LST. Homogenous LST-Gs, regardless of size, are at little risk of submucosal cancer invasion. By contrast, pseudodepressed LST-NGs have a high risk of submucosal cancer invasion. The frequencies of submucosal cancer invasion by pseudodepressed LST-NGs 10–19 mm and 20–29 mm in size were 28% and 41%, respectively [12], whereas almost all pseudodepressed LST-NGs > 30 mm in diameter are at risk of submucosal cancer invasion. Nodular mixed LST-Gs and elevated LST-NGs have intermediate risks of submucosal cancer invasion. Based on their risk of submucosal cancer invasion, pseudodepressed LST-NGs should be managed by endoscopic en bloc resection, which may also be ideal for nodular mixed LST-Gs and elevated LST-NGs. By contrast, EPMR may be sufficient for homogenous LST-Gs because the latter have little risk of submucosal cancer invasion [13].

Endoscopic Resection Methods

Endoscopic resection methods can be classified based on the use of electrical current and the types of cutting accessories. The decision on which method to use should be based on the characteristics of each resection method, the target lesions to be resected, and the expertise of individual endoscopists.

Cold Biopsy

Diminutive polyps < 5 mm can be removed easily by cold biopsy. Although technically easy and with few complications, cold biopsy may result in the incomplete removal of polyps with minute remnant lesions. A comparison of cold biopsy and cold snare polypectomy showed no difference in the complete resection rate for lesions ≤ 4 mm (97% vs. 100%), but cold biopsy showed a lower complete resection rate than cold snare polypectomy for lesions > 5 mm in size (70% vs. 94%) [14]. Therefore, cold biopsy may be indicated for removal of diminutive colorectal polyps < 5 mm in diameter.

Cold Snare Polypectomy

Cold snare polypectomy is usually indicated for polyps 5–7 mm in diameter. Because it does not utilize electrical current, only mechanical guillotining, it may leave a viable remnant tumor. Therefore, a small amount of normal surrounding mucosa should be snared along with the polyp itself (Fig. 12.11).

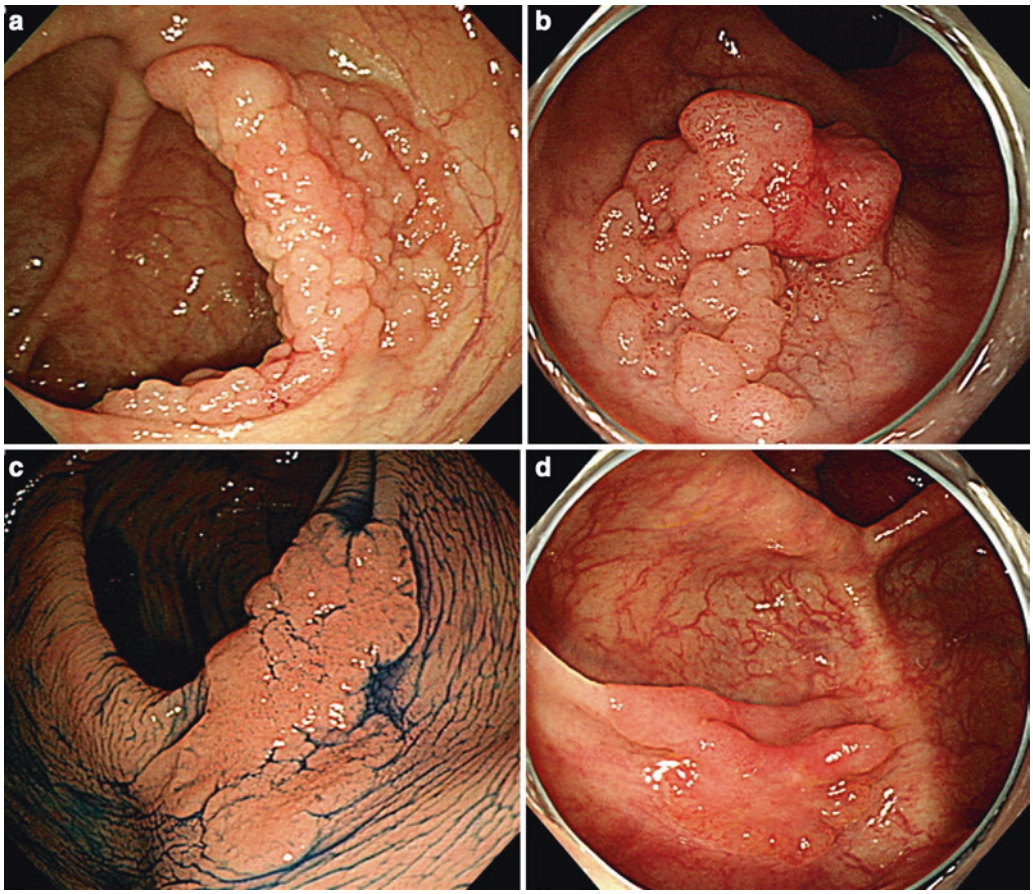


Fig. 12.10 Laterally spreading tumors (LST). (**a**) Granular LST (LST-G) of homogenous type, (**b**) nodular mixed LST-G, (**c**) nongranular LST (LST-NG) of elevated type, and (**d**) pseudodepressed LST-NG

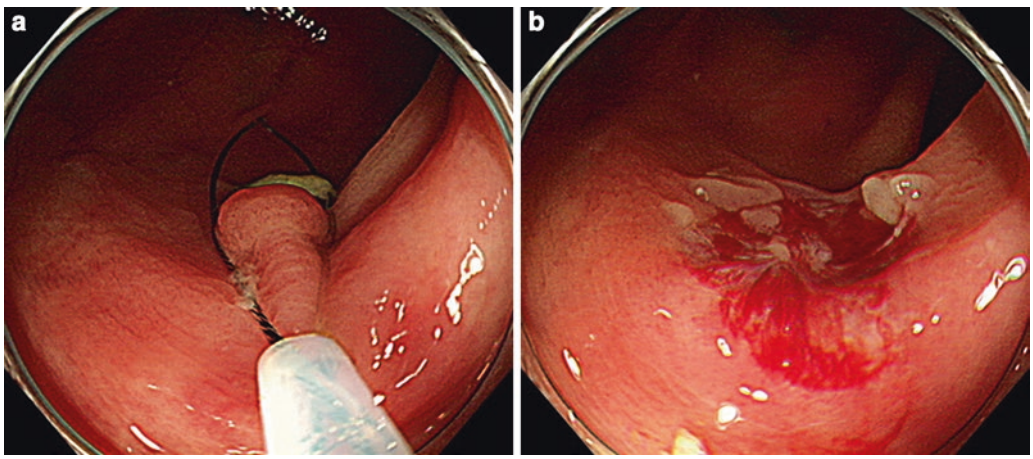


Fig. 12.11 Cold snare polypectomy. (**a**) A small amount of normal surrounding mucosa was snared, along with the polyp itself. (**b**) Clear post-polypectomy site with no remnant polyp tissue

Injection-Assisted Snare Polypectomy (Endoscopic Mucosal Resection, EMR)

EMR is one of the most commonly used endoscopic resection methods. Because it provides a submucosal cushion, it may reduce the risk of perforation while obtaining sufficient tumor-free resection margins. Therefore, EMR may be the preferable method for *en bloc* resection of adequately sized early CRCs.

EPMR

EPMR is indicated for the resection of large benign premalignant polyps that cannot be resected *en bloc* by EMR. Homogenous LST-Gs, which have little risk of submucosal cancer invasion, is an indication for EPMR. Assessment of 1000 colorectal tumors ≥ 20 mm in diameter, most of which were resected by EPMR, found that tumors had recurred in 16.0% (95% CI, 13.6–18.7%) of patients after 4 months. Of these recurrences, 95% were managed again by repeat endoscopic resection. Of patients who did not show recurrence at 4 months, 4.0% showed late recurrence at 16 months, with 94% of the latter managed by repeat endoscopic resection [15]. In summary, although the recurrence rate of large premalignant tumors, such as homogenous LST-Gs, is not low after EPMR, most recurrences can be managed by repeat endoscopic resection. These findings suggest that EPMR may be a good option for resection of large benign colorectal polyps such as homogenous LST-Gs. Risks of local recurrence may be reduced by applying argon plasma coagulation to the base and edge of post-EPMR ulcers.

Endoscopic Submucosal Dissection (ESD)

ESD can achieve high *en bloc* resection rate even for large colorectal tumors. The *en bloc* resection rate for colorectal tumors > 20 mm in diameter has been reported to be approximately 80–95%. Despite this high *en bloc* resection rate, ESD has not been widely utilized because of its long procedure time and high perforation rate. The time required to perform colorectal ESD is about 1–2 h, with 5–10% of these patients developing perforations. Thus, colorectal ESD should be performed only in patients requiring *en bloc* resection, but in whom *en bloc* resection may not be possible using conventional resection methods such as EMR. Large superficial submucosal CRCs > 20 mm in diameter may be the best indication for colorectal ESD, with nodular mixed LST-Gs and LST-NGs included in this category.

Colorectal ESD-associated perforations usually occur during submucosal dissection with knives. Because most perforations can be detected by endoscopists during these procedures, the perforations should be closed by endoscopic clipping, thus allowing most ESD-associated perforations to be managed without surgery. Snaring after sufficient submucosal dissection may reduce the risk of perforation and shorten the procedure time, (Fig. 12.12). This procedure, called hybrid ESD, was comparable to ESD in *en bloc* resection rate and complications, but shortened procedure time [16].

Postpolypectomy Surveillance

Several professional societies have published postpolypectomy surveillance guidelines, with surveillance intervals based on the risk of metachronous neoplasms. The latter may be influenced by the findings of baseline colonoscopy. High-risk findings for recurrence or metachronous neoplasms include resection of ≥3 adenomas, adenomas ≥ 10 mm in diameter, adenomas with villous component, adenomas with high-grade dysplasia, and invasive cancers. The surveillance colonoscopy interval is usually 3 years in patients with high-risk findings, 5 years in patients with low-risk adenomas alone, and 10 years in patients without baseline colorectal neoplasia. Detailed surveillance guidelines by the US Multi-Society Task Force on CRC are summarized in Table 12.8 [17].

Conclusion

Several recently developed colonoscopy techniques have contributed to the effective detection, characterization, and treatment of premalignant and malignant colorectal polyps. White light endoscopy, pit pattern analysis by high definition endoscopy with or without chromoscopy, and equipment-based image-enhanced endoscopy such as NBI enable accurate real-time histological diagnosis. Not only premalignant adenomas but superficial submucosal CRCs without any histological features indicative of poor prognosis can be managed by endoscopic resection. Colonoscopists should choose the most ideal endoscopic resection methods based on the characteristics of these methods, the target lesions, and the expertise of individual endoscopists. Proper surveillance colonoscopy intervals may minimize the risk of interval cancer.

Pearls and Pitfalls

- Assessment of gross morphology, pit pattern analysis, and evaluation of image enhanced endoscopy findings are tools for the differential diagnosis of colorectal polyps.

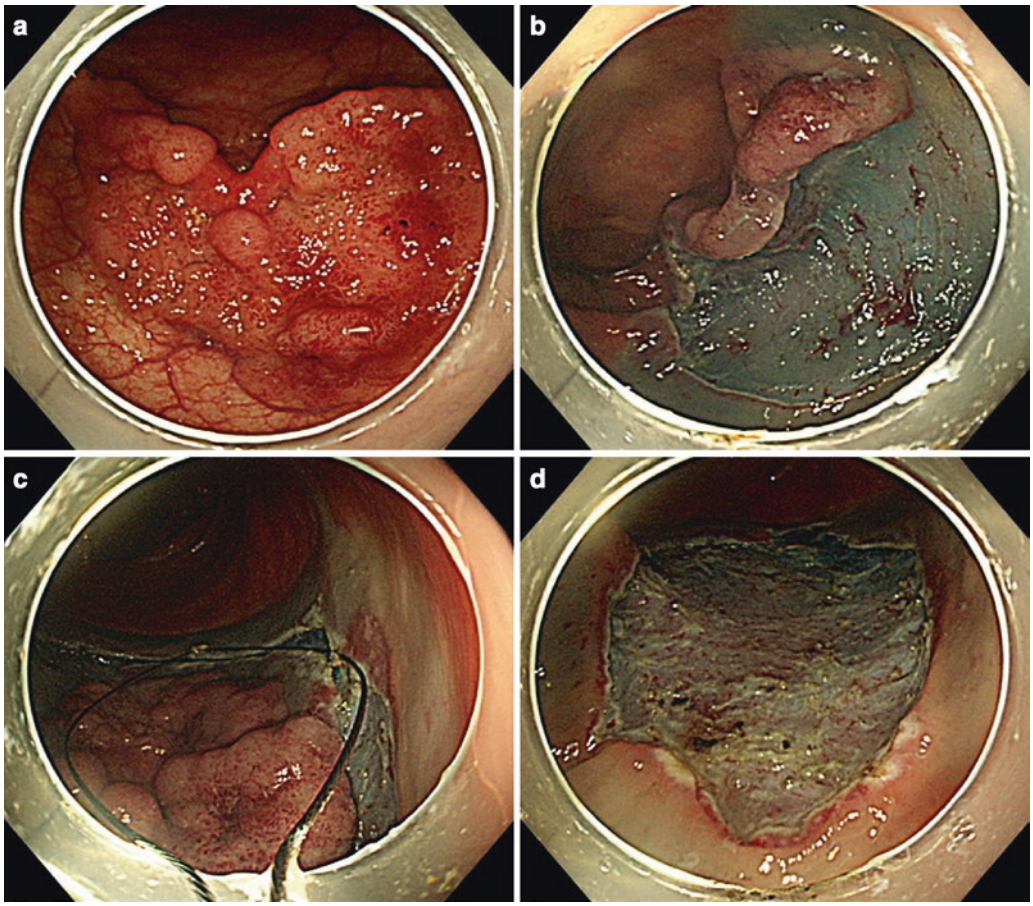


Fig. 12.12 Hybrid endoscopic submucosal dissection (ESD) of (**a**) a large, nodular mixed LST-G. (**b**) A sufficient amount of submucosal dissection was performed, followed by (**c**) snaring to finish the resection procedure. (**d**) A clear posthybrid ESD ulcer is observed

Table 12.8 US Multi-Society Task Force on CRC 2012 recommendations for surveillance intervals [17]

Baseline colonoscopy: most advanced findings	Recommended surveillance interval (years)
No polyps	10
Small (<10 mm) HPs in rectosigmoid colon	10
1–2 small (<10 mm) tubular adenomas	5–10
3–10 tubular adenomas	3
> 10 adenomas	<3
One or more tubular adenomas ≥ 10 mm	3
One or more villous adenomas	3
Adenoma with high-grade dysplasia	3
Serrated lesions	
SSA/P < 10 mm without dysplasia	5
SSA/P ≥ 10 mm or SSA/P with dysplasia or TSA	3
Serrated polyposis syndrome[a]	1

HP hyperplastic polyp, *SSA/P* sessile serrated adenoma/polyp, *TSA* traditional serrated adenoma
[a]Serrated polyposis syndrome is defined when one of the following criteria is met: [1] at least five serrated polyps proximal to the sigmoid, with two or more ≥ 10 mm; [2] any serrated polyps proximal to the sigmoid with a family history of serrated polyposis syndrome; and [3] > 20 serrated polyps of any size throughout the colon

- Most benign adenomas can be managed by endoscopic resection. Early CRCs such as mucosal and superficial submucosal CRCs can be also managed by endoscopic resection.
- Endoscopic piecemeal mucosal resection can result in local recurrence, whereas endoscopic submucosal dissection has a higher perforation rate.

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Detection: (CQI) Quality Measures and Tools for Improvement

13

Matthew M. Philp

Abbreviations

ABCRS	American Board of Colon and Rectal Surgery
ABS	American Board of Surgery
ACG	American College of Gastroenterology
ADR	Adenoma detection rate
AGA	American Gastroenterological Association
APC	Adenomas per colonoscopy
ASGE	American Society for Gastrointestinal Endoscopy
CE	Chromoendoscopy
CQI	Continuous quality improvement
CRC	Colorectal cancer
EHR	Electronic health record
FES	Fundamentals of Endoscopic Surgery
MNA	Mean number of adenomas
NBI	Narrow band imaging
PDR	Polyp detection rate
PDSA	Plan-Do-Study-Act
PQRS	Physician Quality Reporting System
QCDR	Qualified Clinical Data Registries
RCA	Root cause analysis
SSA	Sessile serrated adenoma
VCE	Virtual chromoendoscopy

Key Points

- All endoscopists should be aware of their personal quality metrics. When performing below acceptable levels, targeted interventions should be done. Participation in a cycle of continuous quality improvement (CQI) is advised to continually evaluate and refine performance.
- The adenoma detection rate (ADR) is the most important quality measure in colonoscopy. It should be ≥30% for males and ≥20% in females in screening examinations. Endoscopists with high ADRs reduce the incidence of interval colorectal cancer and death.
- Detection of precancerous polyps requires adequate bowel cleansing and meticulous technique. Maintaining a withdrawal time of ≥6 min is a *minimum* requirement during evaluation of the colonic mucosa. It is a less useful measure in endoscopists with high ADR but is a strategy for CQI in those with low ADR.
- There are various technical advancements being developed to improve the quality of colonoscopy, specifically the ADR. These include image processing techniques, mucosal enhancement, scope attachments, and wide-angle or rear-viewing colonoscopes. Data is largely mixed on their effectiveness and cost is a consideration.
- Payers are increasingly looking at quality measures in respect to procedure reimbursement. Volume is being devalued. Endoscopic specific quality data will be published and available to the public in the future.

Introduction

The concept of quality in healthcare has never been more important than it is today. Most practitioners are well aware of the ever-increasing fiscal expenditure on healthcare delivery in the United States. This pure economic concern of increasing cost is compounded by the fact that, by many indices of measurement, we are also not seeing a proportional increase in improved medical outcomes.

Because colonoscopy is performed in large volumes, in various clinical settings, and by different types of practitioners, it is not surprising that large variations in quality have been observed. With ten million colonoscopies being per-

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formed annually in the US, resulting in $10 billion in direct healthcare cost, this is an active area of interest for both insurance payers and the public [1]. As healthcare professionals, we are clearly motivated to provide high-quality colonoscopy for our patients. In theory, improving the quality of colonoscopy leads to better clinical outcomes (reduced incidence of colorectal cancer (CRC) or advanced lesions requiring surgery, minimizing periprocedural complications, etc.), and this should reduce cost overall in the system. This may or may not be true. But moving forward, it is clear that reimbursement for procedures will be directly tied to various quality measurements. The traditional fee-for-service model where each procedure is reimbursed at a certain level, and doing more equals greater reimbursement, is rapidly being phased out.

This chapter will discuss some basic principles of the quality improvement process and specifically how it relates to colonoscopic procedures. Specific colonoscopy quality measures will be discussed in detail, including clinical relevance, supporting literature, and application in clinical practice.

Continuous Quality Improvement

Continuous quality improvement (CQI) is a thoughtful, structured methodology for maximizing the efficacy of a defined process. Originally arising in the manufacturing engineering industry, CQI methods have been applied to many fields in medicine. Much like a car on a factory assembly line, the patient and their global colonoscopy experience is a process and can be broken down into components. Some CQI examples from industry include General Electric's Six Sigma, and the Toyota Production System, also referred to as Lean methodology. Although each CQI method has a different focus, Six Sigma in reducing variability and Lean in reducing non-value-added steps in a process or elimination of waste, they all require data-driven attention to the details of a process.

Another way of conceptualizing CQI is through the Plan-Do-Study-Act (PDSA) cycle, also known as the Deming cycle (Fig. 13.1). Before attempting to improve a process, planning must occur. It is imperative to gather consensus among involved practitioners. Involving other members of the team (office staff, endoscopy nurses) can provide insight physicians may not have and can be invaluable. This increases the chances of success. Finding common goals or so called "burning platforms" is useful (e.g. reimbursements will cut if ADR is not maintained above thresholds) as motivation to succeed. The planning phase should include data gathering. This can be a time-consuming step. Reviewing thousands of endoscopy records and pathology reports is tedious. This is one area where the standardized reporting and searchability of electronic health records (EHR) is invaluable. After planning is complete and an intervention, or group of interventions, is decided upon they should be implemented. In contrast to what is typically taught in the scientific method, modifying one variable and measuring its effect on the outcome measure, in quality improvement often "bundling" or multiple interventions implemented simultaneously is done to attempt to maximize the outcome of focus. The intervention(s) should then be studied for their effect on the

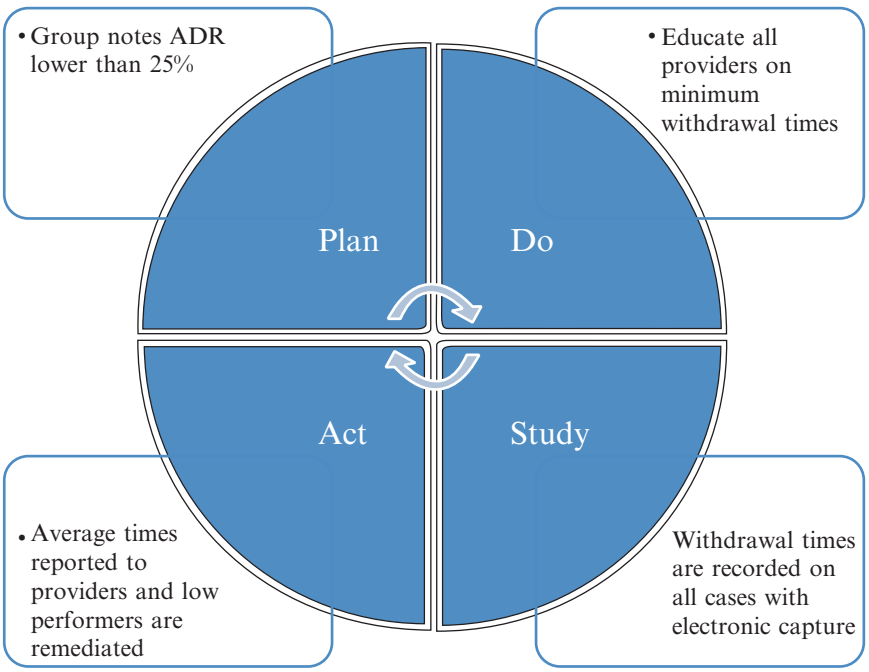

Fig. 13.1 PDSA cycle to improve adenoma detection rate

outcome measure. Again, standardized collection of data here is crucial for efficiency and in planning the next step of the cycle. At this point, the cycle should continue until the desired end point is reached. When it is, ongoing monitoring should continue to ensure no lapses occur.

Quality Metrics in Colonoscopy

The original publication on quality measures in colonoscopy was published in 2002 by the U.S. Multi-Society Task Force on Colorectal Cancer [2]. More recent iterations have subsequently been published in 2006 and 2015, giving an excellent overview of the field and its supporting literature [3, 4]. The authors stated a variety of reasons for initial formal recommendation of quality. First was the beginning of Medicare coverage for screening colonoscopies, and the anticipated increase in what was already a high-volume procedure. This is even more relevant today. The Patient Protection and Affordable Care Act (PPACA) has eliminated patient cost sharing for preventative cancer screening tests. Although there has been some confusion in implementing this (billing those found to have polyps removed during a screening examination), the intent clearly is to reduce any financial barrier for a patient to receive cancer screening examinations and would be expected to increase demand. Second was the large variation reported in the literature regarding neoplasia detection rates. Specific quality measures electronic will be categorized into the three phases of colonoscopy: preprocedure, intraprocedure, and postprocedure. Table 13.1 summarizes the recommended quality measures discussed in this chapter.

Table 13.1 Recommended colonoscopy quality metrics [4]

Measure	Performance target
Preprocedure	
Indication is documented and included in a published standard list of appropriate indications	>80%
Informed consent obtained	>98%
Interval for colonoscopy is appropriate	>90%
Screening exams of appropriate interval in colitis	≥90%
Intraprocedure	
Preparation quality documented	>98%
Adequate bowel preparation	>85%
Adenoma detection rate	Males ≥30%
	Females ≥20%
	Mixed ≥25%
Cecal intubation rate	≥95% screening
	≥90% all exams
Withdrawal time	≥6 min
	>98% documentation rate
Biopsies obtained for indication of chronic diarrhea	>98%
Endoscopic removal of polyps <2 cm attempted prior to surgical referral	>98%
Postprocedure	
Perforation rates	<1:1000 screening
	<1:500 therapeutic
Postprocedure bleeding	<1% incidence
	≥90% managed nonoperatively
Colonoscopy done for appropriate indication	>80% of exams
Appropriate recommendation for repeat colonoscopy, documented, given to patient	≥90%

Preprocedure

General Evaluation

The preprocedural evaluation of the patient prior to colonoscopy is a crucial step in maintaining high-quality colonoscopy. This may be done by the endoscopist or by the referring physician. The latter being common when patients are referred via open access systems. Criteria regarding who can, and more importantly, cannot be scheduled via open access systems should be well defined. Patients with significant medical comorbidities should most likely be evaluated by the performing endoscopist well in advance of the planned day of colonoscopy. Patients with known history of difficult examinations or suboptimal bowel preparations should be seen early as well. Although screening exams can be done anticoagulated, patients will undergo additional cost and inconvenience to return for a therapeutic procedure if polyps are detected.

The appropriateness of cancer screening should be determined, weighing risks and benefits, given patient comorbidities and age. Perioperative medication management should be reviewed with the patient. This is critical for those on anticoagulant medications. Consultation should be obtained if necessary prior to withholding anticoagulation in patients with cardiovascular stents or conditions. Informed consent must be obtained from patients. This should include common risks like bleeding or sedation complications. Risk of perforation should be discussed, and individualized if intervention is planned. Interval cancer and possibility of missed lesions should also be addressed. A target of >98% has been proposed for obtaining informed consent [4]. Ideally anything less than 100% compliance with this measure should ideally trigger a Root Cause Analysis (RCA) and evaluation of process, as this is a serious medicolegal liability.

Possibly the most important step of the preprocedure evaluation is the discussion of the bowel preparation with the patient. Bowel preparation for colonoscopy is discussed

extensively in Chap. 4. However, the influence of colonic cleaning on other quality measures cannot be understated. A clean colon, devoid of stool, will allow for an efficient, high-quality examination of the colonic lumen and optimal detection of polyps. Inadequately prepped patients will require longer intubation times, possibly increasing the pressure on the endoscopist to compensate with faster withdrawals. Poor preparation may preclude intubation of the cecum. Puddles have to be cleared, and those that cannot may hide adenomatous lesions. Inadequate preparation will require patients to typically be reexamined within a year, and increases cost. Endoscopists may be less likely to feel comfortable recommending 10-year screening intervals if no adenomatous polyps are found during an examination with only marginal preparation. Stressing the importance of the preparation to patients is paramount. Written instructions should be provided. Follow-up phone calls and reminders may aid in improving compliance. Patients with history of prior poor preparation should merit special consideration and planning for extended preps, although data guiding this is limited. Increasingly, split dosing preparation regimens are being employed to improve the quality of cleansing. Patient satisfaction and compliance with these regimens remains high, even for those with early procedure times who are required to awake early to complete the second dosing schedule. Same-day preparation, adhering to American Society of Anesthesiology guidelines allowing clear liquids up to 2 h prior to sedation, may be another strategy to improve success.

The plan for sedation during the procedure should be decided upon during preprocedure evaluation. Adequate patient sedation facilitates completion of the procedure and provides a level of comfort for the patient. The endoscopist must decide if sedation will be administered by the provider or an anesthesia specialist. This is an important topic in today's healthcare economic discussion. Sedation from an anesthesiologist or certified registered nurse anesthetist clearly increases the overall cost of the procedure. However, having a provider skilled in sedation and airway management enables the endoscopist to focus primarily on the technical performance of the colonoscopy itself and allows for expert rescue if airway trouble arises. This may allow for overall improvement in the quality of the colonoscopic examination.

Appropriateness of Procedure

The indication for colonoscopy must be appropriate and well documented. Chapter 10 discusses in detail the current guidelines for colonoscopy and appropriate intervals for reexamination. Recommendation for adherence to published guidelines for the appropriate indication for colonoscopy has been recommended to be >80% [4]. It is likely in the future that this area will be closely monitored by payers (refer to section on "Reporting and Payment Policy"). Nonindicated colonoscopy is a cause of increased cost in the healthcare system. Documentation of the clinical decision-making process is crucial when the endoscopist feels examination is warranted but falls outside published guidelines. Guidelines should never supplant individual physician decision making for specific clinical situations, but, increasingly, supporting documentation must be done.

Also recommended is adherence to published guidelines for intervals between screening exams for average-risk patients, postcancer surveillance, and for surveillance in patients with history of polyps. Previous colonoscopy date and histology of polyps, if known, should be documented. Recommended compliance is ≥90% [4]. Again, this is an area that will be closely monitored in the future.

Surveillance colonoscopy for patients with ulcerative colitis or chronic Crohn's colitis is another area with suggested quality indicators. Surveillance examinations for colitis patients are done outside of exams necessary for changes in clinical condition, like bleeding or worsening symptoms when treatment changes may be indicated. Current American Society for Gastrointestinal Endoscopy (ASGE) guidelines recommend starting surveillance after 8 years of ulcerative colitis (exclusive of limited proctitis) or Crohn's colitis involving more than a third of the colon [5]. Intervals of 1–3 years are recommended, with patients having primary sclerosing cholangitis and severe inflammation being at increased risk of malignancy. Recommended performance target for appropriate screening intervals in colitis is ≥90% [4].

Intraprocedural

Cecal Intubation Rate

High-quality colonoscopy mandates complete examination of the colon. By definition, this requires advancement of the tip of the colonoscope to the caput of the cecum. The ileocecal valve is the most reliable landmark of cecal intubation. It is critical to examine the portion of the cecum that lies immediately medially and behind the valve. This is a critical region where pathology can be missed. The appendiceal orifice at the convergence of the teniae coli is another important landmark. The terminal ileum can be intubated to ensure the cecum has been reached. Ileal mucosa is distinct from colonic with prominent villi. Transillumination and palpation in the right lower quadrant are unreliable predictors of cecal intubation and are not recommended. Photographic images of important landmarks documenting cecal intubation should be recorded in the endoscopy record. This is important both from a quality assurance standpoint but also from a medicolegal one. Still images may be equivocal at times. Video capture is typically not feasible for all examinations but can be useful for targeted review. Reductions in the cost of digital archiving may make this a more attractive method of CQI in the future.

Cecal intubation rates for patients undergoing routine screening examinations should exceed 95% [4]. Cases aborted due to inadequate bowel preparation or severe colitis, where there is concern for perforation, can be excluded from the denominator. Supportive photo documentation is important in these situations. Cases with a newly identified stricture or malignancy that is not traversed are typically counted. Therapeutic procedures for stricture are not. Another proposed metric for provider cecal intubation rate is ≥90% when all indications are considered [4].

Withdrawal Time

Typically during proximal advancement of the colonoscope, the endoscopist is focused on reaching the cecum or ileum if that is the planned extent. Withdrawal of the scope is usually when the mucosal surface is closely examined and inspected for polyps or lesions. Methodical examination, clearing puddles, and looking behind haustral folds are intuitively necessary for the detection of polyps. Initial recommendations for withdrawal time were 6–10 min [2]. This was based on evidence showing polyp detection rate was positively correlated with longer withdrawal times. This correlation is strongest for smaller polyps [6]. The ASGE continues to recommend withdrawal times of ≥6 min in its most recent guidelines, and that measurement is documented in >98% [4]. Withdrawal time should be calculated beginning when the cecal caput is intubated and the endoscopist begins to evaluate the colonic mucosa, and ending at scope removal from the anus. This time is independent from any time spent taking biopsies or performing polypectomy.

Withdrawal times should be documented during the procedure and recorded. This process measure is relativity easy to collect and utilize as a benchmark for CQI. It should be noted that this measure is relatively easier for a provider to manipulate (waiting in the rectum until 6 min is reached). Increasing withdrawal times for endoscopist with high adenoma detection rates is unlikely to be an effective intervention but can be useful for those with lower rates. The technique and thoroughness of mucosal examination during withdrawal is likely more important than simply the duration [7]. While this metric may not be entirely valid in those patients who have previously undergone resection, it is still worth noting that it may be tracked.

Adenoma Detection Rate

Detection and removal of precancerous polyps is the goal of screening colonoscopy. This was initially supported by retrospective studies showing lower rates of colorectal cancer in those patients having polyps removed. More recently, strong evidence of the effectiveness of polyp removal on reducing CRC rates has been published [8]. Adenoma detection rate (ADR) for a provider is defined as the number of patients having at least one adenomatous polyp removed divided by the number of screening examinations. Sessile serrated and hyperplastic lesions are not counted. Tandem colonoscopy studies and studies involving CT colonography have shown that the polyp miss rate during colonoscopy can be distressingly high. This is even true for larger, more advanced adenomas. Patients who have missed adenomas are not moved to shorter surveillance intervals and are at increased risk for development of interval CRC. Fear of missed adenomas and interval cancer is a primary reason why endoscopists recommend nonstandard screening intervals. This increases the financial burden on the healthcare system. High-quality colonoscopy screening programs with high ADR providers will allow for detection of patients who require short intervals and prevent unnecessary examinations in those who do not.

ADR is an important quality metric for colonoscopy. ADR will vary based on the patient population of the endoscopist. Initial recommendations were for ADR rates to be ≥25% for a male screening population, and ≥15% for a female one [2, 3], and were set below what was known to be the actual incidence of adenomatous polyps. These have been recently increased to ≥30% male and ≥20% female [4], for reasons discussed later. A provider with a balanced cohort of screening patients would be expected to have an ADR of ≥25% overall.

More recently, ADR has been shown to have a dramatic impact on patient's risk of developing interval colorectal cancer. In a study of over 250,000 colonoscopies with 712 interval colorectal cancers, examination by a high ADR provider was inversely correlated with development of interval cancer or cancer death [8]. ADR rates of the endoscopists in the study ranged from 7.4 to 54%. With the lowest ADR quintile as reference (ADR 7.35–19.05%), having colonoscopy by an endoscopist in the highest quintile (ADR: 33.51–52.51%) conferred essentially a 50% reduction in the risk of interval CRC (HR 0.52, 0.39–0.69, 95% CI). Each 1% increase in ADR reduced the risk of interval cancer by 3%. This evidence was cited by the ASGE in raising the performance target for ADR in the most recent guideline iteration.

Based on supporting evidence, ADR is now primarily considered an outcome measure, rather than a measure of process of care. ADR can be more labor intensive to track than other quality indicators. Accurate measurement of ADR requires follow-up reporting of pathology results. In the future, this may be more easily done by integration of electronic endoscopy and pathology reporting systems. However, currently this remains a manual process for the most part.

Because of difficulties centered on calculating ADR, other methods of providing similar information have been investigated. Polyp detection rate (PDR) is the proportion of screening examinations with any polypoid lesion being removed. PDR is attractive in that it could be automatically calculated without the need for manual correlation with pathology results. One problem with PDR is that it could

Table 13.2 Recommended subject areas of the standardized colonoscopy report

Patient demographics and history
Assessment of patient risk and comorbidity
Procedure indication(s)
Procedure: technical description
Colonoscopic findings
Assessment
Interventions/unplanned events
Follow-up plan
Pathology

encourage removal of obvious hyperplastic polyps, without clinical benefit to the patient, to simply improve or be in compliance with a set rate. Studies have shown that, in general, ADR and PDR correlate well for individual endoscopists. Adenomas per colonoscopy (APC) is another measure that has been evaluated. APC in theory rewards removal of the maximum number of polyps, avoiding the temptation with ADR to not search actively after the first adenomatous lesion is identified. Other possible future quality metrics include the mean number of adenomas (MNA) or polyps (MNP) per exam. MNA has been shown to correlate with the ADR and also provides a better level of discrimination between providers with similar ADRs [9].

There is increasing awareness regarding flat lesions and their role in interval cancer. A disproportionate number of interval CRCs are right sided and have microsatellite instability (MSI). This implies lesions are being missed or progress at a more rapid rate than are being detected via current screening guidelines. The sessile serrated adenoma (SSA) is thought to represent an alternative pathway to invasive cancer than the traditional adenoma to carcinoma sequence. Currently, SSAs are treated similarly to adenomatous polyps when calculating surveillance intervals. However, SSAs are typically excluded from calculation of ADR. High SSA detection rate may confer protection from these types of interval cancers and may be monitored separately from ADR in the future.

Resection of Polyps

Endoscopists should possess the skills for basic polypectomy. Referral for polypectomy increases the cost and inconvenience to patients. Most small polyps under 2 cm can be removed endoscopically. Another proposed quality measure is ≥98% attempt rate of removal for polyps <2 cm before surgical referral [4]. Photos of polyps should be documented and can allow for review of quality in the CQI process, as well as for consultation with more advanced interventional endoscopists to possibly attempt endoscopic management.

Adequacy of Bowel Preparation

As previously described, adequate bowel preparation is essential to high-quality and efficient colonoscopy. Adequate bowel preparation is defined as being able to exclude lesions over 5 mm in size. This simple description is clearer than descriptive terms (poor, fair, good, excellent) and easier to implement than some of the complex preparation quality scales (Chicago, Boston). Irrespective of the method used to describe the bowel preparation, it should be documented in the endoscopy report in ≥98% of examinations [4]. A quality process measure has been recommended that ≥85% of outpatient examinations have preparations adequate to exclude lesions over 5 mm [4]. Inpatient examinations are well known to have higher rates of inadequate preparation. Endoscopists should track their bowel preparation success rate as part of the CQI process. Those falling below should examine their methods including selection of preparation, patient education, and use of techniques like split dose or day of procedure preps. Chapter 4 provides more details on strategies to increase bowel preparation success rates.

Documentation

Detailed and accurate reporting of colonoscopy is important for quality assessment, communication with referring physicians, and legal purposes. Standardized colonoscopy reporting templates have been proposed [10]. Table 13.2 lists the major topics that should be addressed in every colonoscopy report. Commercially available software packages are available to produce endoscopy reports, and probably provide better standardization than natural language dictation.

Postprocedure

Perforation

Perforation is probably the most feared complication of colonoscopy, despite its actual incidence being quite low. Rates of perforation should be less than 1 in 500 for therapeutic procedures and 1 in 1000 for screening examinations [4]. Individual perforation rates can be difficult to interpret given the relative infrequency of events. Also a provider's patient mix needs to be considered; perforation rates may be higher for someone doing complex polypectomy with advanced techniques.

The rarity of perforations lends well to the performance of RCA. Cases should be reviewed by the provider and local peers in a nonaccusatory, constructive fashion. Factors that could have contributed to the perforation can be identified and plans made to prevent future ones from occurring. RCA often uncovers etiologies for an event that were not initially expected. For example, rather than poor insertion technique, a provider may have consistently inadequate preparations, leading to increased difficulty in advancing the scope. Without RCA, unnecessary interventions may be implemented instead of focusing on the major underlying problem.

Bleeding

Bleeding remains a risk after colonoscopy when an intervention is performed. This is probably highest for patients undergoing polypectomy. Predictors of bleeding include proximal polypectomy and removal of pedunculated polyps. Rates of postcolonoscopy bleeding should be less than 1% [4]. Rates noted to be higher should trigger RCA to ensure best practices are being used to minimize bleeding risk. Chapter 21 provides details on steps that can be taken to reduce bleeding and intervention if it occurs. Patients that do have postprocedure bleeding should be managed without the need for surgery in ≥90% of cases [4]. Early endoscopic intervention is safe and effective treatment for postpolypectomy bleeding and can minimize the need for transfusions.

Screening and Surveillance Intervals

After completion of a screening examination, the endoscopist should assign an interval for repeat examination. Assuming an average patient risk, adequate bowel preparation, and no polyps detected, this should be a 10-year interval. If polyps are removed, their histology must be reviewed before making determination on the surveillance interval. There is evidence that recommended exam intervals are often not followed by endoscopists. This significantly increases cost in the healthcare system and may expose patients to unnecessary procedural risk. Appropriate recommendation for repeat colonoscopy should be given to the patient in ≥90% of exams [4].

Strategies for Improvement

Although multiple quality measures of colonoscopy have been discussed, increasing ADR likely remains the most important target for endoscopists in most practices. High ADR is clearly associated with decreased rates of CRC [8]. High-quality bowel preparation is imperative. Improvement in this area lends itself well to the CQI process, and steps like split or same-day bowel preparation should be implemented if not already being utilized.

The literature on systematic approaches to improving ADR has generally not been impressive [11]. In a review of seven published studies on CQI for ADR, only one showed improvement. This study paired an audible timer for withdrawal pace and provided feedback on examination techniques to the endoscopist. There was a 50% increase in ADR for 12 endoscopists from 23.5 to 37.4%.

In addition to improving patient factors and endoscopist performance issues, there has been significant use in employing technology to aid in the detection of adenomatous polyps. These include mucosal enhancement techniques, both topical and virtual, scope add-ons to improve visualization behind folds, and wide-angle or rear facing endoscopes.

High definition video is becoming more prevalent as the technology expands and the cost of acquisition drops. High definition endoscopes provide higher resolution video, typically defined as 1080p or higher. In theory, the higher resolution may aid in detection of smaller polyps or flat lesions, although one would expect the effect to less important for advanced adenomas. High definition endoscopes are also available with wide viewing angles (170° vs. standard 140°). A meta-analysis showed a small pooled incremental increase in ADR with high definition endoscopy of about 3.8% [12]. As expected, there was no difference in detection of advanced adenomas. Wide variation in ADR was noted among the studies examined in the review and was discussed as a limitation. This is common theme for much of the ADR literature. Studies are often conducted with endoscopists having high baseline ADR and intervention has little effect. It is difficult to extrapolate the effect of an intervention to an endoscopist with a low ADR, where a potentially greater impact may be seen.

Chromoendoscopy (CE) is the application of dye to the colonic mucosa to aid in detection of polyps. Methylene blue and indigo carmine are two commonly use dyes. CE has been shown to be effective in increasing the diagnostic yield when performing surveillance biopsies for patients with chronic colitis. Because dysplasia in the setting of chronic colitis often arises from flat lesions, CE allows for improved differentiation from surrounding mucosa and improves detection of these lesions. The use of CE in detection of polyps for a screening population does not have strong supporting evidence with most trials showing no difference. The European Society for Gastrointestinal Endoscopy (ESGE) recommends against the routine use of CE for screening average-risk patients [13]. They cite increased cost of dyes, 30–40% increase in procedure time, and the lack of supporting data showing increased detection of advanced adenomas.

Virtual chromoendoscopy (VCE) uses imaging processing techniques to manipulate the endoscopic image and improve detection and identification of lesions. Narrow band imaging (NBI) is one such technique that is widely available, and different endoscope manufacturers have proprietary

variations of it available. NBI filters out higher wavelengths of red light, favoring lower wavelength blue and green light, which lie in the absorptive spectrum of hemoglobin. This provides a more contrasted appearance of mucosal blood vessels. Meta-analysis has shown no benefit of VCE techniques over white-light endoscopy in ADR [14], and its routine use is not recommended [13].

A number of endoscope add-ons and improvements have also been studied. Many of these are discussed in more detail in Chap. 14. These include add-on caps or cuffs to flatten out the haustral folds during withdrawal. This allows for improved detection of small polyps on the backs of the folds. Rear-viewing cameras can be introduced through the working channel, again providing an improved examination on the back of the haustral folds. A specialty endoscope with integrated side-viewing cameras is also available. Also referred to as full spectrum endoscopy, this provides a fused image to the endoscopist with a composite viewing angle of 330°. Initial studies are promising. One showed an adenoma miss rate of 7% with full spectrum endoscopy vs. 41% with standard forward viewing in tandem back-to-back colonoscopy [15]. It remains to be seen if this technology can have an impact on increasing the ADR of low performing endoscopists, and cost concerns of equipment purchase do play a factor.

Training and Credentialing

Colonoscopy remains a procedure that is performed by physicians from various training backgrounds. They include gastroenterologists, general surgeons, colorectal surgeons, internists, and family practitioners. Though pioneered and developed by surgeons, gastroenterologists have assumed a significant proportion of the colonoscopic procedures being performed today. General surgeons perform many endoscopic procedures in rural practice settings, likely due to reduced availability of gastroenterologists, who tend to cluster in urban locations. One study of general surgeon case mix found colonoscopy to be the second most commonly performed procedure [16]. There was also a direct correlation between lower numbers of gastroenterologists in a health service area and the increasing volume of colonoscopy done by general surgeons. Clearly, surgeons are providing access to care where medical gastroenterology specialty care may not be readily available.

There has been recent ongoing debate regarding the training of an endoscopist for colonoscopy. The American Board of Surgery (ABS) has set the minimum number of colonoscopies for a graduating general surgery resident at 50. As would be expected, The American Board of Colon and Rectal Surgery (ABCRS) has more stringent requirements for its residents. The ABCRS requires 140 colonoscopies, with 30 of them requiring intervention (biopsy, polypectomy, injection, stenting, etc). Half of the interventions [15] must be snare polypectomy. The ASGE has also set a minimum of 140 colonoscopies for its fellows "before competency can be assessed." This number is also included in the American College of Gastroenterology (ACG) Core Curriculum. No society espouses that a minimum number of case volume confers proficiency. The ASGE and ACG were concerned that the minimum ABS numbers could place a burden on gastroenterologists who participate in surgical training programs, and that proficiency may be presumed. The ABS and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) in response have developed a standardized endoscopic curriculum for general surgery residents, Fundamentals of Endoscopic Surgery (FES). FES contains standardized didactic learning materials and an objective measurement of simulated endoscopic skills. There is also a standardized form for assessing performance during live endoscopy. FES certification will be required for ABS eligibility beginning in 2017.

Quality among endoscopic providers is a matter of politics that is worthy of some discussion. The most recent set of quality measures in colonoscopy published by the ASGE cites five articles when stating gastroenterologists are more effective than surgeons or primary care physicians at preventing CRC by colonoscopy [4]. In two of these referenced studies, the lead author is a colorectal surgeon. In one case–control study looking at Medicare data and the effect of colonoscopy on CRC mortality, there was dramatic improvement when colonoscopy was done by any practitioner, with an odds ratio of 0.4 (0.37–0.43, 95% CI) [17]. This effect was most pronounced with distal CRC. However, when the specialty of the endoscopist was considered, there was a variable range of the protective effect. For cancers of all sites, gastroenterologists had the lowest odds ratio of 0.35 (0.32–0.39, 95% CI), followed by primary care physicians at 0.43 (0.33–0.55, 95% CI), and finally by surgeons with odds ratio of 0.55 (0.47–0.64, 95% CI). Similar trends were seen when looking at proximal and distal CRC, again with the protective effect stronger for distally located tumors. This study used administrative data and there was no way to know the indication for colonoscopy, practice patterns of the endoscopists, or the patient's baseline risk for CRC. Surgeons could have been doing a higher risk population (patients referred for large or complex polyps). There is data supporting the fact that surgeons can perform colonoscopy safely and efficaciously [18, 19]. However, these are mostly older studies and currently quality measures like ADR were not reported, a major limitation. At least one more recent report shows specialty colon and rectal surgeons can provide high-quality colonoscopy [20]. It is important for surgeons to be familiar with this literature and ascribe to high-quality standards as discussed in this chapter.

Privileging and credentialing for procedures remains a local facility matter. What is acceptable and customary at an

urban tertiary care endoscopy center with regards to quality measures performance is likely quite different from a rural community hospital or a critical access center. However, each practice location should have a well-defined set of minimum training criteria. The major endoscopic societies have published guidelines on this. Ongoing professional practice evaluation is mandatory for all providers. All endoscopic providers, regardless of background or specialty, should be held accountable to the quality measures determined by the local institution. Remediation should be planned for those who do not meet criteria. Failure of remediation should result in revocation of privileges. However, blanket application of a quality measure without thought to the local practice environment could result in fewer endoscopic providers and reduced access to colonoscopy, which is clearly counterproductive to the overall goal of CRC reduction.

Reporting and Payment Policy

There is an ongoing shift in healthcare payment policy away from traditional fee-for-service models. This is being actively pursued by the government for Medicare beneficiaries and followed closely by private insurance companies. The repeal of the Sustainable Growth Rate (SGR) in 2015, via the Medicare Access and CHIPS Reauthorization Act (MACRA), has sent providers down a new path in payment policy. Providers accepting Medicare patients will be required to participate in alternate payment models (ACO, bundles) or participate in a quality reporting system. The current programs of Physician Quality Reporting System (PQRS), value modifier, and EHR meaningful use will be rolled into one Merit-Based Incentive Payment System (MIPS). By 2019, providers will have as much as a −4% penalty or +12% bonus applied to Medicare payments depending on their performance to benchmarks. Fifty percent of providers' Medicare patients must have quality measures reported to be eligible.

Current colonoscopy specific performance metrics that have been approved for collection in Qualified Clinical Data Registries (QCDR) are shown in Table 13.3. The current PQRS measures focus on avoiding unnecessarily short examination intervals for patient with normal screening exam and those with polyps. ADR is also a primary focus. Physician technical ability is being monitored in cecal intubation rates. Interestingly, data is being collected regarding the adequacy of bowel preparation. Although the bowel preparation process is under the control of the endoscopist and can be improved with CQI methods, it is somewhat sobering to realize that procedural reimbursement may soon be influenced ultimately by the actions of patients (e.g. not taking preparation as instructed). There are currently two QCDRs that groups can join to track their data and provide a mechanism for reporting PQRS to the government. These are GIQuIC, a collaboration between the ACG and ASGE, and the American Gastroenterological Association (AGA) Clinical Data Registry.

Recently with the 2016 Physician Fee Schedule, effective January 1, 2016, a significant reduction in endoscopy reimbursement for Medicare patients occurred. The endoscopy family of codes was initially labeled as mis-valued in 2015 and changes to them were fought by the ACG, AGA, and ASGE. Regardless, reimbursement reductions were enacted, with colonoscopy being reduced 9%, colonoscopy with snare polypectomy reduced 12%, and colonoscopy with biopsy reduced 17%.

It is clear that moving forward there will be increased focus on the costs associated with colonoscopy. Quality measures will be publically reportable in the future to allow patients to select endoscopists. Endoscopists will need to understand, measure, and follow their quality measures not only to achieve maximal patient outcomes but to remain financially viable in our evolving healthcare system.

Pearls and Pitfalls

- Recommended adenoma detection rates for screening colonoscopy.
  - Males ≥30%
  - Females ≥20%
  - Combined ≥25%
- Adequate bowel preparation should be achieved in ≥85% of outpatient examinations. Consider split preparation or same-day preparation to improve success rates.

Table 13.3 Colonoscopy quality measures reported regarding physician-specific quality

Measure	PQRS measure
Endoscopy/polyp surveillance: colonoscopy interval for patients with a history of adenomatous polyps—avoidance of inappropriate use	Yes
Endoscopy/polyp surveillance: appropriate follow-up interval for normal colonoscopy in average risk patients	Yes
Screening colonoscopy adenoma detection rate	Yes
Colonoscopy assessment (procedure adequacy)—assessment of bowel preparation	No
Colonoscopy assessment (cecum reached)—cecal intubation/depth of intubation	No
Unnecessary screening colonoscopy in older adults	No

- Maintain a *minimum* endoscope withdrawal time of 6 min, exclusive of time spent in biopsy and polypectomy. Perform thorough examination of the colonic mucosa, clearing puddles, and looking behind folds. Increasing ADR reduces CRC mortality.
- Achieve cecal intubation in ≥95% of screening examinations. Photo document ileocecal valve and appendiceal orifice to confirm this.
- Make sure the indication for colonoscopy is clearly documented. Examination intervals should follow established guidelines. Reasons for early reexamination need to be well documented.
- Data is powerful. All endoscopy providers and groups should know their own performance with regards to the various endoscopy quality measures. CQI should be in place to monitor and continuously improve outcomes. Reimbursement in the near future will be linked to quality.

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Advanced Endoscopic Imaging: Polyps and Dysplasia Detection

14

Jacques Van Dam and Anna Skay

Abbreviations

ADR	Adenoma detection rate
CLE	Confocal laser microendoscopy
CRC	Colorectal cancer
EUS	Endoscopic ultrasound
HD	High definition
NBI	Narrow band imaging

Key Points

- Two to 6% of CRCs develop in the interval between colonoscopies. These interval cancers are believed to be from missed polyps rather than new neoplastic lesions.
- Chromoendoscopy enhances the observed image through use of dye or optical techniques. Chromoendoscopy also aids in distinction of adenomatous polyps from hyperplastic polyps.
- Adenomatous lesions have a gyrus-like Kudo pit pattern, while hyperplastic lesions have an asteroid pit pattern.
- Dye-assisted chromoendoscopy has been shown to be superior to white light with standard biopsies in detection of dysplasia in Ulcerative Colitis patients.
- Cap-assisted colonoscopies, using various devices, such as the Endocuff and EndoRing can improve detection of diminutive polyps, but data is not strong enough to recommend wide use of these devices.
- Third Eye colonoscopy improved ADR for surveillance and diagnostic colonoscopies but not for screening exams.
- CLE and EUS can prove valuable in evaluation of specific regions or lesions in the colon but have little potential to help improve polyp detection.

Introduction

Colonoscopy is an invaluable tool in colorectal cancer diagnosis and management. Detection and removal of colonic neoplasms are the key elements in screening and prevention of colorectal cancer. A high-quality colonoscopy remains the main screening modality for colorectal cancer. Colonoscopy with polypectomy was shown to decrease mortality from CRC by 53% [1]. Unfortunately, 2–6% of CRCs develop in the interval between colonoscopies and are believed to be from missed polyps rather than new neoplastic lesions [2]. Polyps can be missed due to inadequate bowel preparation, appearance of the polyps, as flat polyps may resemble normal mucosa, and technical challenges, especially if polyps are hidden behind folds. Several advances in colonoscopy technique will be discussed in this chapter that have improved visualization and increased polyp detection.

Real-Time Optical Prediction of Polyp Histology

Recent developments in colonoscopy techniques have been designed to improve detection of abnormal lesions in the colon. Certain techniques are used not only to distinguish normal mucosa from abnormal but also to predict histology based on endoscopic appearance. Chromocolonoscopy,

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which can be performed with dye or with varying light frequency, not only characterizes abnormal mucosa, but also can act as an "optical biopsy" by predicting the lesion's microscopic morphology.

Chromocolonoscopy

Dye-Assisted Chromocolonoscopy

Chromoendoscopy enhances the observed image through use of dye or optical techniques. It improves distinction of normal mucosa from neoplastic lesions by enhancing the borders and surface morphology of pathologic lesions. Chromoendoscopy also aids in distinction of adenomatous polyps from hyperplastic polyps. Small hyperplastic polyps (of less than 5 mm) are generally considered benign without risk of malignancy. As cost of colonoscopy is rising, predicting histology of small polyps can cut down on excessive pathology fees.

White light endoscopy does not allow for clear distinction between adenomatous and hyperplastic polyps. Chromoendoscopy improves distinction of the mucosal morphology, allowing the endoscopist to predict histology. The neoangiogenesis of adenomatous polyps results in different "pit patterns" of the mucosa, which can be seen with dye or optical techniques. The NICE (NBI International Colorectal Endoscopic classification) was developed to determine type I (hyperplastic) and type II (adenomatous) lesions based on appearance of color, surface pattern, and vessels (Table 14.1) [3].

Dye-based chromoendoscopy uses dyes that either absorb into the mucosa (vital dye) or remain on the surface of the mucosa (nonvital). The dye can be applied to targeted areas or to the entire colon (pan-chromoendoscopy). The dyes enhance topography of neoplastic lesions or the pit pattern. Kudo et al. showed the endoscopic pit pattern of dye-enhanced lesions correlated to histology [4]. Adenomatous lesions have a gyrus-like pit pattern, while hyperplastic lesions have an asteroid pit pattern.

Most commonly used dyes are indigo carmine and methylene blue, which both have a blue appearance endoscopically. Both are equally effective to distinguish abnormal mucosa. Indigo carmine is a nonvital dye that coats the mucosa and outlines the pit pattern, enhancing the contrast between varying mucosal morphology. It is applied with a concentration of 0.03–0.5% and lasts a few minutes. Because it is not absorbed, it disappears as it becomes diluted throughout the colon. Methylene blue is a vital dye, which actively absorbs into the intestinal epithelial cells (Fig. 14.1). Neoplasia and inflamed mucosa do not absorb the dye, making it appear brighter than normal mucosa. It is applied at a concentration of 0.1%. After application, the dye stains tissue for approximately 1 min and lasts up to 20 min [2]. Both stains have been shown to be safe with no significant side effects. There was concern that methylene blue may cause DNA damage, but no clinically significant DNA injury has been proven [2].

Adequate visualization of mucosa with chromoendoscopy requires excellent bowel preparation. Any remaining material in the colon should be aspirated by the endoscopist when advancing through the colon. The dye is applied upon reaching the cecum directly into the accessory channel using a 60-mL syringe or a spray catheter. The dye can also be diluted into 1 L of sterile water and applied by the endoscopist by pressing the foot pedal of the water pump. The dye coverage is improved if the colon is decompressed. For pan-chromoendoscopy, segments of 20–30 cm are sprayed. Immediate inspection can be done with indigo carmine, while methylene blue requires 60 s to absorb. Methylene blue-coated tablets have been reported for the use in chromoendoscopy, with delivery of dye directly to the colon, but more studies will need to be done to determine the efficacy of this dye delivery [5].

In average-risk individuals, dye-based chromoendoscopy, in comparison with white light endoscopy (or high definition (HD) endoscopy) has shown significant benefit in detection of lesions that are commonly missed: diminutive polyps, proximal adenomas, and flat polyps. Adenoma detection rate (ADR) has been studied in chromoendoscopy, in comparison with white light colonoscopy. In comparison with standard white light colonoscopy, or HD colonoscopy, chromoendoscopy showed a small increase in ADR or no effect on ADR. The significant benefit of chromoendoscopy was shown to detect more diminutive polyps per person using dye-based chromoendoscopy [6]. Chromoendoscopy increases detection of more proximal, flat, and serrated lesions. Although this technique can significantly increase

Table 14.1 NICE criteria

NICE criterion	Type 1	Type 2
Color	Same or lighter than background	Browner relative to background
Vessels	None or Isolated lacy vessels	Brown vessels surrounding white structures
Surface pattern	Dark or white spots of uniform size, or Homogenous absence of pattern	Oval, tubular, or branched white structures surrounded by brown vessels
Likely pathology	Hyperplastic	Adenoma

Adapted from Hewett, D.G., et al., *Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging.* Gastroenterology, 2012. 143(3): p. 599–607 e1

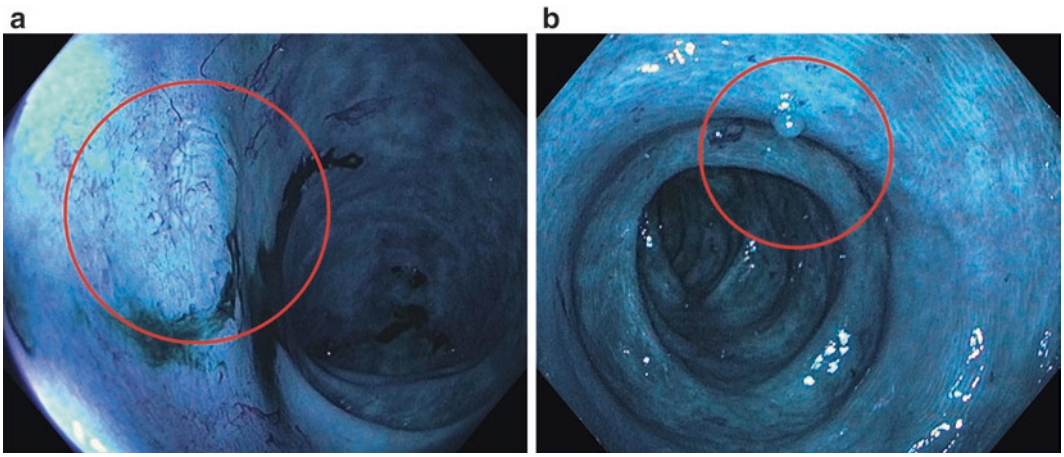

Fig. 14.1 Chromoendoscopy with methylene blue in a patient with ulcerative colitis. (**a**) Flat lesion with pale appearance was a tubular adenoma by histology. (**b**) Inflammatory polyp showed the same uptake of dye as surrounding tissue without the typical pale appearance or changes in the pit pattern. © Aquilant Endoscopy Ltd. with permission

detection of the often missed lesions, the main disadvantage of dye-assisted chromocolonoscopy is the length of the procedure.

Patients with Inflammatory Bowel Disease (IBD) are at increased risk for colorectal cancer and require dysplasia surveillance after 8 years of diagnosis. Dye-assisted chromoendoscopy is superior to white light with standard biopsies and improves dysplasia detection by 3- to 4.5-fold [7]. Currently, European guidelines recommend chromocolonoscopy with standard biopsies for dysplasia surveillance in IBD patients. In the USA, chromoendoscopy is used commonly and is the preferred choice for dysplasia screening in IBD patients; however, this is currently not considered standard of care. More studies need to be done prior to establishing chromoendoscopy as the gold standard. Of note, the pit pattern may not be as clear in patients with long-standing inflammation as the background mucosa may appear abnormal. Because dysplasia may not be clear to identify, the American Gastroenterology Association recommends only experienced physicians perform chromoendoscopy.

Digital Chromocolonoscopy

Dyeless or digital chromocolonoscopy uses imaging-enhanced optical techniques. This technique uses optical technology to enhance lesions. Narrow band imaging (NBI) uses optical filters in the light source to enhance superficial and deep vessels (Fig. 14.2). Normally, white light bandwidth has red–green–blue. Hemoglobin absorbs green and blue light. NBI filters the white light to allow blue (415 nm) and green (540 nm) to pass but blocks red wavelengths. Neoplastic lesions in the colon tend to have altered mucosal vessels, which absorb the light, while normal mucosa reflects it. As a result, neoplastic lesions are enhanced under NBI.

Studies have compared ADR using NBI or white light colonoscopy. NBI improved ADR in comparison with conventional white light colonoscopy but was the same in comparison with HD colonoscopy [8]. The main disadvantage of NBI is the dark color, which limits its use as a screening technique (Fig. 14.3).

Another form of digital chromoendoscopy is the iScan (Pentax, Japan), which is a digital filter, which enhances certain wavelength patterns that are absorbed. The software is designed to enhance certain characteristics of the mucosa. Some studies showed that iScan may improve adenoma detection, which were mostly diminutive and hyperplastic.

Fujinon Intelligent Color Enhancement (FICE, Fujinon Inc., Japan) is similar to the iScan. FICE captures the whole white light spectrum. As the light is captured, a computer-based algorithm enhances certain combinations of wavelengths. FICE allows for better visualization of mucosal morphology and enhances vascular and pit patterns, but data showed that it did not improve ADR.

Improvement in Visualization

Several modalities have been developed to improve visualization in the colon. Diminutive polyps have a very low malignancy risk, but three or more predict risk of future colonic adenocarcinoma. The number and size of polyps at the time of the screening colonoscopy determines the subsequent screening intervals. Therefore, not missing polyps is crucial in determining a patient's future risk and screening intervals. Diminutive polyps are more likely to be missed, especially if located behind folds, where a colonoscope cannot easily visualize the mucosa. Several colonoscope accessories have been created in order to improve visualization.

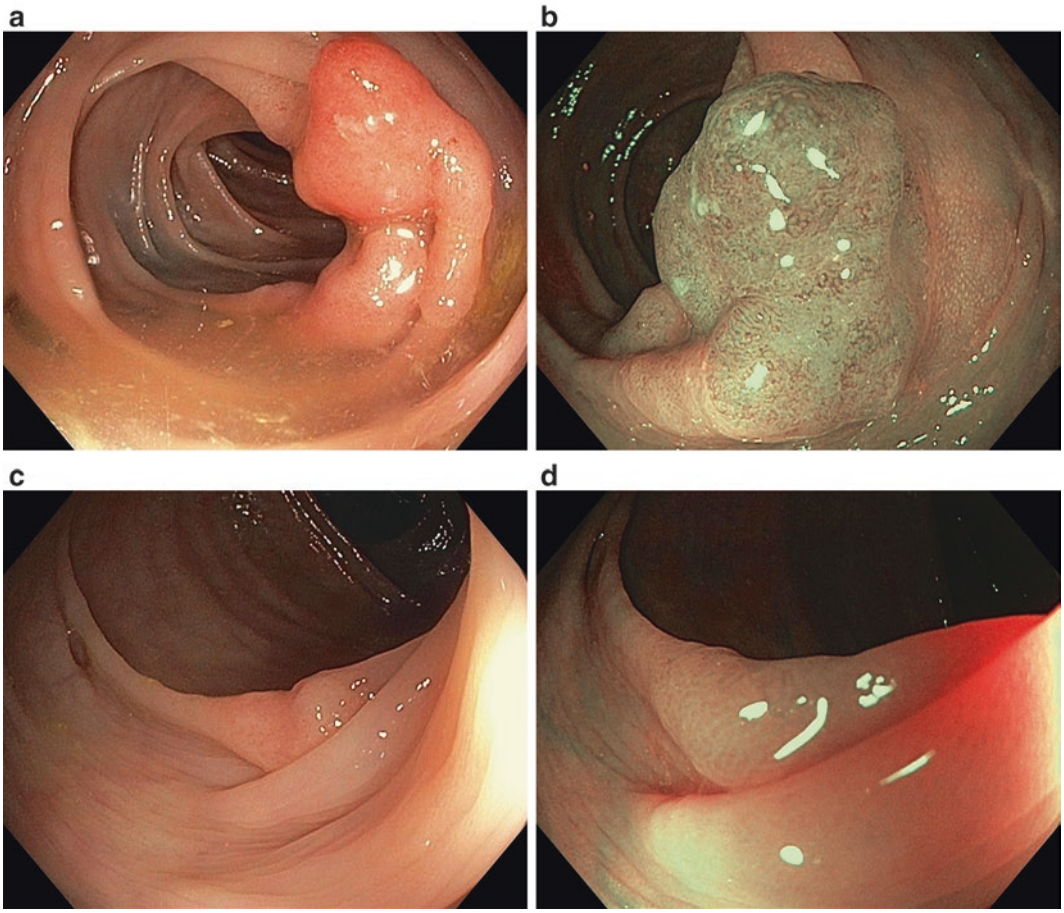

Fig. 14.2 Narrow band imaging (NBI) of tubular adenomas of the colon in a single patient. (**a**) White light and (**b**) NBI showing a large flat tubular adenoma with polypoid component extending onto the folds. NBI delineates the adenomatous lesion from surrounding normal mucosa and so-called chicken skin mucosa. (**c**) White light and (**d**) NBI depicting a flat tubular adenoma. The pit pattern is accentuated by NBI in a lesion that appears subtle under white light

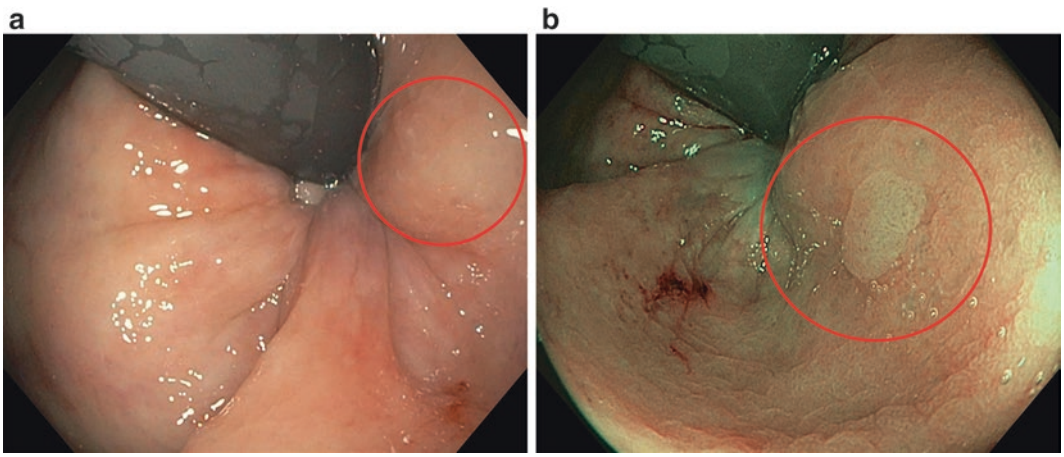

Fig. 14.3 NBI of a hyperplastic polyp. (**a**) *White light* and (**b**) NBI show a hyperplastic polyp in the rectum

Cap-Assisted Colonoscopy

Cap-assisted colonoscopy (Fig. 14.4a) is performed with a 4 mm clear plastic cap on the end of the colonoscope. This device is designed to improve mucosal visualization by pulling back folds, where polyps may hide. The cap is also meant to avoid a "red-out" during advancement to the cecum, when maneuvering around flexures. A randomized,

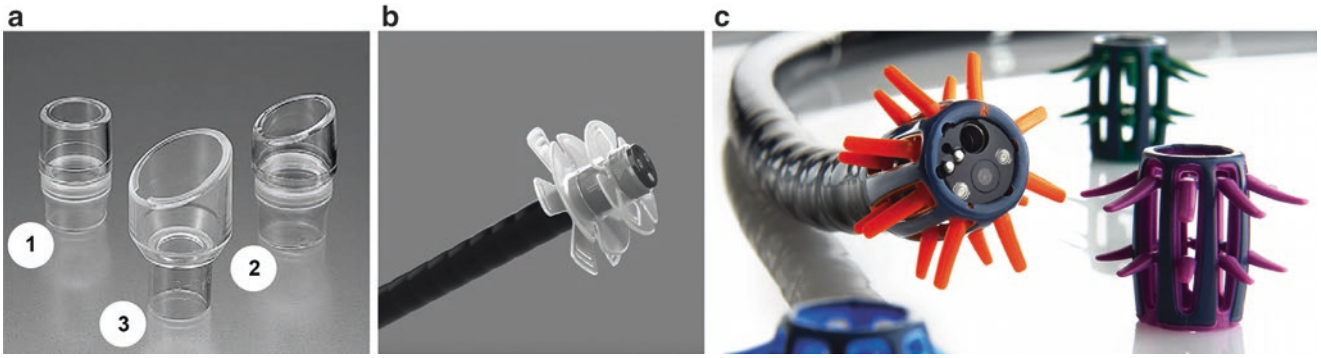

Fig. 14.4 Devices that attach to the distal tip of colonoscopes. (**a**) Endoscopic caps: (1) Hard straight cap. (2) Hard oblique cap. (3) Large caliber soft oblique cap. With permission Sumiyama, K, Rajan E. Endoscopic caps. Tech Gastroinest Endosc 2006; 8(1):28–31 [20]. © 2006 Elsevier Inc. (**b**) EndoRing®. (**c**) Endocuff®

prospective trial did not find significance in the adenoma detection rate but had shown an improvement in the cecal intubation rate [9].

EndoRing

The EndoRing (EndoAid Ltd., Caesarea, Israel) (Fig. 14.4b) is a circular colonoscope cap device that fits on the end of most colonoscopies. It has 3 layers of clear, soft, and flexible rubber-silicone rings, which help to flatten folds upon withdrawal. The rings are soft and should allow for terminal ileum intubation. This device was studied in a randomized controlled multicenter study, the CLEVER study [10]. The investigators compared tandem colonoscopies: EndoRing-assisted colonoscopy, followed by immediate standard exam, versus a standard colonoscopy followed immediately by EndoRing-assisted colonoscopy. This study (funded by EndoAid) compared adenoma miss rate of the two groups. The group that received the EndoRing-assisted colonoscopy first had a statistically significant lower rate of polyp miss rate (10.4%), compared with 48.3% adenoma miss rate in the group that started with a standard colonoscopy. Of note, the EndoRing-assisted colonoscopies had statistically significant longer procedure time, which may account for the difference in adenoma detection. Overall, this device increased adenoma detection, without significant hindrance to the endoscopist, especially diminutive polyps in the proximal colon, where the majority of polyps are missed.

Other similar devices have been studied in the past, with similar transparent caps or hoods for the colonoscopes. The studies compared cap-assisted colonoscopies to standard exams to study an effect on cecal intubation times and adenoma detection. Findings have been mixed with some studies showing a benefit to the cap, while others found no difference when using it [11].

Endocuff

The Endocuff (Arc Medical Designs, Leeds, England) (Fig. 14.4c) is another type of colonoscope cap device that was approved by the FDA in 2012. Endocuff serves the same purpose to flatten folds and increase ADR as the EndoRing, with a different appearance. The Endocuff has two rings of thin projections of soft and flexible material. The projections are hinged at the base in order to not interfere with forward movement of the colonoscope. There are several sizes available for various colonoscopes. The Endocuff was evaluated with a randomized, multicenter study comparing Endocuff-assisted colonoscopies to standard colonoscopies [12]. The Endocuff-assisted colonoscopies had higher detection of flat lesions and diminutive polyps less than 6 mm, but overall adenoma detection was not significantly different. The device also hindered advancing in the left colon when diverticulosis was present and it had to be removed to complete the exams. This study did not address intubation of the terminal ileum.

The two devices have never been compared head to head to study their benefits in ADR or their pitfalls. Each has shown some benefit in detection of diminutive polyps, which are the polyps that are most commonly missed. Meta-analyses reviewing studies using the clear cap use showed mixed results. There are studies that show increase in adenoma detection, while others showed no difference [13]. At this time there is not enough data to recommend the use of these devices, but there are studies suggesting they may benefit adenoma detection.

New Colonoscopy Technology

Advancements in colonoscope technology have been developed to improve mucosal visualization. Some new colonoscopes have built-in technology that increases the endoscopist's

field of view with improved optics, while others add an extra camera. Several of these unique adjustments to the standard colonoscope have shown promise in trials to improve ADR.

Third Eye Retroscope

The Third Eye Retroscope (Avantis, Sunnyvale, CA, USA) passes another endoscope through the working channel of the colonoscope. The small endoscope is retroflexed in the colon, allowing the endoscopist to see mucosa which is behind the folds. The endoscopist has simultaneous endoscopic views of the forward-viewing colonoscope as well as the retroflexed view of the Third Eye retroscope. The TERRACE study evaluated ADR and polyp miss rate, in an open-labeled study that randomized patients to tandem exams, with Third Eye colonoscopy (TEC) followed by a standard colonoscopy [14]. The Third Eye colonoscopy increased overall ADR by 23.2% (p = 0.029). This study showed stronger data for increased ADR for surveillance (35.7% increase) and diagnostic exams (55.4% increase), and less for screening colonoscopies (increase of 4.4%). The benefit of TEC was found to be statistically significant for surveillance and diagnostic colonoscopies but not for screening exams. Authors also noted that the withdrawal time was longer in the TEC compared with standard exams.

Fuse® Full Spectrum Endoscopy Platform

EndoChoice (Alpharetta, GA, USA) is a full spectrum system, with an endoscope that has extra optics at the end. This system results in a 330° field of view for the endoscopist. The colonoscope has three additional imagers and light-emitting diodes (LEDs) at the end of the colonoscope. Three images from the three cameras at the tip of the colonoscope are projected to three video monitors. Polyp miss rate was evaluated in a multicenter, international, randomized trial in which patients received tandem colonoscopies with full spectrum colonoscopy followed by a standard colonoscopy or vice versa [15]. The polyp miss rate was statistically significantly lower in the full spectrum colonoscopies, compared with standard colonoscopies. There was no difference in withdrawal time in the standard colonoscopies compared to full spectrum colonoscopies.

Balloon Colonoscopy

NaviAid G-EYE colonoscope (Smart Medical Systems Ltd., Ra'anana, Israel) (Fig. 14.5a) has a balloon at the end of the colonoscope that can be inflated to flatten folds to improve visualization. This novel colonoscope was studied in a tandem study to evaluate adenoma miss rate. The adenoma miss rate was significantly higher in the standard colonoscopies compared with the NaviAid G-EYE balloon colonoscope (Fig. 14.5b) (7.5% vs. 44.7%, respectively, with p = 0.0002) [16]. The study also showed a higher additional adenomas detected by the balloon colonoscopy (81%). The cecal intubation time was similar in the two groups, but withdrawal time was longer in the balloon colonoscopy group.

Extra-Wide-Angle-View Colonoscope

Extra-Wide-Angle-View colonoscope (Olympus, Tokyo, Japan) has a 170° view and high definition video. This platform showed promise in a prospective study with a statistically significant increase in ADR [17]. This colonoscope has a forward-viewing lens as well as a retrograde/ side-viewing lens. Images from both lenses are projected simultaneously as one image on the monitor. The combined images of the two lenses results in a wide-angle image that improves visualization of the difficult to see mucosa.

Other Modalities

There are advanced technologies developed for the upper gastrointestinal tract and pancreatico-biliary anatomy, such as confocal laser endomicroscopy (CLE) and endoscopic ultrasound (EUS). CLE is a real-time in vivo evaluation of microscopic cell structures during the endoscopy. It has been shown to have diagnostic yield in various upper GI tract disorders. It has been shown to be valuable in predicting relapse in quiescent ulcerative colitis. Recently, it has also shown to detect reproducible changes in the terminal ileum of patient with Crohn's disease that are predictors of disease flare [18]. There is little role of CLE in polyp detection. The CLE probe is able to visualize a very small area at a time; so, this technology is best to evaluate specific areas. CLE is not practical for evaluation of an entire colon.

EUS is a minimally invasive method that uses high-frequency sound waves to create an image. EUS is helpful to visualize deeper organs without invasive surgery, such as the pancreas, lymph nodes, liver, lungs, as well as various others. EUS is widely used in the esophagus, stomach, and duodenum to evaluate depth and type of submucosal lesions. In the colon, EUS can be performed using the miniprobe with 12 or 20 MHz transducers providing 360° radial images (Olympus UM-2R® and UM-3R®). A study evaluated 60 individuals with the miniprobe, showed that EUS may be valuable for local and regional staging of colon cancer [19]. The EUS miniprobe can be helpful in characterization of a specific lesion but does not have a role in polyp detection.

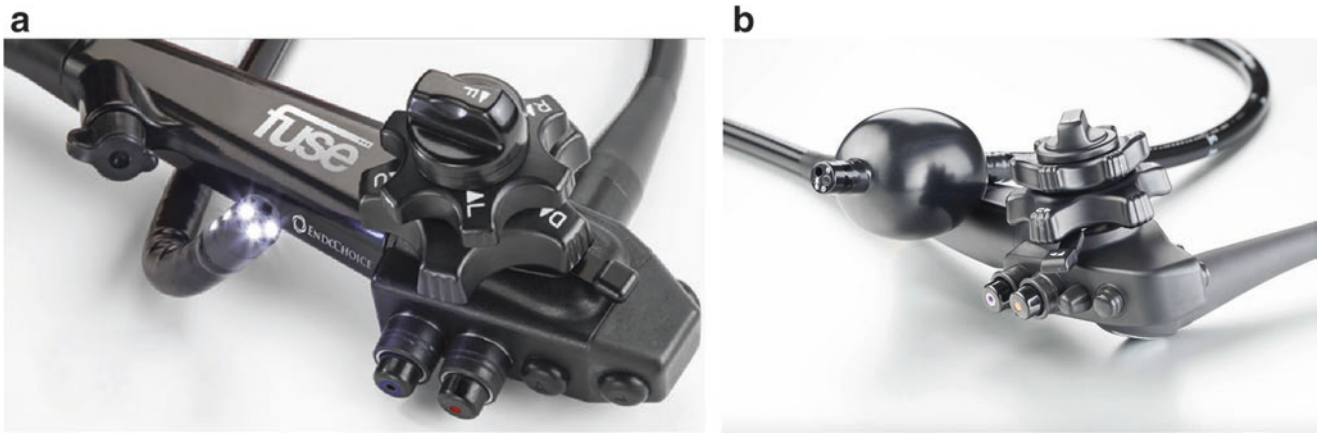

Fig. 14.5 New colonoscope systems. (**a**) Fuse® Full Spectrum Endoscopy Platform. (**b**) NaviAid G-EYE colonoscope

Summary

Colon cancer remains a major cause of morbidity and mortality in the US, although it is one of the few malignancies that are both preventable and curable. Colonoscopy remains the gold standard for screening and surveillance of polyps. Adenoma detection rate (ADR) has been established as the marker of colonoscopy quality. Adenoma detection improvement starts with having an adequate bowel cleanse, sufficient withdrawal time, as well as appropriate surveillance intervals. To improve upon the endoscopist and patient factors, several technological advances have been made.

Chromocolonoscopy, both dye-assisted and digital, has been shown to aid in finding abnormal colonic lesions. The "pit pattern" seen during chromocolonoscopy can distinguish adenomas from hyperplastic lesions, allowing to possibly decrease the pathology fees by discarding the hyperplastic lesions. This modality is proving highly useful in patient with Ulcerative Colitis for dysplasia screening. Chromocolonoscopy is not yet recommended widely for all colonoscopies due to lack of strong evidence for average-risk patients, and the procedure can be more cumbersome.

Cap-assisted colonoscopies have been studied to improve the field of vision. Several devices have been developed to assist the endoscopist to see behind folds and in flexures. The clear cap, the Endocuff and the EndoRing have been studied and have shown some promise to decrease missed polyps, especially diminutive polyps. At this time, the data is not strong enough to support these devices to become standard of care.

New colonoscope platforms, such as the Fuse® full spectrum endoscopy platform, the wide angle colonoscope are designed to increase the field of view by improving optics and adding imagers. The Third Eye colonoscopy device uses an endoscope introduced into the working channel of the colonoscope that is able to retroflex and show the mucosa behind the folds has also shown promise to improve ADR. Balloon colonoscopy with an integrated balloon on the end of the colonoscope has been shown to flatten folds and increase ADR. These novel devices increased the endoscopist's field of view, but require having a different platform and may increase withdrawal time compared to standard colonoscopy. CLE and EUS can prove valuable in evaluation of specific regions or lesions in the colon but have little potential to help improve polyp detection.

In summary, polyp detection is the cornerstone of colorectal cancer screening. Currently, several technological advances can help improve polyp detection, and as a result prevent colon cancer and even death.

Pearls

- Every endoscopist should strive to improve upon the ADR.
- While not the "standard of care," learning techniques like chromoendoscopy may result in improvement in ADR and differentiation between various polyp types and malignancy.
- Technological advancements are on the horizon that may improve polyp detection.

Pitfalls

- Missed polyps lead to advanced lesions and malignancy.

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Endoscopic Mucosal Resection (EMR)

15

Husayn Ladhani, Helmi Khadra, and Jeffrey Marks

Abbreviations

APC	Argon plasma coagulation
C-EMR	Cap-assisted EMR
CT	Computed tomography
DW	Dextrose water
EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
EUS	Endoscopic ultrasound
FM	Fibrinogen mixture
HA	Hyaluronic acid
HES	Hydroxyethyl starch
HPMC	Hydroxypropyl methylcellulose
HS	Hypertonic saline
I-EMR	Injection-assisted EMR
L-EMR	Ligation-assisted EMR
NS	Normal saline
PPS	Postpolypectomy syndrome
U-EMR	Underwater EMR

Key Points

- Endoscopic mucosal resection and endoscopic submucosal dissection have provided new alternatives for minimally invasive treatment of colorectal adenomas and early stage cancers that involve minimum risk of lymph node metastasis.
- Endoscopic mucosal resection is typically used for removal of mucosal lesions smaller than 20 mm or piecemeal resection of larger lesions, whereas endoscopic submucosal dissection is reserved for *en bloc* resection of lesions larger than 20 mm.
- The technique used for resection depends on the location of the lesion, equipment available, and the expertise of the endoscopist.
- Various submucosal injection solutions are available and the type of solution used for resection should be chosen on a case-by-case basis, taking into account the location and size of lesion and the type of resection being performed.
- The major complications related to endoscopic mucosal resection in the colon and rectum include hemorrhage, perforation, and development of postpolypectomy syndrome.
- Patients with lesions that are concerning for malignancy during colonoscopy or resected lesions with high-risk features should undergo segmental colectomy as the risk of lymph node metastasis is high.

Introduction

Wolff and Shinya performed the first polypectomy using snare electrocautery in 1969, merely 3 months after developing the technique of fiberoptic colonoscopy. Prior to the advent of polypectomy such potentially precancerous lesions required a laparotomy and colectomy. In 1973, they reported a series of 499 colonic polypectomies with only one incidence of postpolypectomy bleeding, one incidence of minimally symptomatic perforation, and no mortality [1–3].

Although the standard snare polypectomy technique described in Chap. 9 is sufficient for the majority of lesions encountered during colonoscopy, several types of lesions require advanced resection techniques. These include sessile or flat lesions more than 15 mm in size, occupying more than one-third to one-half of the wall circumference, extending

Electronic supplementary material: Supplementary material is available in the online version of this chapter at 10.1007/978-3-319-48370-2_15. Videos can also be accessed at http://www.springerimages.com/videos/978-3-319-48368-9.

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over more than two folds, or wrapped around a fold in a clamshell fashion. These lesions are generally considered 'difficult' and comprise about 10–15% of all lesions encountered during colonoscopy [4]. Endoscopic techniques have significantly improved over the past few decades, allowing a greater number of difficult lesions to be successfully resected endoscopically.

Endoscopic mucosal resection (EMR) was first developed in Japan in 1984 for the treatment of early gastric cancer [5]. It has since expanded to include the treatment of early colorectal malignancies and precancerous lesions and is typically used for removal of mucosal lesions smaller than 20 mm or piecemeal removal of larger lesions. Even with piecemeal resection, incomplete resection is common and can lead to local recurrence. The development of endoscopic submucosal dissection (ESD) has allowed *en bloc* resection of lesions larger than 20 mm. This chapter will discuss the indications, different techniques, and applications of EMR in the colon and rectum. ESD is discussed in greater detail in Chap. 16.

Indications for EMR

EMR is used for minimally invasive curative resection of benign and early stage (T1a) malignant lesions without lymph node involvement throughout the gastrointestinal tract. Indications for EMR in the colon and rectum are listed in Table 15.1 [6].

Patients with lesions that are concerning for malignancy during colonoscopy or resected lesions with high-risk features should undergo segmental colectomy as the risk of lymph node metastasis is high. These high-risk features include positive or indeterminate margins, margin <1 mm, lymphovascular invasion, poor differentiation, deep submucosal invasion (>1 mm), or tumor budding [7].

Table 15.1 Indications for EMR in the colon and rectum [6]

Indications for EMR in the colon and rectum
Nonpolypoid colorectal neoplasms
Lesions greater than 20 mm
Difficult locations
Dentate line
Ileocecal valve
Appendiceal orifice
Folds
Lesions over scars
Lesions in chronic inflammatory bowel disease
Large pedunculated lesions
Rectal carcinoids
Large lipomas
Patients with impaired coagulation
Anticoagulation medication
Antiplatelet medication
Thrombocytopenia

EMR Techniques

Several EMR techniques have been developed over the years based on the principle of "lifting" the target mucosa and performing resection of the target lesion using electrocautery. The type of EMR technique used depends on the location of the lesion, equipment available, and the expertise of the endoscopist. The main approaches are as follows:

- Injection-assisted EMR (I-EMR)
- Cap-assisted EMR (C-EMR)
- Ligation-assisted EMR (L-EMR)
- Underwater EMR (U-EMR)

Prior to beginning resection, the extent of the target lesion should be clearly identified because once resection has commenced mucosal landmarks may become obscured and visible abnormalities in early neoplastic lesions may become difficult to ascertain. Saline or water irrigation is used to clear the field and spraying 1% acetylcysteine aids in the dissipation of adherent mucus. It is also useful to mark the periphery of the lesion using cautery prior to beginning the resection.

Injection-Assisted EMR

Injection-assisted ("inject-and-cut") EMR is the most commonly used EMR technique in the colon and consists of submucosal injection of a lifting agent followed by application of snare electrocautery for resection. Submucosal injection is a well-established technique that creates a submucosal cushion underneath the lesion, mitigating the risk of transmural thermal injury during the application of electrocautery and allowing *en bloc* resection of the target lesion.

The goal of submucosal injection is to elevate and bring forward the lesion into the lumen to provide good visualization of the margins and allow assessment for resection. Before injection, the assistant should prime the needle with saline solution to prevent injection of air into the bowel wall causing iatrogenic pneumatosis. Injection should begin at the proximal aspect of the lesion, the side farthest from the scope, and proceed distally. If it is started at the distal aspect of the lesion, the lesion may fall away from the scope, reducing visualization and making resection difficult. Whenever possible, the injector needle should be placed tangential to the mucosal surface; this facilitates insertion of the needle into the submucosal plane and decreases the risk of intraperitoneal injection. Puncture is made immediately adjacent to

the lesion [4, 8]. Injecting directly through the lesion has raised some concerns regarding the risk of needle tracking of neoplastic cells into deeper layer of the wall [9].

Injection begins when the needle touches the mucosa and is continued as the needle is advanced towards the submucosa. There is immediate elevation of the lesion upon entering the submucosal space. This confirms injection into the correct plane. Lack of elevation or intraluminal extravasation of injection solution may mean lack of injection into the correct plane. In this instance, the needle can be advanced or withdrawn until the correct submucosal plane is identified. When resecting large lesions in a piecemeal fashion, segmental injection and resection is recommended, especially when using normal saline (NS) as the injection solution. The volume of injection solution used during the entire procedure varies and depends on the size of the lesion and type of solution used.

If there is lack of elevation despite appropriate injection technique, this 'nonlifting sign' (Fig. 15.1) may indicate fixation of the lesion to the underlying submucosal tissue. This can be due to fibrosis from previous resection attempts, underlying colitis, or malignant infiltration into the deeper tissues. Occasionally, even benign lesions without underlying colitis or fibrosis may fail to elevate. Intervention in these cases is often limited to a biopsy, and presence of more invasive disease on the biopsy necessitates surgical resection [4, 8].

Following submucosal injection, resection is performed using an endoscopic snare. A variety of snares are available ranging in size, stiffness, configuration, and shape. The snare is placed on top of the lesion, opened, and placed around the base of the lesion with the scope angled downwards. The assistant then begins to close the snare while advancing the catheter, to maintain the position of the snare at the base of the lesion. Once the snare is closed at the base, transection of the lesion is performed using electrocautery. Large size snares are often employed as they allow *en bloc* resection of the target lesion and piecemeal resection of large lesions in as few pieces as possible. The supplementary Video 15.1 provided with this chapter shows endoscopic resection of a mucosal resection using I-EMR.

All attempts should be made to perform an *en bloc* resection. This allows for evaluation of resection margins for completeness of resection, provides for more accurate histopathological assessment, and also reduces the risk of recurrence when compared to piecemeal resections. If *en bloc* resection is not possible piecemeal resection is performed starting at one margin of the lesion and proceeding until the entire lesion is resected. Care must be taken to include the margin of previous resection, so that residual tissue bridges are not left behind. Once piecemeal resection is complete, the lesion site should be inspected for presence of residual tissue. If present, the residual tissue should be resected using an appropriate sized snare [4]. Figure 15.2 depicts piecemeal resection of a lesion greater than 20 mm.

Following complete resection of the lesion, some endoscopists choose to ablate the resection margin and any residual tissue to decrease the risk of local recurrence. Options include argon plasma coagulation (APC), thermal ablation with the tip of the snare (snare tip soft coagulation), and hot biopsy forceps (hot avulsion technique) [8, 10].

Cap-Assisted EMR

First described by Inoue in 1990 [11] and most commonly used for resection of mucosal lesions in the esophagus, this technique can also be employed in the colon and rectum. Like I-EMR, it also uses submucosal injection to lift the target lesion following which resection is performed using dedicated mucosectomy devices. These are single-use devices that have a cap fixed to the tip of the scope and are equipped with a specially designed electrocautery snares. Caps are available in various sizes and have either a flat, cylindrical, or oblique end.

To begin resection the snare is opened and positioned on the internal rim at the tip of the cap. The scope with the

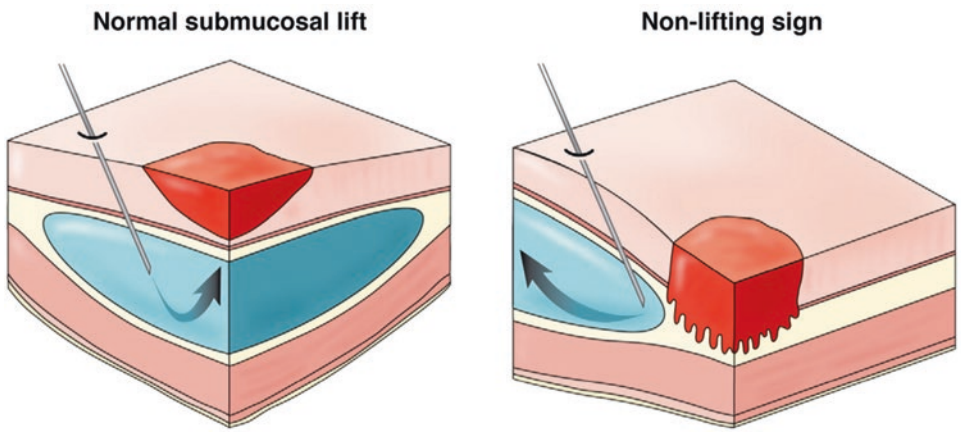

Fig. 15.1 Normal submucosal lift and the 'nonlifting' sign. With permission from Chandrasekhara V, Ginsberg GG. Endoscopic mucosal resection: not your father's polypectomy anymore. *Gastroenterology.* 2011;141:42–9 [10] © Elsevier

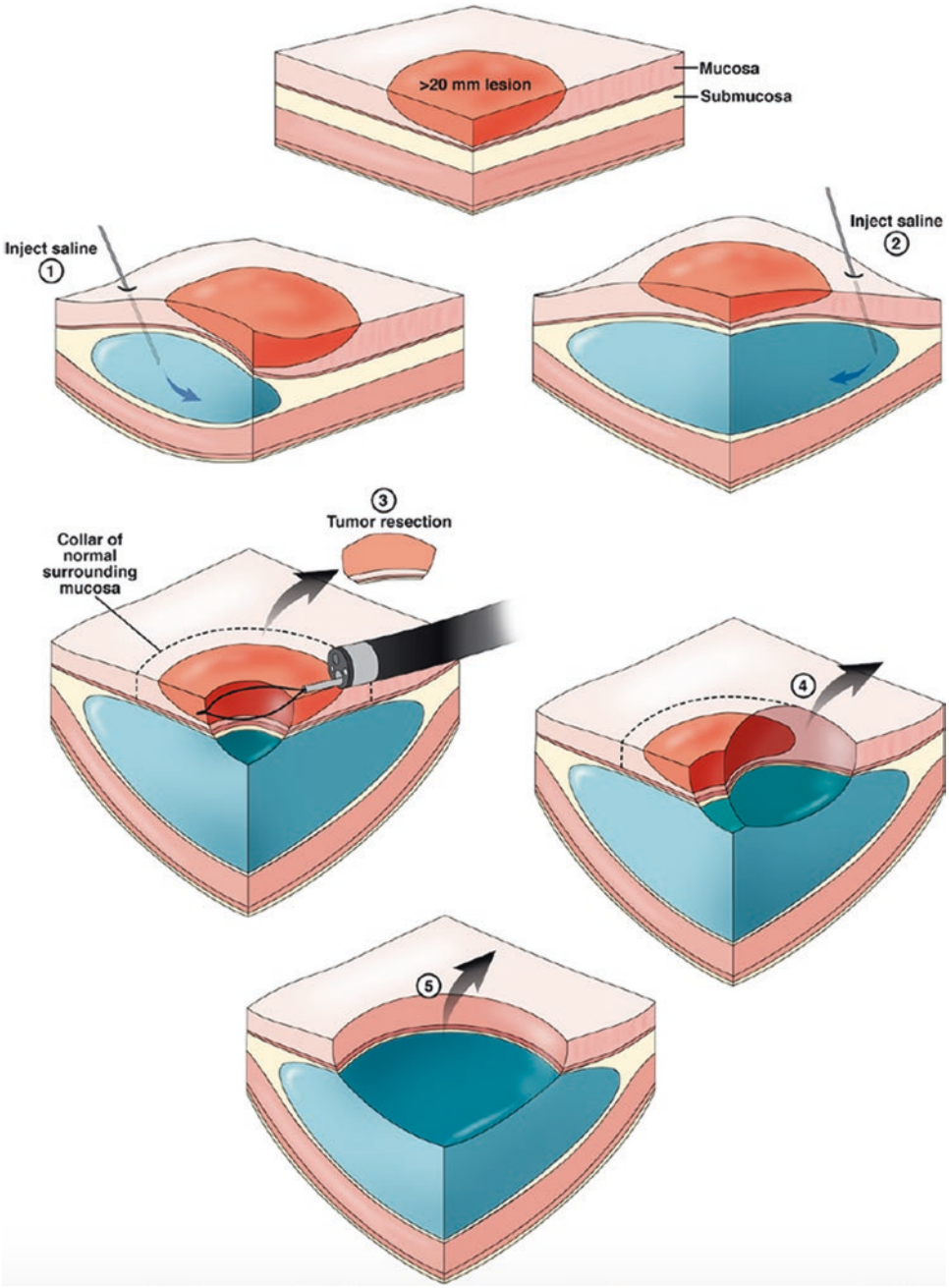

Fig. 15.2 Piecemeal resection of lesion greater than 20 mm using I-EMR. With permission from Chandrasekhara V, Ginsberg GG. Endoscopic mucosal resection: not your father's polypectomy anymore. *Gastroenterology.* 2011;141:42–9 [10] © Elsevier

attached cap is then positioned on top of the target lesion. Suction is applied to capture the lesion into the cap and the snare is deployed at the base of the lesion. Finally, electrocautery is applied to resect the target lesion [8]. Figure 15.3 shows resection of a mucosal lesion using this technique.

One must be careful when applying suction to capture the lesion as it may involute the full thickness of the wall resulting in capture of the muscularis propria in the snare. It also tends to collapse the lumen which compromises the endoscopist's view. Concern over the risk of full thickness resection has limited its application in the colon.

Ligation-Assisted EMR

Originally extrapolated from variceal band ligation, this technique is somewhat similar to C-EMR. Specially designed band ligation devices with caps are used to create a neo-polyp. These devices are attached to the tip of the endoscope and positioned on top of the target lesion. Suction is applied to retract the lesion in the cap following which the band is deployed at the base of the lesion. Standard snare electrocautery is then used to resect the neo-polyp above or below the band [8]. Figure 15.4 shows resection of mucosal lesion without the use of submucosal injection.

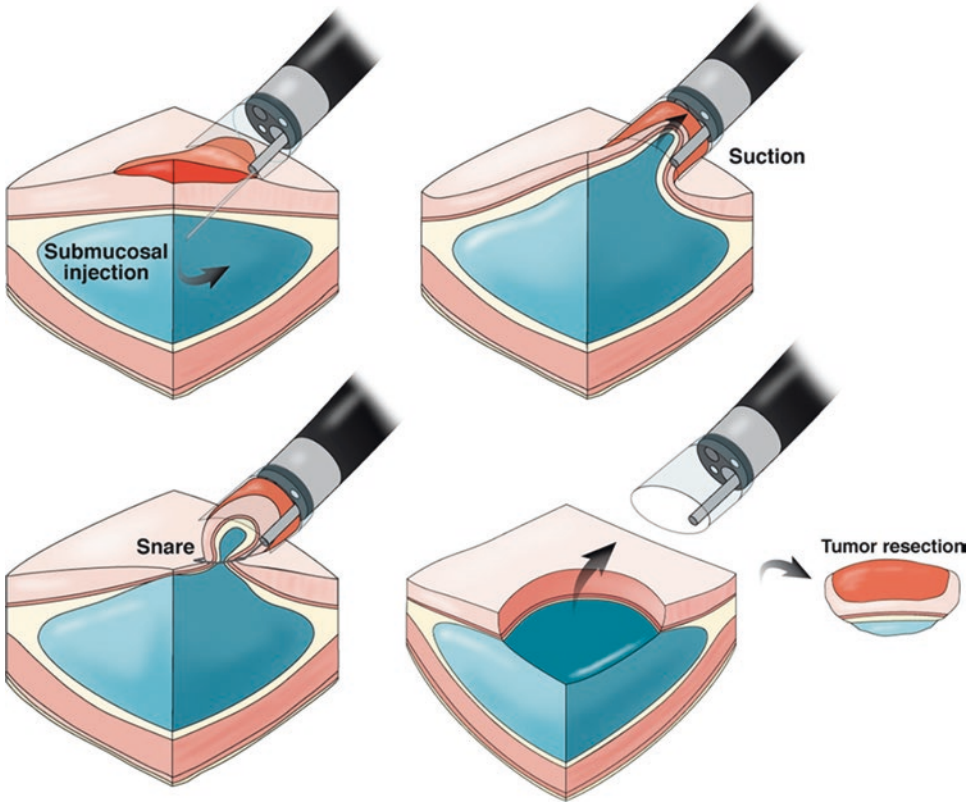

Fig. 15.3 Resection of mucosal lesion using C-EMR. With permission from Chandrasekhara V, Ginsberg GG. Endoscopic mucosal resection: not your father's polypectomy anymore. *Gastroenterology.* 2011;141:42–9 [10] © Elsevier

Underwater EMR

Binmoeller et al. in 2012 described a novel technique of performing resection by immersing the lesion under water. This was based on their observation of the colonic wall when viewed with an endoscopic ultrasound (EUS). They noted that when filled with water, the muscularis propria remained circular and mucosa and the submucosa remained involuted. Furthermore, the buoyancy effect of the disease-affected mucosa allowed the mucosa and the submucosa to "float" away from the deeper muscularis propria eliminating the need for submucosal injection and the costs associated with injection needles and specialized injection agents.

Water immersion enhances the sensitivity of endoscopy by creating an optical "zoom" effect that magnifies the mucosa. Narrow band imaging can be used to further enhance the contrast between the diseased and normal mucosa. On the other hand, lack of air insufflation prevents overdistention and subsequent thinning of the wall thus decreasing the risk of perforation.

A routine adult-sized single-channel colonoscope with an auxillary water jet is used for this technique. Upon reaching the target lesion luminal air is suctioned and sterile water is instilled to fill the lumen. Between 500 and 1000 mL of sterile water at room temperature is needed to achieve complete filling of the lumen. Continuous water infusion can be used to limit contractility which can compromise visibility. Margins of resection are marked using the APC probe tip prior to resection.

Duckbill snare is used to perform resection. Starting at the margin of resection the snare is opened, pushed against the bowel wall, and torqued to capture a piece of the tissue. The snare is then closed and electrocautery is applied to transect the tissue. Large lesions may require piecemeal resection taking care not to leave behind any residual tissue. Remnant tissue too small to ensnare can be coagulated with hot biopsy and forceps and APC can be used to ablate the resection margins [8, 9, 12].

Mucosal Lifting Agents

The success of EMR depends on the formation of an adequate submucosal cushion to decrease tissue resistance within the transection place and allow *en bloc* resection of the lesion. It also reduces the risk of perforation and transmural thermal injury by separating the lesion from the underlying muscularis propria. The ideal solution used for this purpose should be inexpensive, readily available, nontoxic to the tissue, easy to prepare and inject, and should provide a long-lasting submucosal cushion [4, 8].

Currently, there are no FDA-approved solutions for submucosal injection during EMR in the US. Various solutions have been used over the years, none of which can be consid-

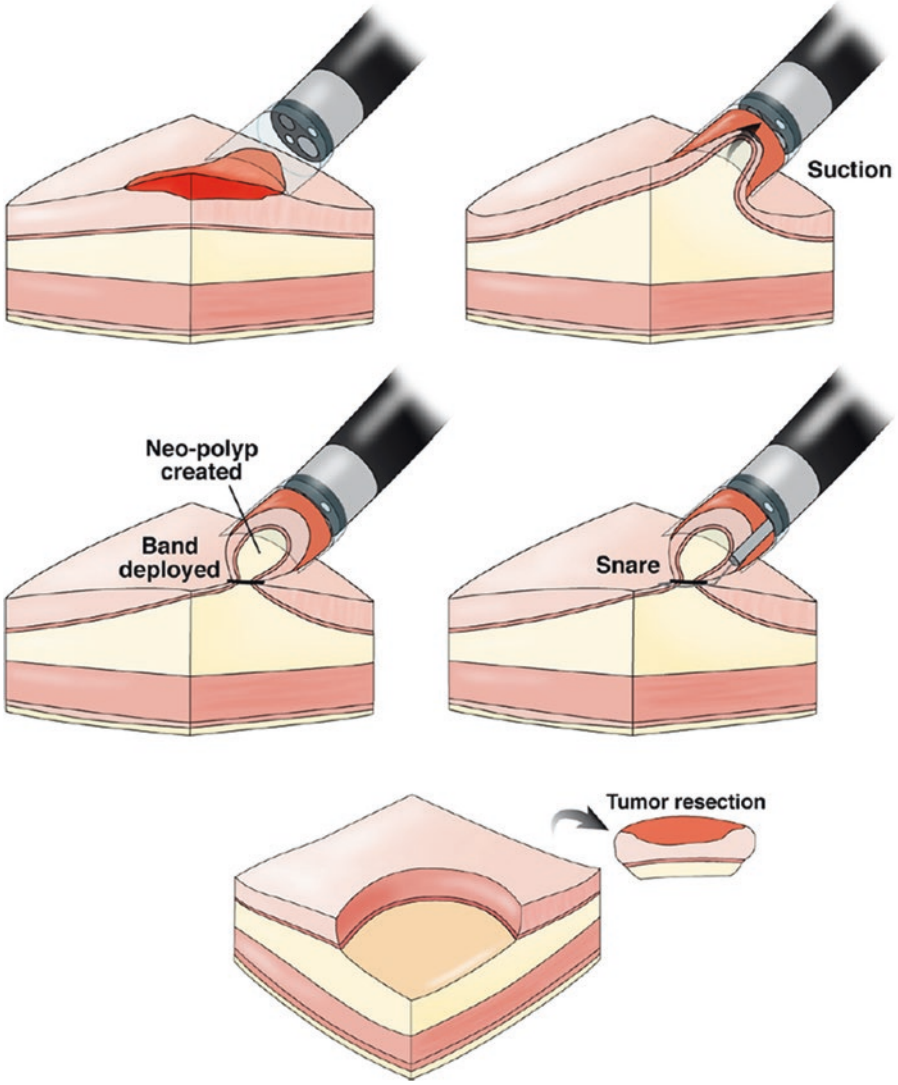

Fig. 15.4 Resection of mucosal lesion using L-EMR. With permission from Chandrasekhara V, Ginsberg GG. Endoscopic mucosal resection: not your father's polypectomy anymore. *Gastroenterology.* 2011;141:42–9 [10] © Elsevier

ered ideal, and these solutions differ in terms of effectiveness, cost, availability, and risk profile. Table 15.2 lists some of the solutions currently used and under investigation for use during EMR. The appropriate submucosal injection solution used for EMR should be chosen on a case-by-case basis taking into account the location and size of lesion and the type of resection being performed.

Normal saline 0.9% (NS) solution is most commonly used in the US for submucosal injection. It is widely available, easy to use, and inexpensive. However, the cushion provided by NS dissipates within minutes thus requiring repeated injections. In recent years, various injection solutions have been demonstrated to provide longer lasting submucosal cushion compared to NS.

Hypertonic saline 3.75% (HS) solution in readily available, inexpensive, and has been shown to provide a higher cushion compared to NS but creates tissue damage and local inflammatory reaction at the injection site. Dextrose water (DW) solution is also inexpensive, easily available, and produces a higher and longer lasting cushion compared to NS but has also been reported to cause tissue damage, delay ulcer healing, and cause postpolypectomy syndrome (PPS) at concentrations ≥20%.

Hyaluronic acid (HA), a type of glycosaminoglycan found in connective tissue, has been shown in clinical practice to provide greatest elevation and longest lasting cushion allowing greater number of successful *en bloc* resections and lower perforation rates, especially for colorectal ESD. A 0.4% HA solution is currently approved for use during EMR in Japan. It has several shortcomings, however; it is expensive, has limited availability, requires dilution to facilitate injection, and has been reported to stimulate the growth of residual tumor cells making it unsuitable for use during piecemeal resections. A low-cost mixture of high-molecular-weight HA and glycerol has recently shown good outcomes with ESD.

Table 15.2 Solutions for submucosal injection during EMR [4, 6, 8, 13]

Solution	Duration of cushion	Advantages	Disadvantages
Normal saline (0.9%)	+	Inexpensive, readily available, easy to inject, safe	Dissipates rapidly
Hypertonic saline (3.75%)	++	Inexpensive, readily available, easy to inject	Tissue damage, local inflammation, delayed healing
Dextrose water	++	Inexpensive, readily available	Tissue damage, local inflammation, delayed healing, increased risk of PPS at concentrations ≥20%
Hyaluronic acid	++++	Longest lasting cushion	Expensive, limited availability, very viscous, may stimulate growth of residual tumor cells
Hydroxypropyl methylcellulose	+++	Long-lasting cushion, less expensive	Tissue damage and local inflammation, very viscous, risk of antigenic reactions
Succinylated gelatin	++	Inexpensive, readily available, easy to inject	Contraindicated in gelatin hypersensitivity
Glycerol	++	Inexpensive, readily available	Produces smoke with use of electrocautery, use not reported in US
Albumin	++	Readily available, easy to inject	Expensive
Fibrinogen mixture	+++	Long-lasting cushion, easy to inject, hemostatic effect	Expensive, risk of transmission of viruses, use not reported in US
Autologous blood	+++	Long-lasting cushion, easily available	Limited human data, can clot in syringe, may hamper visualization
Hydroxyethyl starch	+++	Long-lasting cushion	Lack of human data, increased risk of bleeding

Hydroxypropyl methylcellulose (HPMC), a cellulose derivative, is less expensive than HA, provides longer duration of cushion compared to NS, and causes minimal tissue reaction but is very viscous and must be diluted for injection. It is a synthetic product and has the potential to cause antigenic reactions. Glycerol (10% glycerin and 5% fructose in NS) solution has been shown to increase *en bloc* resection rates compared to NS but produces smoke with use of electrocautery during the procedure.

Fibronogen mixture (FM) provides a long-lasting submucosal elevation compared to NS and also has a microvascular hemostatic effect but has a risk of transmission of hepatitis or other viruses. Autologous blood has shown encouraging results with longer mucosal elevation than other solutions. Furthermore, it is safe, readily available, easy to inject, and promotes local hemostasis. However, autologous blood can hamper visualization during the procedure, may clot in the syringe if injection is delayed, and currently has no human data regarding its use during EMR [4, 13].

Hydroxyethyl starch (HES) has also been investigated and has shown to provide long-lasting cushion in ex vivo animal studies. However, there are some reports that suggest that HES may promote bleeding by exerting adverse effects on plasmatic coagulation and platelet function [14].

Other novel submucosal injection solutions such as sodium alginate, injectable drug-eluting elastomeric polymer, sodium carboxymethyl cellulose hydrogel, photo-crosslinkable chitosan hydrogel, and polyethylene glycol maleate solutions are under investigation and have limited human data [4, 13]. Further comparative research is needed to identify the optimal injection solution for use during EMR.

Dilute epinephrine (1:100,000–1:200,000) and staining dyes are often added to the injection solution. Dilute epinephrine is generally safe and well tolerated. It minimizes the risk of immediate bleeding, provides a sustained cushion, and facilitates endoscopic visualization by maintaining a dry resection field but has not shown to prevent delayed bleeding. Systemic side effects such as hypertension, tachycardia, and intestinal ischemia are rare and only reported at higher concentrations of epinephrine used for hemostasis. Staining dyes, such as 0.004% indigo carmine or methylene blue facilitate identification of lesion margins and help distinguish between the submucosa and the underlying muscularis propria [8].

Clinical Outcomes of EMR

Most colorectal lesions can be successfully resected using traditional EMR techniques, either *en bloc* or in piecemeal fashion. However, local recurrence has been observed and rates differ between *en bloc* and piecemeal techniques. A recent meta-analysis found the overall mean recurrence rate to be 15% and this rate to be significantly higher for piecemeal resection (20%) than for *en*

bloc resection (3%). In multivariable analysis piecemeal resection was found to be the only independent risk factor for recurrence [15].

There are no established guidelines for surveillance following EMR. After successful *en bloc* resection, surveillance colonoscopy can be performed at 1 and 3 years but patients with larger lesions should undergo 3 successive yearly exams. Following piecemeal resection, repeat colonoscopy should be performed at 3–6 months to assess for local recurrence. Scars from previous resection sites should be biopsied. Repeat EMR can be performed for local recurrence but patients with submucosal invasion or lesions not amenable to EMR should be referred for segmental colectomy [16].

Data regarding outcomes of the novel U-EMR technique is limited. When compared to I-EMR, a nonrandomized clinical trial showed the complete removal rate to be higher and the recurrence rate to be significant lower for U-EMR. Complication rates have also been low. Besides being the initial technique for resection, it has also shown to be efficacious for managing recurrences after previous EMR as well in patients with partial resections and lesions that are difficult to lift with submucosal injections [8, 12].

Complications and Management of Complications

EMR is generally safe in experienced hands though several complications have been described. The major complications related to EMR in the colon include hemorrhage, perforation, and PPS. These complications and their management are discussed in greater detail in Chap. 21.

Hemorrhage

It is the most common complication of EMR and can occur at the time of procedure (immediate bleeding) or hours to weeks (delayed bleeding) after the procedure. The reported risk is 1–11% but higher rates have also been reported in some studies, especially for lesions greater than 20 mm. Several variables have been associated with increased risk of postprocedure bleeding. These include, but are not limited to, lesion size greater than 10–20 mm, flat or laterally spreading lesions, pedunculated polyps with thick stalks, right-sided colonic lesions, type of electrosurgical current used, and use of anticoagulants.

Endoscopic therapy for immediate bleeding should be reserved for active bleeding that interferes with completion of the procedure or for persistent oozing that has not ceased by the end of the procedure. Often times constricting the residual stump with a snare and holding pressure may be sufficient. Dilute epinephrine (1:10,000 solution) can be injected in the base of the lesion to reduce or stop bleeding but this is only a temporary measure and should be followed by more definitive therapy, such as endoscopic clips, hemostatic spray or gel, detachable snare (endo-loop), direct suture ligation, or grasping coagulation forceps using a soft coagulation mode. Whenever possible, mechanical devices to achieve hemostasis should be used as they do not extend the depth of tissue injury.

Management of patients with delayed bleeding should begin with general principles employed in lower gastrointestinal bleeding. They must be triaged appropriately based on severity, fluid and blood transfusions should be given, and anticoagulants and antiplatelet medications should be held. Endoscopic therapy, including endoscopic clips, direct suture ligation, or grasping coagulation forceps may be necessary. Uncontrolled bleeding may require angiographic embolization, or rarely, surgery.

Perforation

It is a serious complication that can occur in up to 5% of patients undergoing EMR. Successful outcome depends upon the immediate recognition and management of the perforation. Appropriate workup may include abdominal X-rays or computed tomography (CT). Perforations less than 1–2 cm in size are generally amenable to endoscopic closure. Options include clipping with through-the-scope or over-the-scope clips or endoscopic suturing using various devices. Surgery is indicated in cases of large perforation, failed endoscopic closure, gross feculent peritoneal contamination, residual lesion, and clinical deterioration.

Postpolypectomy Syndrome

This is secondary to transmural thermal injury without perforation following snare resection. The incidence is less than 3% with EMR and occurs most often after resection of large (>20 mm) sessile polyps, particularly in the thin-walled right colon, and with longer duration application of electrosurgical current. Patients present within hours to few days with localized abdominal pain, peritoneal signs, fever, and/or leukocytosis. Abdominal computed tomography is the best radiographic test and shows localized colonic wall thickening and adjacent fat stranding without extraluminal air. PPS has an excellent outcome with conservative management [8, 17].

Comparison with ESD

ESD was originally developed for *en bloc* resection of larger, flat gastrointestinal tumors but carries a greater risk of perforation in the colon due to thin colonic wall. When compared

to EMR, ESD achieves higher *en bloc* resection rates and lower recurrence rates. However, longer procedure times, higher complication rates, technical difficulty, and lack of expertise have limited its use in the US [8, 18].

Pearls and Pitfalls

- Prior to beginning resection the extent of the target lesion should be clearly identified because once resection has commenced mucosal landmarks may become obscured and visible abnormalities in early neoplastic lesions may become difficult to ascertain.
- Submucosal injection should begin at the proximal aspect of the lesion because if it is started at the distal aspect of the lesion, the lesion may fall away from the scope reducing visualization and making resection difficult.
- Injection should be done immediately adjacent to the lesion since injecting directly through the lesion may cause tracking of neoplastic cells into deeper layers of the wall.
- The 'nonlifting sign' may indicate fixation of the lesion to the underlying submucosal tissue secondary to fibrosis from previous resection attempts, underlying colitis, or malignant infiltration into the deeper tissues.
- All attempts should be made to achieve an *en bloc* resection because incomplete resection increases the risk of local recurrence.
- The success of EMR depends on the formation of an adequate submucosal cushion to decrease tissue resistance and reduce the risk of perforation and transmural thermal injury.
- There is no ideal solution for submucosal injection and the type of solution used for resection should depend on the location and size of lesion and the type of resection being performed.

Conclusion

EMR provides a minimally invasive alternative for the treatment of various benign, precancerous, and early stage malignant lesions with low risk of lymph node involvement in the colon and rectum. Resection rates are high and the risk of complications in experienced hands is low using all the various resection techniques. However, lack of established guidelines for surveillance following resection, as well as the technical difficulty and lack of expertise have limited its widespread use.

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Endoscopic Mucosal Dissection

16

Cigdem Benlice and Emre Gorgun

Abbreviations

CT	Computerized tomography
EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
LCS	Laparoscopic colorectal surgery
SM	Submucosal invasion status

Key Points

- Up to 15% of colon polyps require advanced polypectomy techniques due to their size, location, or appearance; ESD has unique advantages over other methods in this setting.
- The colonoscopy report and pathology results should be reviewed prior to ESD as these details can influence treatment decisions.
- Polyps should be localized first endoscopically and marked using hyperosmolar injectate diluted with methylene blue.
- Bleeding encountered during dissection should be coagulated immediately and potential perforations should be closed using endoclips.
- If a target lesion demonstrates features of malignancy, the procedure can be converted to laparoscopic colectomy.
- If endoscopic submucosal dissection is successful, but final pathology reveals carcinoma, patients may then require colectomy.

Introduction

Screening colonoscopy and polypectomy decreases the incidence of colorectal cancer and its related mortality [1]. While most colorectal polyps can be removed with simple snare or forceps techniques, some lesions may not be amenable to conventional colonoscopic removal. Up to 15% of colonic polyps require advanced polypectomy techniques due to their size, location, or appearance [2].

A recent study estimated the cancer risk in patients with endoscopically benign-appearing unresectable colon polyps referred for surgery. Over a 15-year period, 439 patients underwent colectomy for polyps that were deemed unsuitable for endoscopic removal; only 8.4% of these patients were found to have cancer. In other words, more than 92% of patients undergoing colectomy for an endoscopically unresectable, benign-appearing colon polyp did not have invasive cancer in the final pathology [3]. Nonetheless, all apparently benign polyps that cannot be removed endoscopically should be resected via colorectal resection in accordance with oncologic principles. However, more than 90% of patients are overtreated by oncologic colorectal resection and bowel resection carries risks of major complications including mortality. Advanced polypectomy techniques such as endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), or hybrid procedures have been proposed to remove large colorectal lesions. Technique selection is prominently influenced by lesion morphology, size, location, patient condition, and existing skill set and expertise.

ESD was first popularized in Japan for the treatment of early esophageal and gastric cancers in the 1990s [4] and is ideal for cancers in the stomach because the thick gastric

Electronic supplementary material: Supplementary material is available in the online version of this chapter at 10.1007/978-3-319-48370-2_16. Videos can also be accessed at http://www.springerimages.com/videos/978-3-319-48368-9.

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Table 16.1 Indications for colorectal endoscopic submucosal dissection (ESD)

Indications for colorectal ESD
1. Large (>20 mm in diameter) lesions amenable to endoscopic submucosal resection and in which *en bloc* endoscopic mucosal resection is difficult
Laterally spreading tumor-nongranular: particularly of the pseudodepressed type
Lesions showing Kudo type-V invasive pit pattern
Carcinoma with submucosal infiltration
Large depressed-type lesion
Large elevated lesion suspected to be a cancer
2. Mucosal lesions with fibrosis
3. Local residual early carcinoma after endoscopic resection
4. Sporadic localized tumors in chronic inflammation, such as ulcerative colitis

wall allows for safer dissection. Using this technique, surgeons can achieve *en bloc* margin-negative resection of tumors allowing detailed histopathological analysis while avoiding invasive surgery and preserving the native organ [5]. ESD has not yet been established as a "standard" therapeutic method for removing colorectal lesions; however, data from early studies is promising and further research is continuing [6]. It is important to understand the indications and limitations of ESD, so that patients are appropriately counseled and treated. This chapter reviews the details of ESD including indications, equipment, technique, outcomes, and complications.

Indications

The indications for ESD (as recommended by the Japan Colorectal ESD Standardization Implementation Working Group) include lesions difficult to remove *en bloc* endoscopically, lesions with underlying fibrosis, sporadic localized lesions in patients with ulcerative colitis, and local residual lesions after prior EMR (Table 16.1) [4, 7]. Although there has not been an extensive experience with colorectal ESD in the United States, a proposed management algorithm for the care of patients with difficult colorectal lesions is summarized in Fig. 16.1.

How and What to Inject

To perform the ESD safely, it is necessary to create and expand a potential submucosal space to allow dissection between the mucosa and muscle wall. This is done via submucosal injection and reduces the risk of perforation and transmural thermal injury by separating the lesion of interest from the deeper muscularis propria layer and decreases tissue resistance within the transection plane [2]. The first injections are made around the perimeter of the lesion to provide a margin of safety when incising the mucosa; subsequent injections are made beneath the lesion during submucosal dissection.

The submucosal injection should be performed in such a way that the lesion is elevated into the lumen to improve exposure and visualization of the margins. If the polyp is situated on a fold, the first submucosal injection site should be along the proximal margin of the lesion to allow the polyp to fall forward into view. If the submucosal injection is started along the distal portion of the polyp, there is a danger of the polyp falling backward away from the view of the scope, which increases the difficulty of ESD. To create the submucosal cushion, the needle tip is advanced into the mucosa while the assistant starts injecting. As the needle tip advances into the submucosal space, there is an immediate elevation of the mucosa, confirming entry into the correct plane. If the lesion does not lift or the injectate extravasates intraluminally, the needle can be gently repositioned until the correct plane is entered. Failure of polyps to lift adequately despite appropriate injection technique (the "non-lifting sign") may indicate the presence of invasive disease requires surgical resection. Non-lifting may also occur as a result of fibrosis from previous polypectomy attempts.

The ideal injection agent should be safe and inexpensive and provide a long-lasting submucosal cushion. The two common elements in the various injection solutions are the colloid (hyperosmolar) solution and an inert dye (like indigo carmine or methylene blue). Several agents have been used for lifting during ESD and each has its own limitations reflecting the absence of a clearly superior solution (Table 16.2). Commonly, ESD solutions contain normal saline, glycerol, and hyaluronic acid. Hypertonic saline solution and dextrose have been noted to cause local tissue damage and were abandoned. Sodium hyaluronate 0.4% (MucoUp; Johnson and Johnson, Tokyo, Japan) is widely reported in the Asian literature but is expensive [4]. Alternatively, hydroxypropyl methylcellulose (Hypromellose) diluted six to eight times with saline can be used and is relatively inexpensive (Fig. 16.2). Injectates are colored with a few drops of dye (typically indigo carmine or methylene

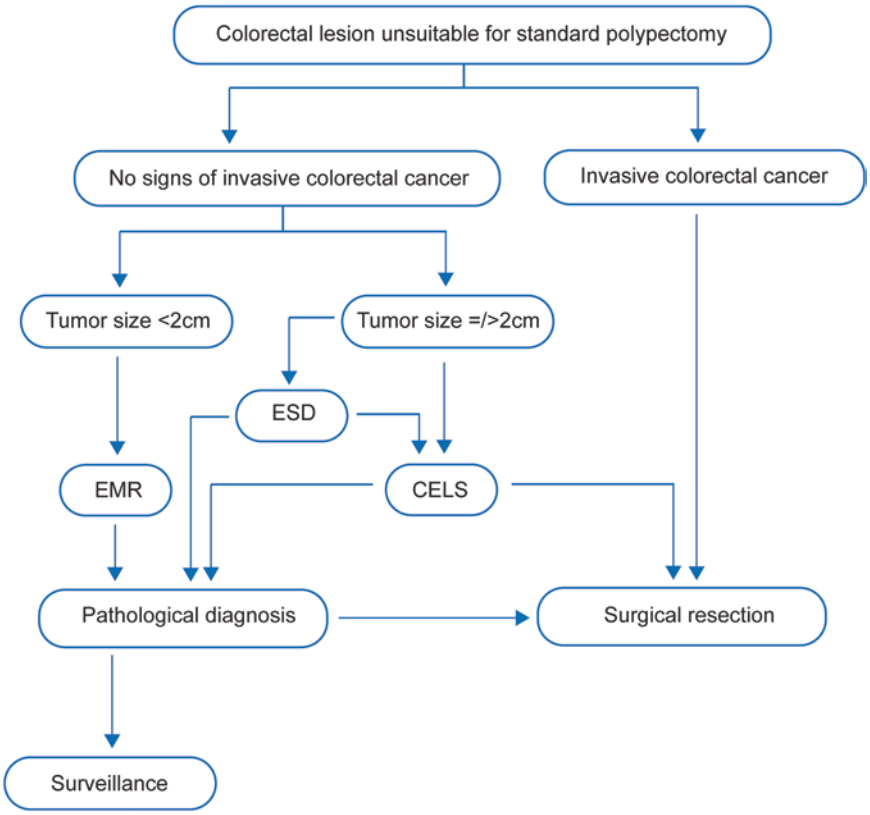

Fig. 16.1 Endoscopic submucosal dissection algorithm. *EMR* Endoscopic mucosal resection, *ESD* Endoscopic submucosal dissection, *CELS* Combined endoscopic laparoscopic surgery

Table 16.2 Submucosal injection solutions for colorectal endoscopic submucosal dissection

	Submucosal lift duration	Advantages	Disadvantages
Normal saline	+	Cheap, readily available, easy to inject, safe	Rapidly dissipates
Glycerol	++	Cheap, readily available	Smoke production
Dextrose	++	Cheap, readily available	Local inflammation, tissue damage
Fibrinogen mixture	+++	Long-lasting cushion, easy to inject	Limited availability, risk of infection
Hyaluronic acid	+++	Produces the longest lasting cushion, high successful en bloc resection rate, low perforation rate	Expensive, limited availability, very viscous
Hydroxypropyl methylcellulose	+++	Long-lasting cushion, relatively inexpensive	Local inflammation, tissue damage, very viscous

blue) to improve visualization and facilitate differentiation of tissue planes [8].

Injectates are typically delivered with a 21- to 25-gauge injection needle catheter while viscous injectates require a larger bore needle. Some ESD knives have an integrated water jet channel within the device catheter. The Hybrid Knife (ERBE, Tuebingen, Germany), the only integrated device currently available in the United States, features an ultrafine water jet powered by a foot pedal that is powerful enough to penetrate the mucosal layer in a needleless fashion for lifting purposes.

Cautery Principles

Electrocautery facilitates polyp removal by tissue cutting (snare closure) and coagulation (thermal energy). Cautery energy applied at the cellular level produces heat due to tissue resistance which leads to tissue disruption or coagulation with hemostasis, depending on the chosen waveform. A variety of instruments can be used with electrocautery including probes, snares, forceps, and knives. Monopolar devices transmit current from an electrode in the instrument's tip

through the patient's body to a remote grounding plate (usually on the leg or thigh) to complete the circuit. Bipolar devices have both active and return electrodes in the instrument tip obviating the need for a grounding plate. Each of the following tools is best used for specific steps and maneuvers (Fig. 16.3) [9]:

Dual Knife

The single-use Olympus *DualKnife*™ (Olympus America Inc., Center Valley, PA) electrosurgical knife features an adjustable two-step knife length and a dome-shaped cutting section designed to simplify marking and enable incision and dissection in all directions (Fig. 16.3a). Distinct blue marks visible on the sheath provide endoscopic verification of cutting depth. The channel diameter is 2.8 mm, the working length is 230 cm, and the cutting knife length is 1.5 mm for colon applications. The short cutting length helps prevent accidental perforation of the thin-walled colon. Closing the handle and pulling the tip into the sheath facilitate the functions of marking and hemostasis. Opening the handle and deploying the knife facilitate incision and dissection.

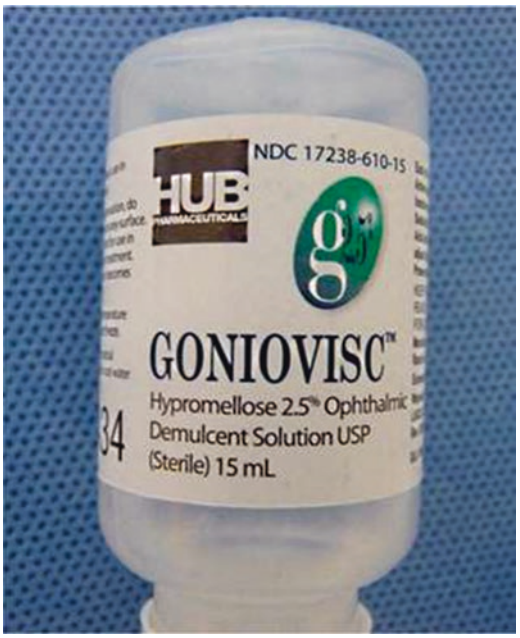

Fig. 16.2 Hypromellose solution. A hyperosmolar injection solution provides superior lift to a polyp compared to saline

Hook Knife

The *HookKnife*™ (Olympus America Inc., Center Valley, PA) is an L-shaped hook with rotational function that allows for precise incision and dissection in longitudinal and lateral directions (Fig. 16.3b). This tool is used to hook the tissue and draw it away from the mucosa while applying diathermy, thus minimizing the risk of perforation. The turn-and-lock feature is simple to deploy and ensures the cutting wire is locked at the desired position during the procedure. Different lengths can be chosen based on procedural technique and lesion location.

Coagrasper

The single-use *Coagrasper*™ (Olympus America Inc., Center Valley, PA) hemostatic forceps provides precise and effective hemostasis by grasping a bleeding point or a visible vessel and delivering targeted monopolar coagulation (Fig. 16.3c). Excellent rotational function increases the accuracy of the grasper and the device is available in two types of cup shapes and opening widths. Using a combination of

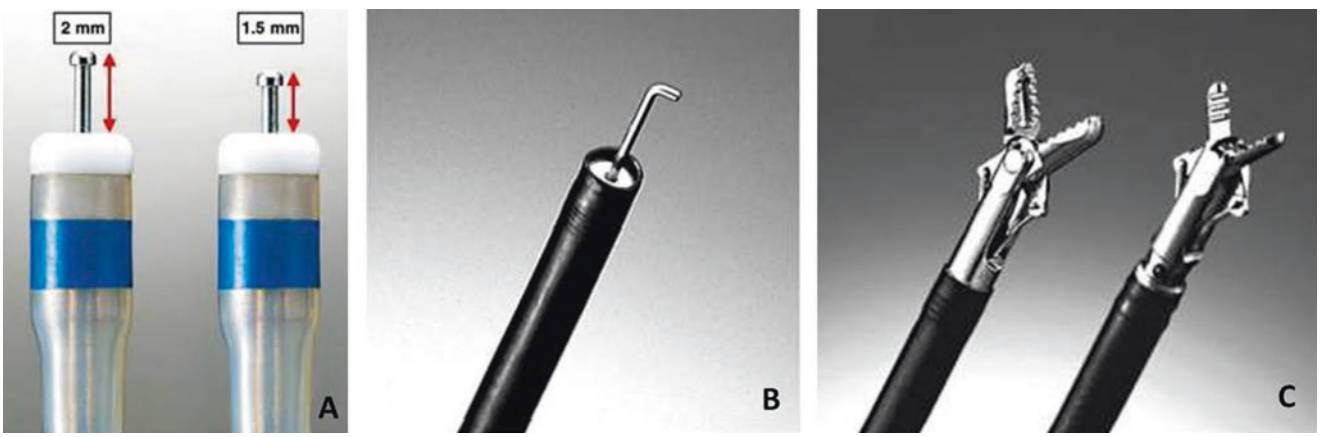

Fig. 16.3 Endoscopic submucosal dissection tools. (**a**) Dual knife: Useful for marking and dissection (Courtesy of Olympus). (**b**) Hook knife: Controls depth of penetration as tissues are pulled away while energy is applied (Courtesy of Olympus). (**c**) Coagrasper: Helpful for larger submucosal vessels (Courtesy of Olympus)

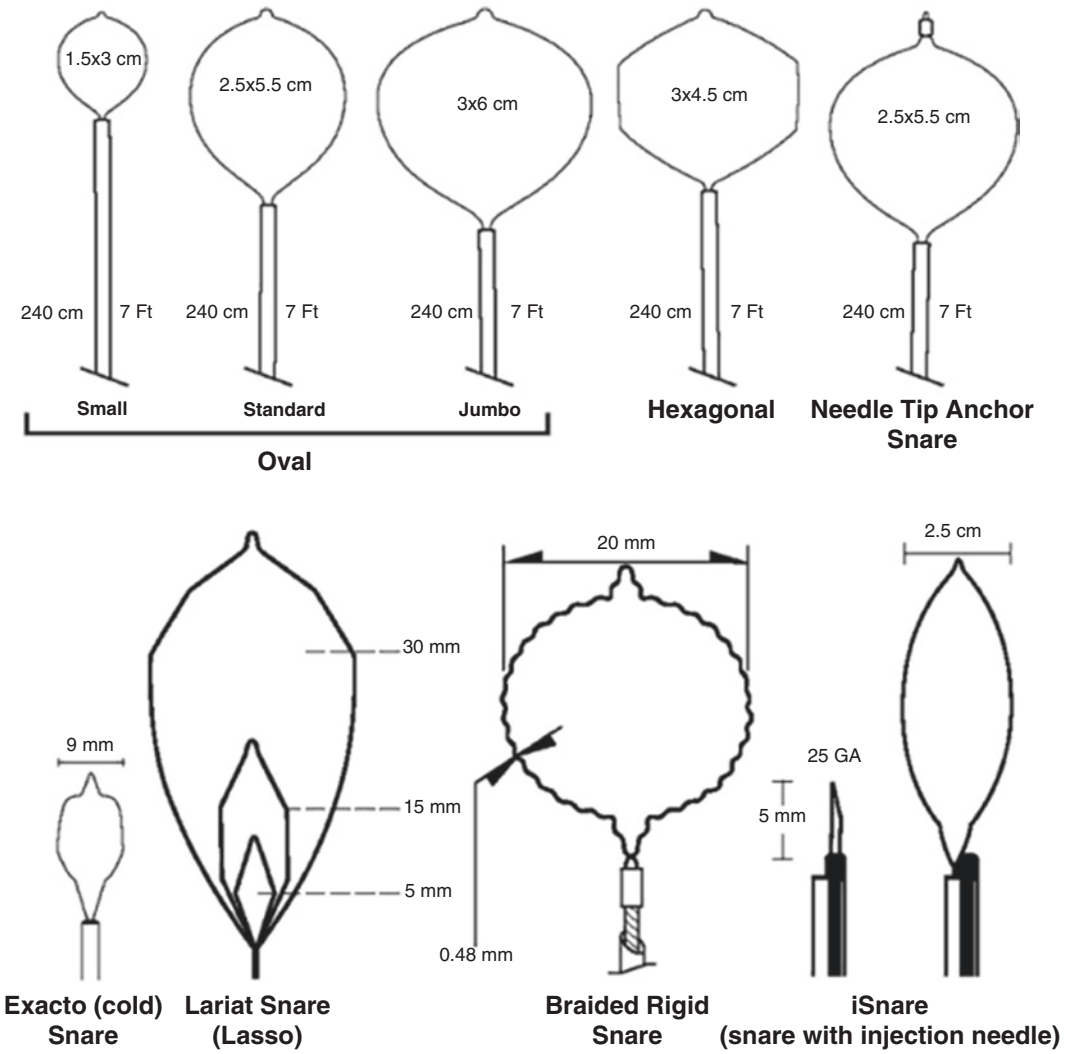

Fig. 16.4 Snare types used for advanced endoscopic resection techniques

mechanical and energy-based hemostasis, the Coagrasper can isolate a vessel from the healthy surrounding mucosa, so that thermal coagulation occurs only where needed.

Snare Selection

A variety of snares are available for use in advanced endoscopic resection techniques. The choice of a specific snare is influenced by lesion size, morphology, and location and personal preference (Fig. 16.4). While EMR techniques mainly involve polyp removal with snare or strip biopsy, the hybrid ESD technique uses a circumferential mucosal incision followed by *en bloc* resection of the lesion with snare (see Video 16.1). This technique can be considered a bridge between EMR and ESD. When lesions are difficult to access via the mucosal plane, hybrid ESD may achieve better results than EMR [10].

Technique and Results

ESD involves several basic steps (Fig. 16.5). First, the lesion is delineated, although marking the borders in the colon and rectum is usually not necessary (Fig. 16.6). After submucosal injection, a circumferential incision is created beginning at the proximal border. Once half of the circumference is incised, submucosal dissection is performed in this half of the circumference. In some cases, retroflexion may be necessary to complete this step. The circumferential incision is then completed and the submucosa is completely dissected from the distal side. Surgeon may use one or more different types of endoknife combinations during the procedure. The resected lesion is retrieved following complete dissection (Fig. 16.7). Bleeding encountered during dissection should be coagulated immediately and potential perforations should be closed using endoclips.

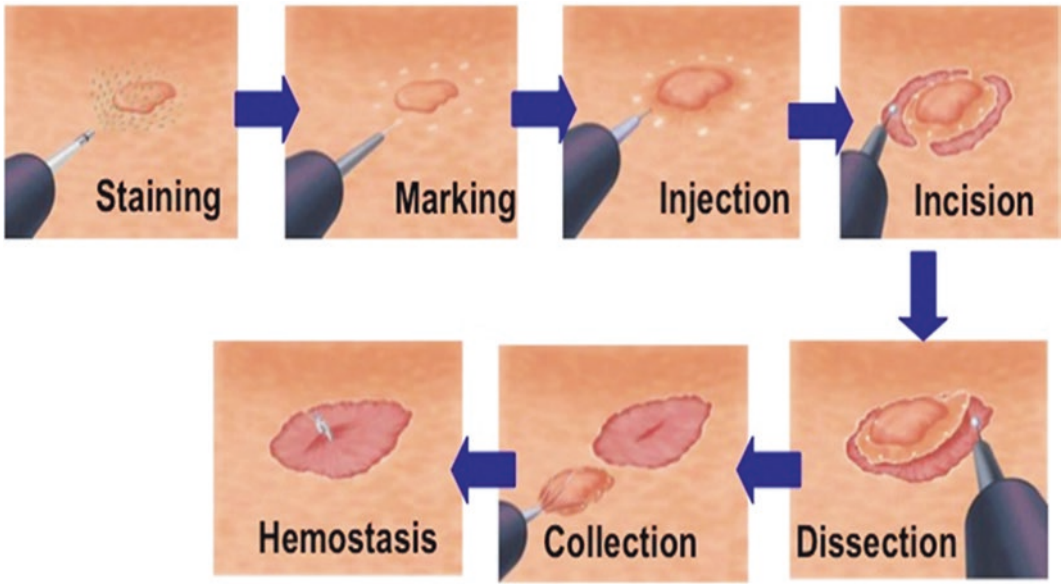

Fig. 16.5 Basic principles of endoscopic submucosal dissection

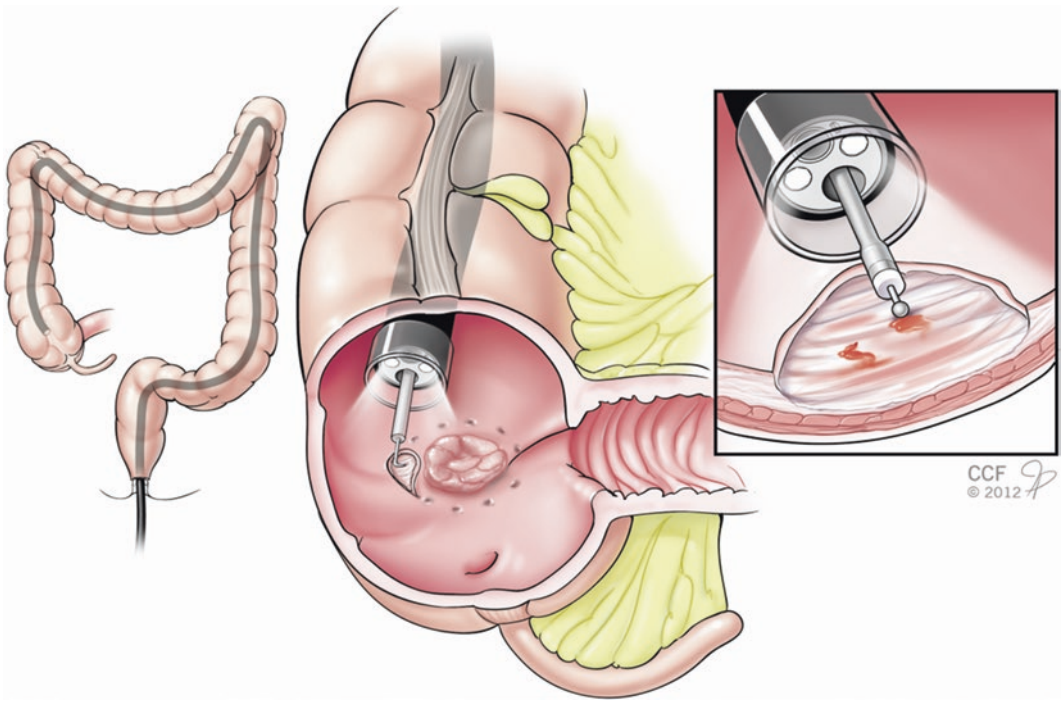

Fig. 16.6 Orientation for endoscopic submucosal dissection and dissection of the submucosal plane

In an ongoing study at Cleveland Clinic, Ohio, selected patients were offered ESD in the operating room with possible bowel resection if ESD could not be successfully completed or was otherwise indicated. Seventy-one patients (mean age 63 years, female 32 (45%), median BMI 29.8 kg/m^2) had indications for intervention including large polyp size (median preoperative endoscopic size 3 cm (range, 1.5–6.5)) and/or difficult location. Lesion morphology was sessile (n = 64, 90%) or pedunculated (n = 7, 10%). The successful advanced endoscopic resection rate was 84.6% (N = 60) (Fig. 16.8). Of these 60 cases, ESD was completed in 41 patients and 19 patients underwent laparoendoscopic intervention. The complication rate was 12.6% (9/71) [delayed bleeding (N = 3), perforation (N = 2), organ-space surgical site infection (SSI) (N = 2), superficial SSI (N = 1), small bowel obstruction (N = 1)]. Out of 71 patients, 12

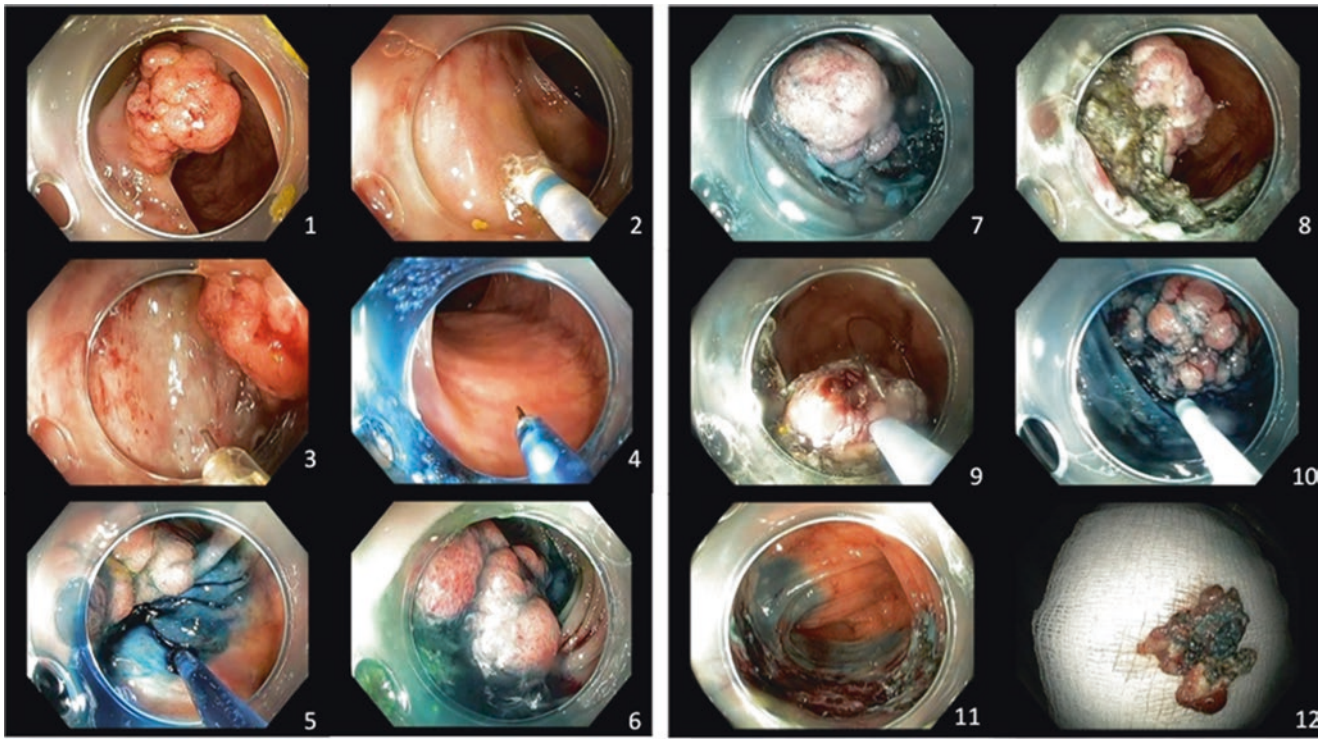

Fig. 16.7 Operative steps. *1*: Lesion arising from the colonic mucosa; *2–6*: Submucosal injection; *7–8*: Circumferential submucosal dissection of the lesion; *9–10*: Snaring the centrally attached portion of the lesion; *11*: Colon lumen and submucosa after removal of the lesion; *12*: Resected specimen

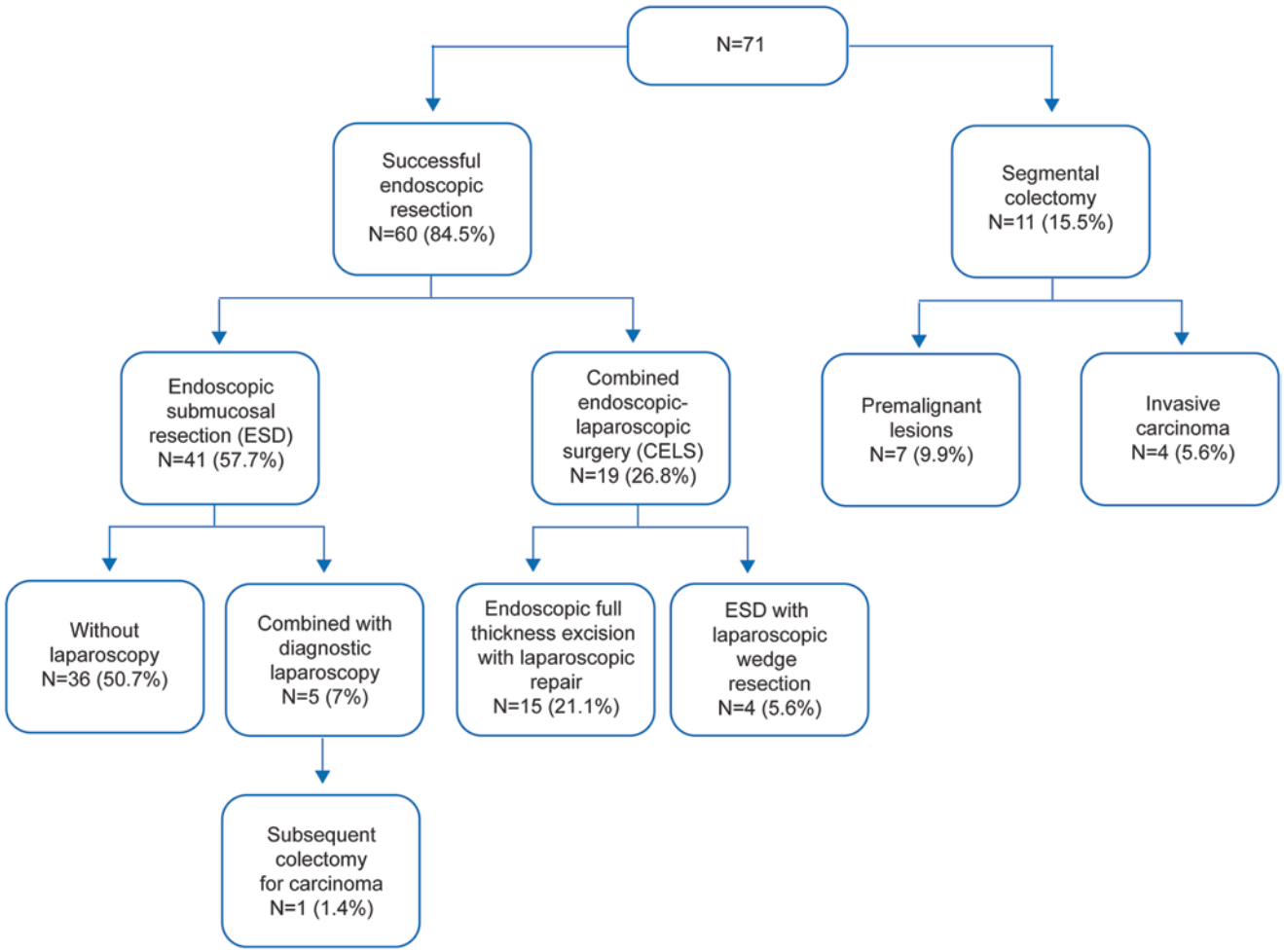

Fig. 16.8 Intraoperative and postoperative outcomes of 71 patients evaluated for advanced endoscopic resection

Table 16.3 Outcomes of ESD for colorectal superficial lesions

Author, year	Lesions included, *N*	En bloc resection rate, *n*/*N* (%)	Bleeding (ESD related)	Perforation (ESD related)	Local recurrence
Repici, 2012 [11]	2841	2727/2841 (96%)	47/2841 (2%)	135/2841 (4%)	1/1397 (<0.1%)
Tanaka, 2012 [12]	2719	2082/2516 (82.8%)	31/2087 (1.5%)	127/2719 (4.7%)	9/768 (1.2%)
Lee, 2013 [13]	1000	973/1000 (97%)	4/1000 (<1%)	53/1000 (5%)	3/722 (<1%)
Oka, 2015 [14]	716	680/716 (95%)	18 (2.5%)	8 (1.1%)	10/716 (1.4%)

(16.9%) required colectomy for technical failure (7 patients) or carcinoma (5 patients). The median operative time was 123 min (range: 40–351) and median length of stay was 1 day (range: 1–9). During a median follow-up of 13 months (range: 1–41 months), 1 patient had adenoma recurrence.

Other outcomes after ESD for colorectal lesions are summarized in Table 16.3 [11–14]. A recent systematic review comprising 22 studies and 2841 treated lesions reported an *en bloc* resection rate of 96% with an R0 rate of 88% [15]. Surgery was necessary in a few cases (2% of lesions) mainly because of incomplete resection or complications (1%). "Intramucosal cancer" was present in 44% of specimens and submucosal cancer was found in 11% [11]. In an analysis of several studies totaling greater than 2719 cases of ESD for colorectal neoplasia, local recurrence rates averaged approximately 1% [12].

After ESD, patients are usually observed for 3–4 h until discharge criteria are met. Patients who had complicated or larger lesions removed with ESD usually stay overnight.

Complications

ESD for colorectal lesions is associated with a variety of complications. While perforation and bleeding are the major complications, colonoscopy-related complications can also occur including splenic injury, post-polypectomy syndrome, mesenteric hemorrhage, diverticulitis, appendicitis, and pancreatitis [7]. Close postoperative follow-up is required. Careful examination of the resected area during ESD is important and early recognition of complications and prompt intervention are crucial.

Bleeding

Bleeding is the most common complication and occurs in up to 7% of colorectal ESD procedures [16]. Bleeding that occurs during the procedure (immediate bleeding) occurs in up to 7% of cases and is rarely serious. Immediate bleeding can be managed with hemostatic clips, coagulation forceps, or snare tip soft coagulation. Delayed bleeding is defined as a decrease in hemoglobin by >2 g/dL or confirmation of marked hemorrhage after endoscopic treatment. Delayed bleeding does not include small amounts of bleeding such as the presence of trace amounts of blood in the stool. The incidence of delayed bleeding is reported to be 1.5–2.8% after ESD and is mainly observed 2–7 days after operation.

Perforation

Colonic perforation occurs in up to 5–10% of ESD procedures [16]. Full-thickness perforation during the procedure (intra-procedural) usually occurs following deep resection and is immediately appreciated and treated. Delayed perforation, most likely caused by coagulation necrosis or other unrecognized injury to the muscular layer, occurs in 0.1–0.4% of ESD cases. Colon perforation that is detected after the scope has been withdrawn following completion of an ESD during which a perforation did not occur is diagnosed on the basis of abdominal pain, abdominal examination, presence of fever, and inflammatory response. Most cases of delayed perforation occur within 14 h of operation but approximately one-third of delayed perforations are diagnosed 24 h after the procedure. Smaller volumes of extraluminal gas can go undetected by X-ray imaging but can be detected by abdominal computerized tomography (CT). In cases where delayed perforation is suspected and X-ray is unrevealing, abdominal CT should be performed. Because of the delayed presentation, peritonitis is often present and surgery is frequently necessary.

Postprocedural Pain

Nonspecific pain after ESD is common especially after large or complex lesions are removed. Excessive distension, serositis, and transmural injection are common causes of pain. Continuous pain, which may be sign of peritonitis, needs further radiologic assessment.

Results for Early Colorectal Cancers

ESD is a reliable method for *en bloc* resection of a polyp when the size and location of the lesion permits; it also may be considered for cases of T_1 colorectal carcinoma.

In the case of early malignancy, microscopic examination of endoscopically resected specimens is of particular importance because a precise histopathological analysis influences the potential need for further surgery [17]. The muscularis mucosa is the landmark that determines invasivity of cancer, and classification of invasion levels of T_1 cancers within the submucosal layers has influenced the management of early colorectal cancers. Kikuchi's classification divides the submucosa into three vertical sections [18]. While early neoplasms invading the upper third (SM1) submucosa can be treated endoscopically, endoscopic removal of tumors invading the mid (SM2) and lower thirds (SM3) of the submucosa is controversial due to the higher risk of lymph node metastases. In order to reduce the number of unnecessary operations after endoscopic treatment of T_1 colorectal carcinoma without lymph node metastasis, ESD may be performed as an excisional biopsy, even if the SM invasion depth is T_{1b} (>1000 μm); the need for additional colectomy is then determined after detailed histopathological examination of resected specimens.

When pT_1 carcinoma is detected in a specimen after endoscopic excision, subsequent therapeutic recommendations should consider the 2014 Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines for the treatment of colorectal cancer [4]. Colorectal resection should be performed for margin-positive lesions as this indicates incomplete endoscopic removal. In cases of complete endoscopic resection, pT_1 carcinoma can be considered cured when all of the following conditions are satisfied: (1) vertical tumor margin-negative (histological complete resection); (2) papillary adenocarcinoma or tubular adenocarcinoma; (3) SM invasion depth <1000 μm; (4) no vascular invasion; and (5) tumor budding grade 1 (low grade). If even one of these five conditions is not satisfied, the estimated rate of lymph node metastasis and the individual specifics of the patient (i.e., age, comorbidities, quality of life) should be comprehensively evaluated in consideration of definitive surgical resection. Alternatively, when a resected specimen satisfies the five conditions detailed above, lymph node metastasis and local recurrence are extremely rare. In cases in which only the SM invasion depth does not satisfy the criteria for a cure and where no other risk factors for metastasis are present, the lymph node metastasis rate has also been reported to be extremely low.

Many experts believe that ESD will someday largely replace colectomy for node-negative colorectal epithelial neoplasia. A large retrospective series from the National Cancer Center in Tokyo compared outcomes of 589 patients with T_1 colorectal cancers who underwent either ESD (n = 297) for apparent mucosal or superficial submucosal neoplasms or laparoscopic-assisted colorectal resection including lymphadenectomy (LCS, n = 292) for apparent deep submucosal cancers [19]. While this study included a large number of patients with colon lesions, 185 who underwent ESD and 243 who underwent LCS, most of the outcomes data were reported for all-comers including patients with rectal neoplasia. In this study, ESD was associated with a shorter procedure time and hospital stay compared to LCS. The *en bloc* and curative resection rates with ESD were 87% and 80%, respectively, and patients with non-curative ESD resections were referred to surgery. The 3-year overall survival rate exceeded 99% in both the ESD and LCS groups and the authors concluded that ESD was associated with a lower complication rate and had favorable *en bloc* and curative resection rates for early cancers with a small risk of lymph node metastasis.

Conclusion

ESD is an innovative, advanced endoscopic therapy for superficial gastrointestinal neoplasms which is increasingly becoming a "standard" treatment option, particularly in Asian medical centers, and has the potential to revolutionize treatment of early alimentary tract cancers in the United States, as well. Colorectal cancer represents an important potential niche for the clinical application of ESD in the United States given the prevalence of these tumors. In order to perform safe and effective ESD, accurate preoperative assessment of the target lesion is essential. It is also imperative that even highly skilled endoscopists undergo specialized training to reduce the incidence of complications. Ex vivo and in vivo training programs must be developed to define the learning curve and educate endoscopists and reimbursement needs to address the time, expert training, and skill set required for this minimally invasive procedure.

Finally, careful pre-ESD tumor analysis is paramount and necessitates additional advanced training in chromoendoscopy and preoperative tumor classification. In order for colorectal ESD to become standard practice in the United States, the prevalence of early colorectal cancer must be further defined and centers of excellence should be developed to offer patients the safest and most efficacious outcomes. An important question remains as to whether the biology of colon cancer in Asia (which has the most ESD experience in the world) differs with respect to the prevalence of lateral spreading cancers and further studies are needed to clarify the epidemiology of early-stage colorectal cancer amenable to ESD to better define the role of this organ-sparing alternative treatment platform.

Pearls and Pitfalls

- For apparently benign polyps an oncologic colorectal resection is overtreatment thus advanced polypectomy techniques have been successfully applied at our institution since 2011.

- In order to start learning ESD, one should have good skills using colonoscopy and perform minimum of 200–300 colonoscopies per year as part of their practice.
- It is strongly recommended to attend didactic and hands-on ESD courses before scheduling initial ESD cases.
- Surgeons should choose appropriate cases (2–3 cm polyps, descending colon, etc.) during early learning period and patients should be consented for possible laparoscopic assistance (laparoscopic intracorporeal suture closure if there is perforation) and bowel resection if ESD cannot be successfully completed.
- To perform ESD technique safely, it is necessary to raise the submucosal plane to form a potential space for dissection between the mucosa and muscle wall.
- Any bleeding that occurs during resection should be coagulated immediately, and any small possible perforations should be closed using endoclips.
- During the ESD procedure, it is important to recognize signs of potential malignancy which can be recognized by direct neoplastic tissue penetration across the submucosal plane into the muscle fibers.
- Overnight observation of the patients after ESD procedure is strongly recommended to recognize any potential early procedure related complications.
- In order to document complete removal of polyp and absence of recurrent adenomatous tissue, a repeat colonoscopy after 6 months of the procedure is indicated.

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Applications of Intraoperative Endoscopy

17

Kyle Cologne and Joongho Shin

Key Points

- In cases where preoperative localization fails, be prepared to perform intraoperative colonoscopy to localize the tumor.
- Flexible CO_2 sigmoidoscopy intraoperative anastomotic leak testing visually confirms the integrity of newly constructed left-sided anastomoses and can also evaluate bowel perfusion.
- Intraoperative or postoperative endoscopy to stop the staple line bleeding is safe and effective.

Introduction

Intraoperative endoscopy is an essential component of the colorectal surgery armamentarium that was first used to localize a tumor during colorectal resection. This was especially helpful when using a laparoscopic approach, where tactile feedback to palpate a tumor is limited [1]. The introduction of CO_2 colonoscopy, a major improvement over using ambient air insufflation, broadened the utility and applicability of intraoperative colonoscopy. The rapid absorption of intra-luminal CO_2 prevents unwanted bowel distension. Conversely, air insufflation persists and jeopardizes the ability to complete an operation laparoscopically. Gorgun et al. compared the operative outcomes of 30 patients who underwent intraoperative colonoscopy during laparoscopic colorectal resection with 30 matched controls and found no difference in perioperative complications such as ileus and anastomotic leak [2]. Over the last two decades, the use of colonoscopy in the operating room during colorectal surgery has steadily increased. Intraoperative colonoscopy has evolved from a diagnostic modality or simple therapeutic tool and has made combined endoscopic-laparoscopic surgery (CELS) a reality [3]. As more advanced endoscopic surgical instruments and platforms come to market, the role of intraoperative colonoscopy is expected to expand.

Equipment and Setup

Before fiberoptic cameras, rigid proctoscopy was the only method for intraoperative endoscopic visualization. Flexible video endoscopy supplanted this technology with its improved visualization and versatile therapeutic applications. In terms of preoperative preparation in anticipation of performing intraoperative tumor localization, it is important to have endoscopic equipment available in the operating room and to bowel prep patients who may require endoscopic localization. Patients are placed in padded modified lithotomy position or split leg position to allow easy access for intraoperative colonoscopy.

Ideally, surgeons have access to dedicated, integrated operating rooms equipped for intraoperative colonoscopy. Alternatively, portable towers that are self-contained units allow surgeons to perform a variety of diagnostic and therapeutic interventions (Fig. 17.1). Typical room setup allows the endoscopic tower to be positioned in such a way that both the endoscopist and the surgeon can visualize the endoscopic picture (Fig. 17.2).

As reviewed earlier, a critical component for intraoperative endoscopy is the ability to use carbon dioxide insufflation which requires an insufflation pump and tank. Colonic CO_2 is absorbed up to 160 times faster than nitrogen and has minimal effects on systemic CO_2, making it ideal for intraoperative use [4]. It is important to monitor

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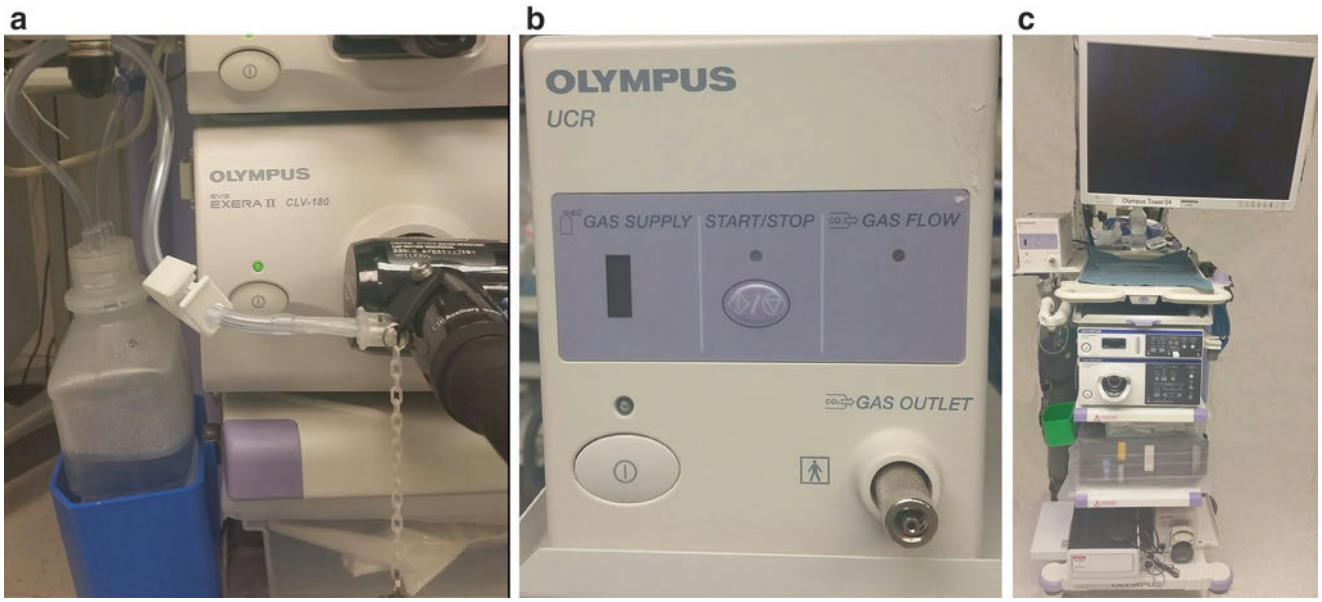

Fig. 17.1 Typical setup of colonoscopy tower with CO_2 insufflator

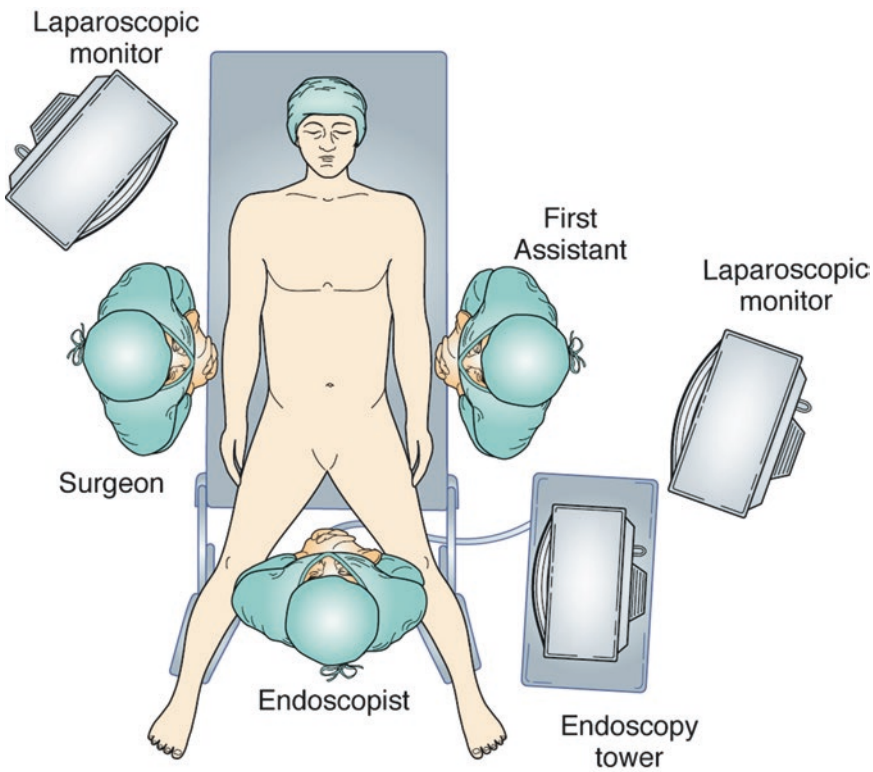

Fig. 17.2 Sample operating room setup

end tidal CO_2 levels and adjust ventilator settings to resolve any transient hypercarbia. The self-contained endoscopic tower also contains a light source, video processor, monitor, irrigation reservoir, and an electrosurgery generator.

Commonly used devices should be readily available including biopsy forceps, clips, snares, specimen retrieval nets, and injection needles for tattoos, epinephrine, or submucosal polyp lift. Depending on the case at hand, it may be useful to have access to endoscopic suturing.

Intraoperative Endoscopic Localization

Tumors, generally, should be tattooed preoperatively for localization purposes unless the tumor is located in the cecum or within a clearly defined relation to the ileocecal valve. In the absence of adequate preoperative localization, intraoperative endoscopic localization will be needed for smaller lesions. Bulky tumors and tumors clearly seen on cross-sectional imaging are usually easily localized intraoperatively without requiring previously tattooing. Three quadrant submucosal injections of ink just distal to the tumor improve the success of localization. Some tumors may not be readily visible at the time of surgery due to tattoos hidden by mesentery or omentum or due to technical failure by injecting ink intramucosally or intraperitoneally. Injecting into the submucosa in tangential fashion and raising a submucosal bleb maximizes efficacy. If the tumor is not confidently localized, intraoperative colonoscopy should be done prior to committing to a resection by ligating a vascular pedicle. Blind resection distal to the mid-ascending colon based on a colonoscopy report risks wrong-site surgery and should not be performed [5]. Once the tumor is localized it is helpful to mark the site with a clip or suture loop placed on an epiploic appendage to facilitate subsequent dissection and resection.

Beyond tumor localization, intraoperative colonoscopy is also useful in ascertaining adequate distal margin during proctectomy for rectal cancer prior to dividing the mesorectum and again prior to dividing the rectum with a stapler. In the case, the stapler is partially clamped at the anticipated transection point while the level is confirmed with a colonoscope.

Completion Colonoscopy During Colon Resection

If not previously performed (due to an obstructing tumor or stricture, for instance), complete colonoscopy can be performed intraoperatively to evaluate for synchronous lesions. The rationale is that more proximal, synchronous cancers were found in 3.5–6.7% of patients who had an incomplete index evaluation. While the detection rate for any type of polyp in the proximal, unevaluated colon can be as high as 24%, the true incidence is difficult to measure as 18–47% of patients never get a follow-up examination [6, 7]. Providers may choose not to perform intraoperative colonoscopy due to reimbursement issues, out of concern for traumatizing a fresh anastomosis or due to technical and resource-related factors. Intraoperative endoscopy may be particularly helpful in patients who would otherwise have a delay in undergoing a postoperative colonoscopy [8]. Intraoperative colonoscopy does not worsen outcomes of laparoscopic surgery and can be safely performed although it requires the ability to prep the colon in advance [2, 9]. Colonoscopy can also be performed during out-patient anorectal procedures depending on patient circumstances and the preferences of the surgeon.

Intraoperative Assessment of Left-Sided Anastomoses

Verifying the integrity of left-sided anastomoses is integral to colorectal surgery and can be performed by instilling a saline solution or by gas insufflation [10, 11]. A leak test with insufflation can be done using a bulb syringe, rigid proctoscope, or flexible sigmoidoscope while occluding the colon and submerging the anastomosis under saline. Riccardi et al. demonstrated that intraoperative leak testing does not increase the risk of postoperative anastomotic leak and that a positive leak test is a significant predictor of postoperative clinical leak [12].

Routinely performing the leak test with CO_2 flexible sigmoidoscopy has multiple advantages over other leak testing methods. First, the health and perfusion of the tissues around the anastomosis can be directly visualized and perfusion can be further assessed using Narrow Band Imaging (NBI), which accentuates mucosal capillary patterns (Fig. 17.3). In selected cases, endoscopic assessment of anastomotic perfusion with indocyanine green fluorescence angiography can also evaluate perfusion [13]. Second, if there is bleeding from the anastomosis, this can be discovered and controlled using a variety of endoscopic maneuvers. Third, if a leak is found, this method aids in critical decision-making allowing the surgeon to repair, revise, or divert the anastomosis.

Management of Postoperative Anastomotic Leak

When a colorectal anastomotic leak is diagnosed and surgical intervention is indicated, intraoperative colonoscopy plays a key role in decision-making as well as treatment. When anastomotic dehiscence is limited to a small area and the anastomosis is well perfused, proximal diversion along with washout is often successful. In contrast, if there is a large area of dehiscence or the anastomosis is ischemic, take-down of the anastomosis and end colostomy is usually required. When the anastomosis is otherwise healthy and there is a pinhole defect (Fig. 17.4), primary repair and transabdominal drainage with proximal diversion, if indicated, is reasonable. When the defect is larger and more dis-

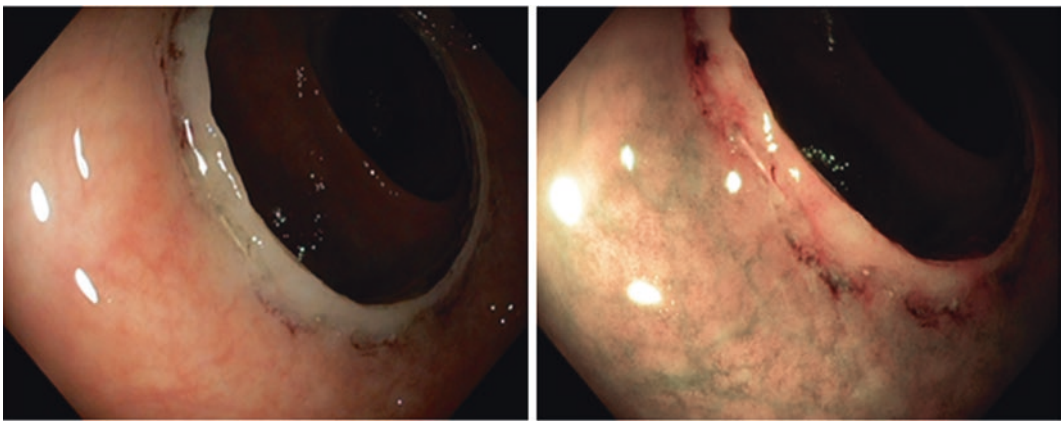

Fig. 17.3 Anastomosis visualized by white light and NBI

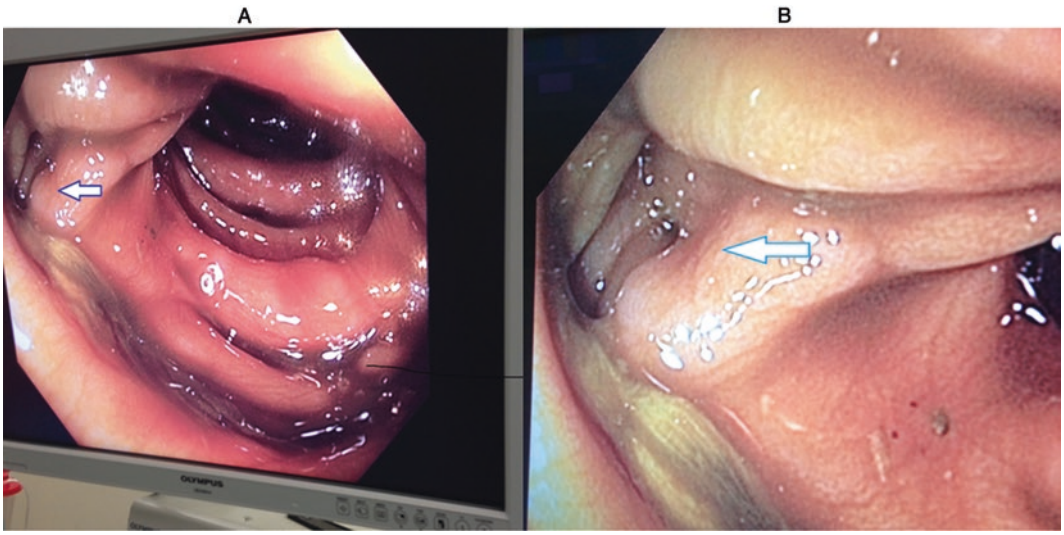

Fig. 17.4 Endoscopic image of salvageable anastomosis with pinhole defect. Whole view of anastomosis (**a**) and close-up view of the defect at the arrow (**b**)

tally located (Fig. 17.5), transanal drainage may be feasible under sigmoidoscopic guidance where the defect is visualized with a colonoscope while a transanal drain is placed into the abscess cavity. Once the drain is placed, it is secured and trimmed so that the end of the drain does not protrude out of anus. As the cavity collapses, the drain is repeatedly exchanged and down-sized until the abscess cavity resolves. In cases where the abscess cavity is well defined and the patient is stable (typically a late anastomotic leak), diversion is not usually required with transanal drainage.

Anastomotic Bleeding

Anastomotic bleeding typically occurs when the staple height is taller than the microvasculature at the level of the anastomosis. If identified intraoperatively, this problem can be addressed endoscopically. The incidence of anastomotic bleeding ranges from 0.6 to 9.6% of cases and is more common in stapled anastomoses rather than hand-sewn anastomoses [14–16]. The most common cause of anastomotic bleeding is thought to be catching the mesentery within the staple line [17]. As the majority of anastomotic bleeding is either self-limited or can be controlled endo-luminally, only a small percentage of patients (1.8%) require additional surgery or blood transfusion [18]. Electrocautery along a bleeding anastomosis should be done with caution, as it may result in anastomotic breakdown. Endoscopic clipping in this setting results in less collateral damage and is readily available. Early postoperative endoscopy to control anastomotic bleeding is safe and effective, with minimal risk of anastomotic complications [19].

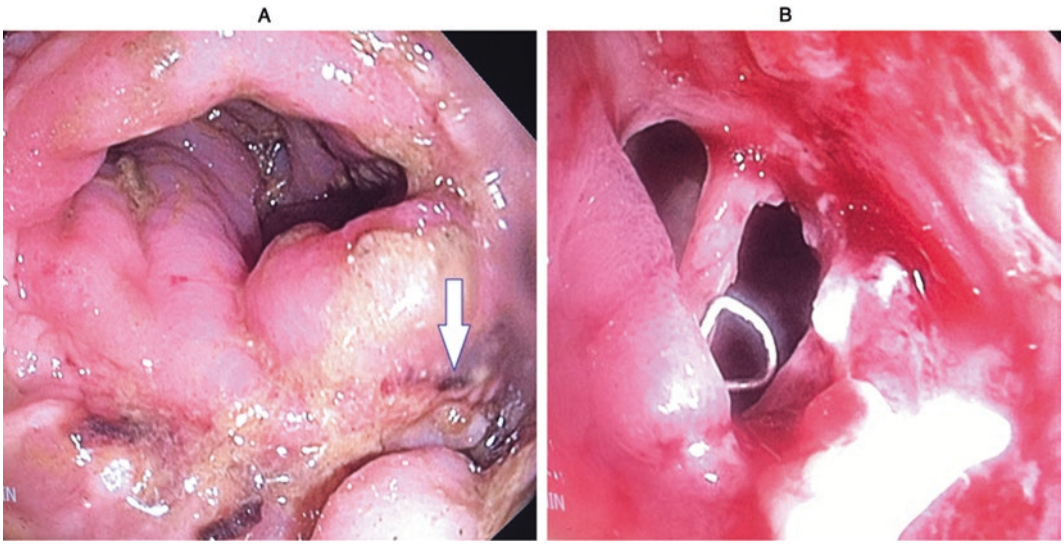

Fig. 17.5 Late anastomotic leak with abscess in stable patient

Pearls and Pitfalls

Intraoperative endoscopy can be a frustrating experience if you do not have the appropriate equipment and personnel. It is very helpful to have a dedicated technician in the operating room to assist with the equipment setup and troubleshoot during the procedure. Additionally, the potential equipment required (clips, injection needle, etc.) should be readily available. Prepackaging a standardized set of endoscopic tools can help ensure that the required equipment is readily available. If intraoperative endoscopy is planned, one must also gauge the anticipated technical difficulty of the procedure; completing an intraoperative colonoscopy to the cecum to localize a lesion for resection requires a different level of skill than testing and inspecting a left-sided anastomosis. Having a second surgeon available with the appropriate endoscopic skill set can be invaluable.

Conclusions

Endoscopy is a versatile tool that augments surgeons' ability to diagnose and manage patients win the operating room. With the correct equipment and a proficient skill set, surgeons should be able to routinely localize target lesions, perform on-table completion colonoscopy and left-sided anastomotic leak tests and control anastomotic bleeding. This experience will enable surgeons to utilize advanced endoscopic platforms to perform more complex intraoperative endoscopic procedure such as CELS and other novel therapeutic procedures like NOTES.

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Combined Endoscopic and Laparoscopic Surgery (CELS)

18

Kelly A. Garrett and Sang W. Lee

Key Points

- During preoperative evaluation, it is important to ensure that the polyp in question is likely to be benign. Surgeons should consider reviewing the pathology slides with pathologists at their own institution. The colonoscopy report as well as the pictures should be reviewed closely.
- It is important to perform colonoscopy in the operating room prior to laparoscopic port placement as the polyp may be amenable to colonoscopic polypectomy.
- CELS technique can be technically demanding, and the surgeon must be proficient in both laparoscopic and endoscopic techniques. For the first several cases, it is useful to have an assistant that is proficient in both of these techniques.
- During the CELS procedure, it is important to recognize the signs of a potential malignancy and to proceed with laparoscopic colectomy if there is suspicion for malignancy.
- Short-interval follow-up colonoscopy should be performed on these patients postoperatively.

Introduction

Large colon polyps and those on or behind a haustral fold can be very challenging to remove endoscopically. Although endoscopic mucosal resection (EMR) and submucosal dissection (ESD) have been performed for these polyps, these techniques are not widely available and do not provide a solution for certain polyps [1, 2]. The most common recommendation for patients who cannot have their polyp removed through endoscopic means has traditionally been segmental colectomy. Many studies demonstrate that laparoscopic colectomy has quicker recovery rates, faster return of bowel function, and earlier return to normal activities in comparison with open colectomy. However, while the laparoscopic approach can minimize the morbidity associated with colectomy, only a minority of the colon resections performed in the United States are being performed laparoscopically [3]. Furthermore, even if a minimally invasive approach is employed, it still entails a major abdominal operation with the potential for associated morbidities. In place of resection, combined endoscopic and laparoscopic surgery (CELS) removal of polyps has been described as an alternative in select patients [3–10].

The technique of laparoscopic-assisted polypectomy was first described in 1993 as a means to avoid the morbidities associated with a major bowel resection [4]. Larger retrospective studies have since been published indicating that the technique is safe and effective [3, 6, 7, 10–12]. The benefits of CELS include mobilization of the colon to make the polyp easier to resect with the colonoscope, the ability to directly observe the wall of the colon laparoscopically to ensure there is not a full-thickness defect, the capacity to repair an injury if there is one, and the option of converting directly to a laparoscopic resection if the polyp cannot be resected endoscopically or there are findings suspicious for malignancy. Many different techniques and approaches have been described including laparoscopic-assisted colonoscopic resection, endoscopic-assisted laparoscopic wedge resection and

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endoscopic-assisted laparoscopic resection [13–15]. The largest study to date was performed by Franklin et al., which included long-term follow-up of 160 patients with 209 polyps. At a median follow-up of 65 months (range 6–196 months), there were no recurrences of completely resected polyps [16].

Indications

Current indications for CELS include large benign colon polyps or polyps in a difficult anatomic location that are unable to be removed using standard colonoscopy techniques. In addition, a polyp that has been incompletely removed colonoscopically may be considered for CELS. Patients should have a benign preoperative colonoscopic biopsy that can include high-grade dysplasia. If patients have other polyps, they should be able to be removed colonoscopically or with CELS techniques. Generally, CELS should not be performed on patients with a known polyposis syndrome. Finally, relative contraindications for CELS would include a history of multiple previous abdominal surgeries or polyps that are too close to the ileocecal valve.

Preoperative Planning

A complete history and physical examination should be performed including past medical and surgical history. If the patient has a history of multiple abdominal operations, then CELS may not be technically feasible. It is important to obtain both the colonoscopy and pathology reports, and, frequently, the pathology slides themselves for internal review. For left-sided polyps, it is often useful to evaluate the area in the office with a flexible sigmoidoscope to determine the exact location, polyp characteristics, and feasibility of CELS.

Patients should undergo a preoperative workup as they would for any other abdominal procedure including blood work, electrocardiogram, and chest X-ray. Patients should receive a full mechanical bowel preparation the day prior to the procedure in order to aid in visualization of the polyp. When discussing the procedure, patients should be informed that if the polyp cannot be resected endoscopically or if there are findings suspicious for malignancy, laparoscopic colectomy will be performed at that point. In addition, patients should be made aware that even if CELS is successful in completely removing the polyp, it is possible that the final pathology may reveal a malignancy that may require colectomy at a later date.

Procedure

Setup

After activating lower extremity compression devices and inducting general anesthesia, a gastric tube and Foley catheter are placed. The patient is positioned in modified lithotomy, ensuring the legs are abducted using padded stirrups to facilitate the insertion and manipulation of the colonoscope during the operation. Both arms are tucked and the hands and wrists are padded. All equipment should be readily available to perform colonoscopic polypectomy as well as laparoscopic and open colectomy, as needed (Table 18.1). Subcutaneous heparin and intravenous antibiotics are given prior to incision, per usual.

Laparoscopic monitors will be placed depending on the location of the lesion. For right colon polyps, monitors are placed on the patient's right side and toward the head of the bed. (Fig. 18.1) For left colon lesions, the monitors are placed at the patient's left and toward the foot of the bed. For transverse colon or flexure lesions, the monitors are placed at the head of the bed as the endoscopist will stand between the patient's legs.

Endoscopic equipment may vary. Surgeons may prefer to use a pediatric or an adult colonoscope. In addition, we feel it is a prerequisite to use CO_2 colonoscopy in the operating room. Simultaneous laparoscopy and colonoscopy with room air present technical challenges that can jeopardize the ability to perform CELS. Colonoscopy insufflation using room air can significantly obscure the laparoscopic view and compromise exposure. In institutions where CO_2 is not be

Table 18.1 Equipment needed for CELS

Adult or pediatric colonoscope with monitor (CO_2 insufflation if available)
Methylene blue diluted with albumin
Endoscopic injector needle
Endoscopic snare
Endoscopic Roth net (US Endoscopy, Mentor, OH)
Suction trap
Bovie cautery
Laparoscopic monitors
High definition flexible tip laparoscope
Trocars: 5 mm × 4, 10 mm × 1, 12 mm × 1
Laparoscopic bowel graspers and scissors
Laparoscopic needle driver
Laparoscopic energy device (surgeon preference)
Micro-laparoscopic (3 mm) instruments if available
Laparoscopic linear stapler with appropriate loads
Endo-Catch bag (Covidien, Norwalk, CT)
Wound protector
Polysorb or vicryl sutures

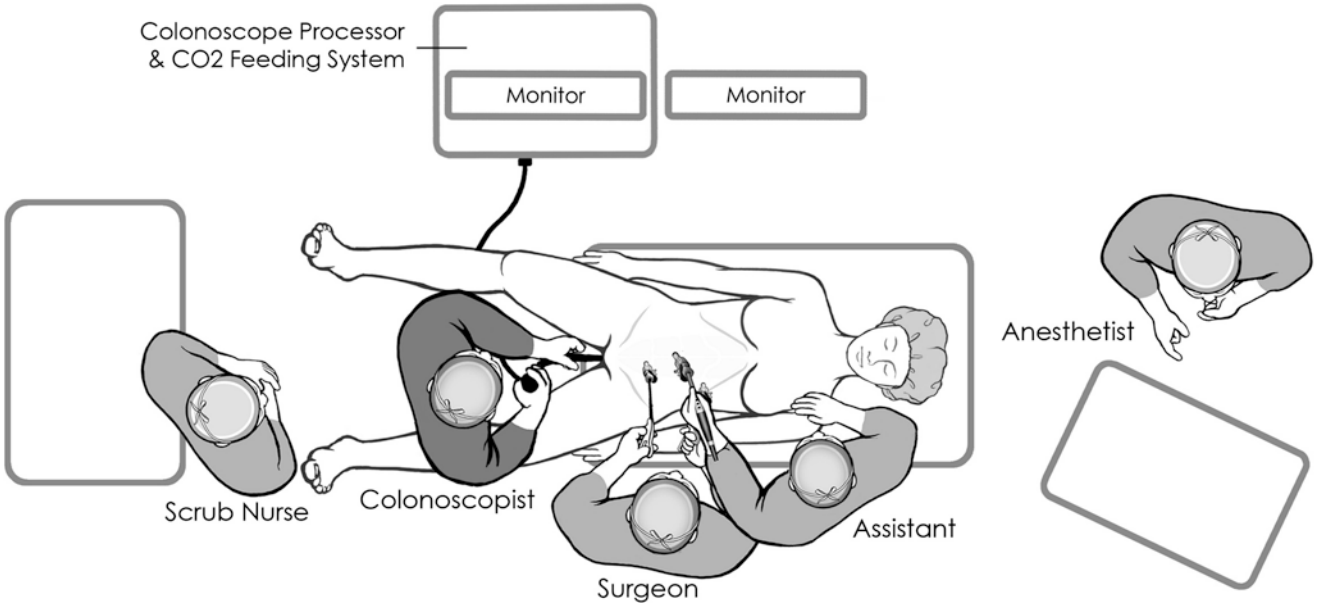

Fig. 18.1 Suggested trocar and monitor placement for CELS technique for excision of a right colon polyp

available for endoscopy, a technique of laparoscopically clamping the terminal ileum to minimize small bowel distention during laparoscopy has been described, but we have found that the colonic distension is still a major impediment to CELS [3, 4]. Since 2003, our group has been performing colonoscopy with the use of CO_2 insufflation during laparoscopy. Because the bowel absorbs CO_2 gas approximately 150 times faster than room air, there is minimal unwanted dilation of the colon and excellent simultaneous endoscopic and laparoscopic visualization. We have previously demonstrated that intraoperative CO_2 colonoscopy is safe during laparoscopy and can be used to avoid excessive bowel dilation during CELS procedures [9, 17]. Therefore, if available, it is preferred to have CO_2 for insufflation during colonoscopy.

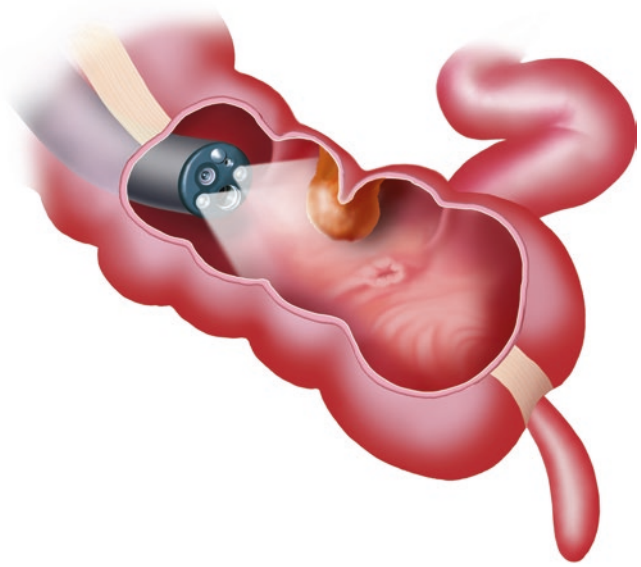

Fig. 18.2 Endoscopic visualization of a right colon polyp

Procedure Steps (Videos 18.1 and 18.2)

Endoscopy

- After the abdomen is prepped and draped in a sterile fashion, CO_2 colonoscopy is performed to locate the lesion (Fig. 18.2). We then use a mixture of 10 cm^3 of 1% methylene blue mixed in 100 cm^3 of 25% albumin to mark the location of the polyp. Submucosal injection is performed under the polyp in order to raise it up.
- If the polyp seems amenable to endoscopic removal alone, then this may be attempted at this point prior to port placement. If patient history suggests that there may be adhesions or a fixed loop of colon that previously prevented endoscopic excision, then pure snare polypectomy may not be feasible.

Port Placement

- *Initial access:* A periumbilical 5 mm port is placed, per usual, and pneumoperitoneum is established. A 5 mm,

high definition flexible tip laparoscope is preferred for enhanced visualization. The abdomen is explored and the polyp is localized using the previously placed tattoo.

- *Secondary trocars:* Depending on the location of the lesion, typically two 5 mm trocars may be placed. For right colon lesions, trocars can be placed in the left lower quadrant and suprapubically. For left colon lesions, trocars can be placed in the right lower quadrant, and suprapubically. For transverse colon lesions, trocars can be placed bilaterally in both the lower and upper quadrants. If available, micro-laparoscopic (3 mm) instruments are used.
- *Optional trocars:* A 12 mm port may be needed for a stapler if a colonoscopic-assisted laparoscopic wall excision is anticipated.

Mobilization

- For laparoscopic-assisted colonoscopic polypectomy, the lesion is located by the endoscopist and its position is confirmed by laparoscopic visualization with the use of transillumination and/or by endoscopic visualization during laparoscopic manipulation of the colon (Fig. 18.3). This maneuver can also expose mucosal areas that were not previously visualized because of folds or segmental kinks of the colon. Appreciating the location of the polyp in relation to the peritoneum is important. Polyps located on the retroperitoneal side or mesenteric side requires mobilization of the colon for adequate exposure.
- If the polyp is in a difficult location (i.e., at a flexure or near the mesenteric border of the colon) and this area cannot be manipulated, the colon will need to be mobilized as in any laparoscopic colectomy procedure. We prefer to use an energy device along the Line of Toldt and the embryonic tissue planes. Once the colon is mobilized adequately, the area of the polyp can then be manipulated.

Polypectomy

- As stated previously, the polyp is lifted with a mixture of methylene blue and albumin. This aids in visualizing the polyp in comparison to the normal surrounding mucosa and also aids in seeing the location of the polyp laparoscopically. It also provides a "buffer" zone to facilitate endoscopic resection without causing a full-thickness injury.
- If the polyp does not lift due to scarring from previous biopsy, either resection or full-thickness CELS can be considered. The possibility of malignancy also needs to be considered in this situation.
- Polypectomy is performed using an electrosurgical snare. This can be done using a single pass or in piecemeal fashion. For polyps that are either flat or are situated in tough location, laparoscopic manipulation of the polyp during snare polypectomy can facilitate delivery of the polyp into the snare (Fig. 18.4).
- During polypectomy, the serosal aspect of the colon should be monitored closely laparoscopically. If there is any subtle change to the area, this can be immediately recognized and then over sewn, if needed (Fig. 18.5). Full-thickness thermal injury or perforation is addressed with suture repair and imbrication. If there is some evidence of blanching or deterioration of muscle layers, the area can also be reinforced to avoid the evolution of partial-thickness to full-thickness injury and perforation in the postoperative period. The ability to laparoscopically repair potential damage allows for a more aggressive polypectomy.

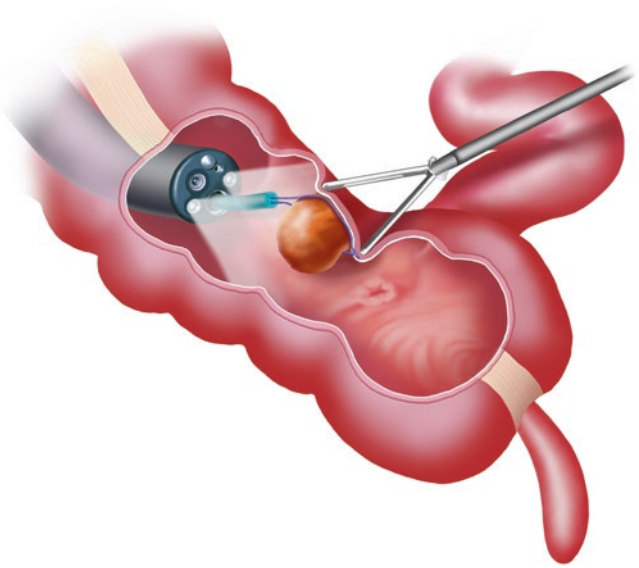

Fig. 18.3 Endoscopic visualization of a colon polyp with simultaneous laparoscopic manipulation of the colon wall

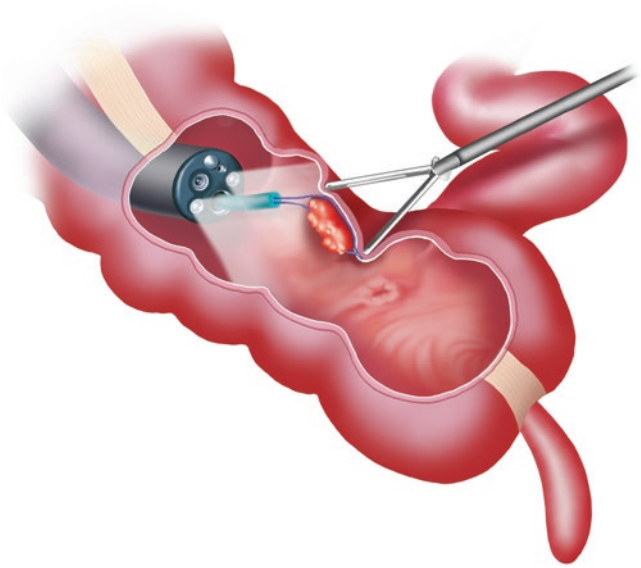

Fig. 18.4 Laparoscopic manipulation of the polyp during a snare polypectomy with laparoscopic delivery of the polyp into the snare

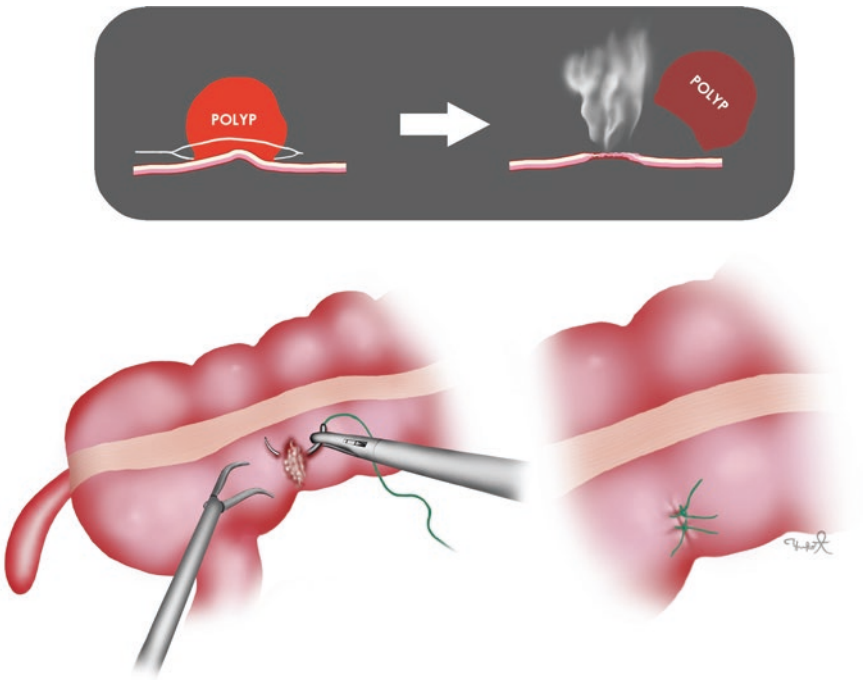

Fig. 18.5 Suture reinforcement of the colon in an area of partial-thickness injury

Colonoscopic-Assisted Laparoscopic Wall Excision

- For polyps that are located in the cecum where the wall of the colon is thinnest, laparoscopic sleeve excision may be indicated.
- Colonoscopy is used to locate the lesion and monitor adequate surgical margins. Polyp location in relation to the ileocecal valve should be noted in order to avoid injury to this structure.
- Sleeve resection is performed using a laparoscopic linear stapler through a 12 mm port (Fig. 18.6). The specimen can be placed within an Endo-Catch bag (Covidien, Norwalk, CT) and brought out through the 12 mm port site. The specimen can be evaluated in the operating room to confirm clear margins.
- Oversewing of the staple line can be performed laparoscopically as needed.

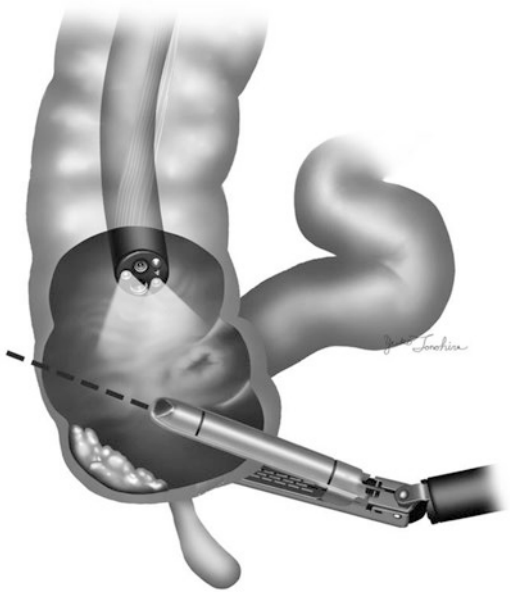

Fig. 18.6 Sleeve resection of a polyp in the cecum using a laparoscopic linear stapler

Full-Thickness CELS Technique

- CELS technique may not be effective when dealing with serrated adenomas or polyps that were scarred from previous biopsies.
- Full-thickness CELS is an extension of CELS that uses standard endoscopic and laparoscopic instruments and techniques. It offers a greater degree of polyp manipulation, enables a full-thickness colon wall resection, and further minimizes the need for colectomy for benign polyps.
- The polyp is lifted using a submucosal injection as described previously. It is critical to the raise the entire circumference of the polyp away from the submucosa (Fig. 18.7). The margins of the polyp are marked in the serosal surface of the colon laparoscopically by using a mono-polar instrument. A laparoscopic hook cautery and/

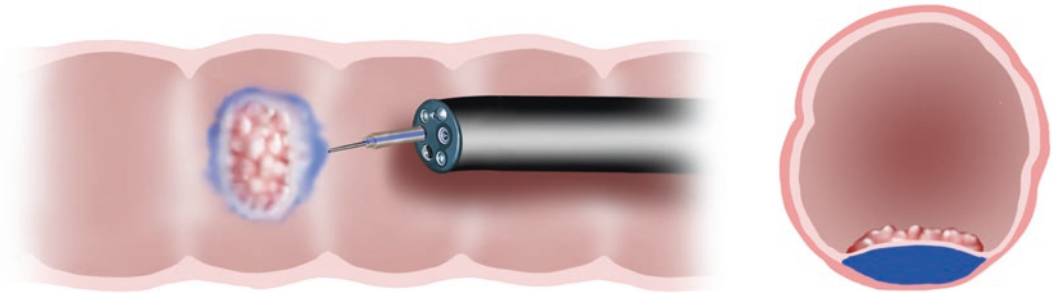

Fig. 18.7 Submucosal injection to lift the mucosa around the polyp away from the muscularis

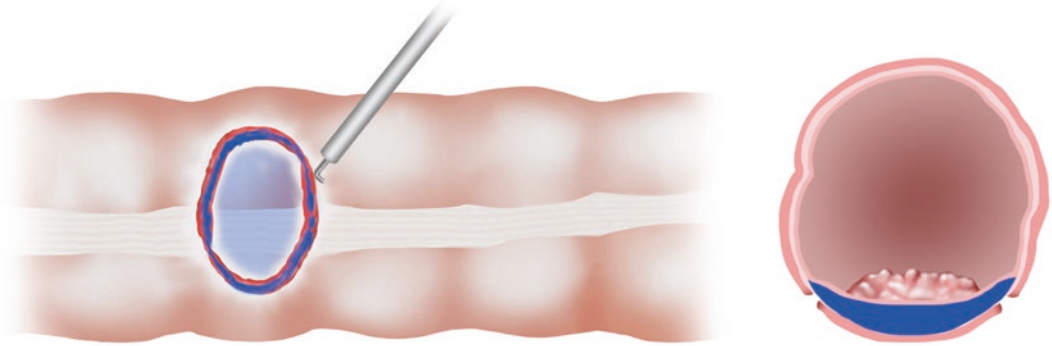

Fig. 18.8 Circumferential dissection of the muscular layer from the serosal side laparoscopically

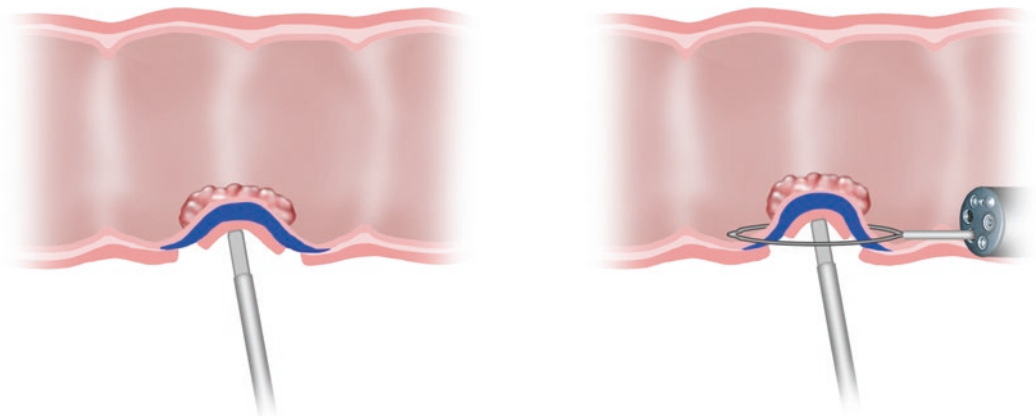

Fig. 18.9 Endoscopic snare is placed around the full thickness of the colon

or scissors are used to create a defect in the seromuscular layer circumferentially along the serosal markings (Fig. 18.8). Care is taken not to enter the mucosa and cause a full-thickness injury.

- Once the muscularis of the colon wall around the polyp is completely disconnected, the dissected area is invaginated into the bowel lumen with a laparoscopic instrument such as a laparoscopic bowel grasper. At this stage, the polyp will become more obvious on the endoscopic monitor. A snare is introduced and looped around the ideally presented full thickness of the colon wall containing the polyp and is cinched down without cutting through (Fig. 18.9).
- The serosal surface is now examined and a pre-excision laparoscopic closure is performed with a running 3-0 absorbable suture repairing the colon defect (Fig. 18.10).

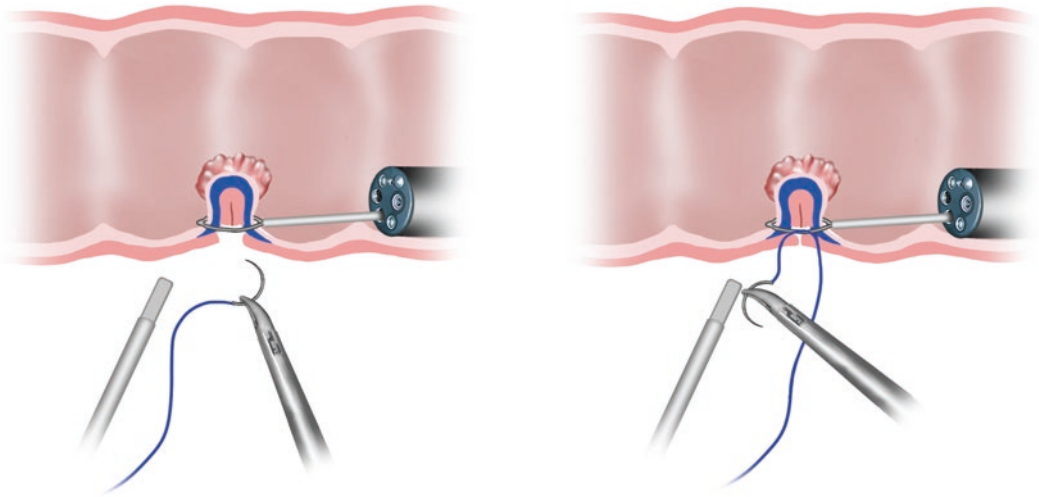

Fig. 18.10 Laparoscopic repair of the colon wall around the specimen

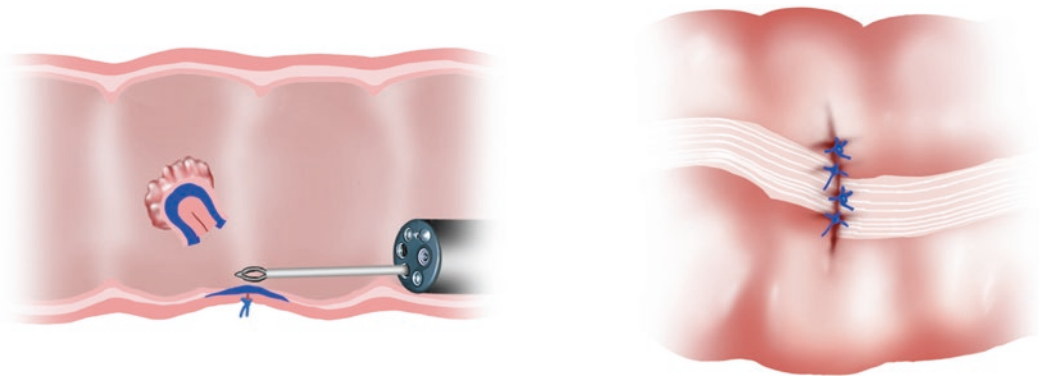

Fig. 18.11 Energy is then applied to the snare and the colon wall containing the polyp is amputated

- Energy is then applied to the snare and the polyp is amputated (Fig. 18.11). The full thickness of the colon wall containing the polyp is removed using an endoscopic Roth net (US Endoscopy, Mentor, OH) and the resection site is carefully examined by endoscopy and laparoscopy.

Leak Test

- A leak test using CO_2 insufflation through the colonoscope and immersion of the bowel segment under saline (using gravity to make the correct area dependent) should be performed.

Polyp Retrieval

- For polyp retrieval, an endoscopic Roth net (US Endoscopy, Mentor, OH) can be used if the polyp is resected en bloc. For polyps that are resected piecemeal, a trap can be added to the suction device and the polyp can be suctioned through the scope.

Postoperative Care

Patients, who undergo standard snare polypectomy without any concerns intraoperatively, may have a very short hospital stay and may even go home the same day as the procedure. Most groups report lengths of stay between 1 and 2 days although some large studies report a mean length of stay of 4–8 days [9, 12, 16]. Patients who have a partial or full-thickness injury or undergo colonoscopic-assisted laparoscopic wall excision are monitored in the hospital as they await return of bowel function. These patients should be admitted to the hospital and treated like any patient who had a laparoscopic abdominal procedure. Patients usually follow

up within 2 weeks to review the final pathology and determine if additional treatment is needed.

Complications

Intraoperative complications can be related to the endoscopic portion of the procedure or to laparoscopic port placement and mobilization.

In a retrospective study of over 80,000 colonoscopies, the risk of perforation for all comers was less than 1% [18]. The benefit of the laparoscopic and endoscopic combined approach is that any full-thickness injury to the colon from electrocautery, barotrauma, or scope trauma can be immediately recognized and repaired. Franklin et al. reported a 10% rate of serosal suture placement [16]. Our group reported a higher rate of 43%; however, none of these patients had a full-thickness injury. These patients underwent serosal repair due to concerns that the wall appeared to have a partial-thickness injury that could easily be addressed at the time [9]. The other benefit of doing a concomitant colonoscopy is that a leak test can be performed to assess the site of injury and repair.

The risk of laparoscopic complications should be similar to any other laparoscopic abdominal procedure and potentially even less if no mobilization of the colon is required. There is risk of abdominal wall and intra-abdominal injury with port placement, bowel injury related to grasper trauma, or the use of an energy device and injury to surrounding viscera such as the bowel, ureter, or the gonadal or iliac vessels.

For patients that undergo a successful CELS procedure, postoperative morbidity is low. Franklin reported a 9% postoperative complication rate, with all complications being minor and mostly consisting of ileus, atelectasis, and seroma [16]. Our group reported an overall rate of 4.2%, with postoperative complications including urinary retention and wound hematoma [7].

Outcomes

There are few large studies that report on the combined approach of laparoscopy and colonoscopy for polyp removal. The longest follow-up for these patients is a median of 65 months and was reported by both our group and Franklin's group [7, 16]. Overall, the long-term outcome of patients undergoing CELS is excellent. For patients with benign polyps that are successfully resected with a CELS technique, there are variable recurrence rates in the literature. Our group reported a recurrence in five patients (10%). Four of these patients underwent a repeat colonoscopic polypectomy and one patient had a subsequent laparoscopic segmental colectomy and all patients had benign pathology [7]. Franklin's group reported no recurrences over a median follow-up of 65 months, but three patients were reoperated for polyps in different locations [16].

There is concern that CELS patients who are ultimately diagnosed with cancer on final pathology may have potential risks associated with perforated cancer. However, in patients with cancer on final pathology who have then gone on to have formal resection there have been no reports of local tumor recurrence [16].

Pearls and Pitfalls

- In the preoperative workup of patients with apparently benign polyps, the CELS surgeon should be aware that there can be discordance among pathologists. Depending on the circumstances, it may be helpful to have pathology slides reviewed by pathologists at your own institution. In addition, the colonoscopy report should be reviewed, as well as pictures of the polyp, to determine if the polyp is suitable for CELS.
- It is important to perform colonoscopy in the operating room prior to placing laparoscopic ports. On occasion, a polyp, previously deemed unresectable by a referring physician, may actually be amenable to traditional colonoscopic polypectomy.
- This combined technique can be technically demanding and the surgeon must be proficient in both laparoscopic and endoscopic techniques. For the first several CELS cases, it is useful to have an assistant that is proficient in both of these techniques.
- During CELS, it is important to recognize the signs of a potential occult malignancy. Polyps that have been biopsied or previously snared are often scarred and difficult to lift with submucosal injection. These findings must be contrasted with characteristics of a possible cancerous polyp like central umbilication, ulceration, vascular pattern detected on narrow band imaging, and firmness. If these findings are present, the surgeon can continue with CELS and perform an intraoperative frozen section or can proceed with formal colectomy. We do not feel it is necessary to perform frozen section on all polyps resected via CELS as this can add to the operative time and cost of the case. In our experience, the rate of cancer in polyps that were thought to be benign was only 2% (1/48). Therefore, frozen section should only be done on patients with a suspicion of malignancy. In our experience, 12 patients underwent colectomy instead of CELS for suspected malignancy and only four (33%) of these patients actually had cancer [7]. Although this demonstrates a low sensitivity, it reflects our overly cautious attempts to avoid performing CELS for potential malignancy.

- Short-interval follow-up colonoscopy should be performed on patients after CELS and is typically recommended at 3 months. In the long-term follow-up of our CELS patients, five patients (10%) had recurrent polyps. Four of these patients underwent colonoscopic polypectomy and one patient underwent laparoscopic segmental colectomy. All of these patients had benign pathologies [7].

Conclusion

Combined endo-laparoscopic surgery (CELS) appears to be safe and effective for the treatment of benign colon polyps and may help to avoid laparoscopic colectomy in most cases.

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Endoluminal Colorectal Stenting

19

Zoltan Lackberg and Maher A. Abbas

Key Points

- Self-expanding metal stents (SEMS) are effective in relieving malignant colonic obstruction.
- Colonic stenting may be used as palliation or a bridge to surgery.
- The oncologic safety of SEMS remains uncertain.
- The most common complications of colonic stenting include perforation and occlusion.
- Use of SEMS for benign colonic obstruction remains controversial.
- Biodegradable stents and drug-eluting stents are under development.

Introduction

There is a 80% incidence of colonic obstructions due to colorectal malignancy and 25% of patients with colorectal cancer present with acute large bowel obstruction, which, in many cases, poses a surgical emergency. Patients presenting with acute malignant colonic obstruction have a 5-year survival rate of less than 20%, which is considerably less than patients presenting without obstruction. Without expeditious decompression of the obstruction, patients can suffer serious complications such as intestinal ischemia and perforation. Emergency colectomy is technically challenging and is associated with a mortality rate as high as 15–20% and a morbidity rate as high as 40–50%.

Emergency surgery for colonic obstruction often requires a multistage procedure with resection, anastomosis, and proximal diversion or resection with end stoma formation followed by stoma reversal. Occasionally, a three-stage approach is used. In cases of left-sided colonic obstruction, the surgical approach is decided by unique patient factors, intraoperative consideration, and surgeon preference. Right-sided colon obstruction can often be managed with resection with primary anastomosis with or without diverting ileostomy. Due to multiple factors, stomas become permanent in more than 40% of patients.

Colonic stenting has become an important alternative treatment for colonic obstruction that can be palliative or a bridge to future surgical intervention. Dohomoto described the procedure in 1991 as a palliative method to relieve obstruction and avoid stoma formation [1]. Tejero et al. first reported the use of self-expanding metal stents (SEMS) as "bridge-to-surgery" to allow bowel decompression prior to a single-stage surgical procedure [2]. Stent decompression of an acute colonic obstruction allows for medical optimization of the patient, proper tumor staging with imaging, and identification of synchronous lesions. In patients with rectal cancer, stenting allows relief of the obstruction and provides the opportunity to administer neoadjuvant chemoradiotherapy prior to surgical treatment.

Colonic stenting for acute colonic obstruction is not without risks with several potential adverse complications like perforation, occlusion, and migration. Furthermore, a major concern regarding long-term survival of patients whose disease is potentially curable is the risk of tumor seeding if perforation occurs during or after stent placement. Additional limitations of endoluminal stents include their limited efficacy in some patients, tumor regrowth, and technical difficulties with placement.

Despite the above limitations and concerns, the use of endoluminal stents continues to grow. Numerous contemporary publications have confirmed the safe and effective use

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of colonic stents and the introduction of new stent technologies. A recent Cochrane review by Sagar compared colonic stenting to emergency surgery in patients with malignant colorectal obstruction [3]. In this meta-analysis, the clinical success rate was statistically higher in the emergency surgery group, but the use of colorectal stents was safe and had advantages of shorter hospital stay, shorter procedure time, and less blood loss.

Stenting Malignant Colonic Strictures

While the majority of malignant colonic strictures are due to a primary colorectal cancer causing intrinsic obstruction, (Video 19.1) extrinsic compression from a non-colorectal malignancy can also occur. Etiologies of extra-colonic lesions include gynecologic cancers, upper gastrointestinal malignancies, and, in rare cases, metastatic lesions such as from breast cancer. It is important to consider that the majority of patients with extrinsic obstruction have incurable disease.

Most of the experience with endoscopic stenting has been gathered from data related to left-sided colorectal malignancy. Stenting of right-sided lesions is feasible although most patients with proximal obstructions can be managed by one-stage surgical resection without bowel preparation or stoma formation. Several studies have shown that SEMS is a reasonable therapeutic option for proximal colonic obstruction with success rates comparable to those seen with distal colonic stenting. Notably, a few studies have reported conflicting results with lower technical success rates. Surgical intervention is currently considered as the treatment of choice for obstructing right-sided colon cancer; however, SEMS placement is an alternative option for elderly and patients with significant comorbidities (Fig. 19.1).

Stenting with Palliative Intent

Patients with acute colonic obstruction and synchronous metastatic disease pose specific challenges. Such patients often present in a debilitated state and have a limited life expectancy. While surgical intervention can be undertaken under such circumstances, less invasive treatment can be beneficial in this group of patients (Table 19.1). Lee and colleagues reviewed their experience with SEMS and found clinical success comparable to surgical intervention; however, SEMS was associated with fewer complications compared to palliative surgery [4]. Despite improved short-term morbidity and mortality, a shorter hospital stay, avoiding stoma formation, and better quality of life, several studies have shown no long-term survival advantage in patients

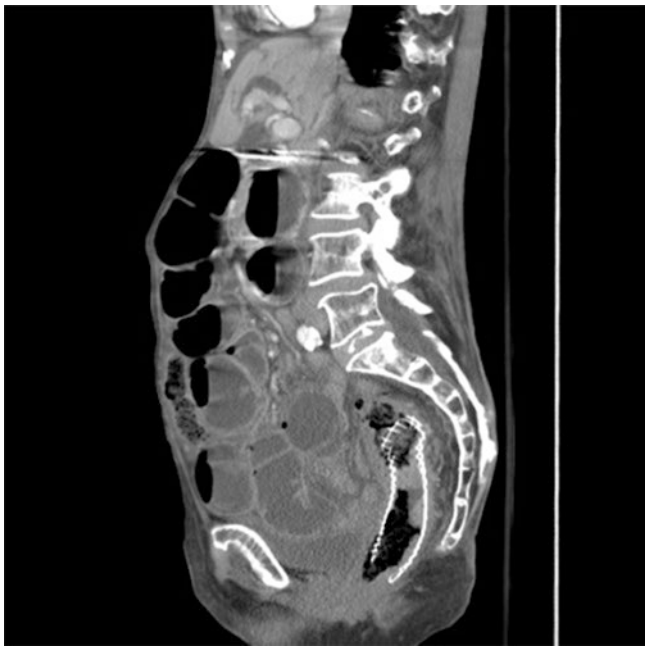

Fig. 19.1 Rectal stent in a 97-year-old woman

treated with SEMS compared to those treated surgically. It is important to note that one study by Súarez et al. reported a significant survival advantage in patients with incurable colorectal cancer treated with SEMS [5].

Colon perforation, a well-known complication of stenting, also occurs in a minority of patients who receive chemotherapy, especially bevacizumab-based chemotherapy. For this reason, stent placement in patients who will undergo palliative chemotherapy remains controversial and patients should be counseled regarding the potential risk of perforation.

Despite the short-term advantages of SEMS, the long-term benefits of SEMS for palliation have not been well established. Lee et al. compared the long-term outcomes of SEMS placement with those of palliative surgery and documented that the patency of the first stent and duration of decompression was shorter but that decompression after a second stent was comparable with surgery [4]. In another study by Small et al., 24.4% of patients decompressed with SEMS experienced long-term complications such as perforation, occlusion, and migration [6]. Fernández-Esparrach et al. showed a long-term clinical failure rate of 51%, with a mean stent patency duration of only 145 days [7].

SEMS in patients with incurable colorectal cancer can improve quality of life with a relatively low risk for early complications and should be considered in patients with limited life expectancy (Table 19.2). However, surgical intervention should be considered in patients who are better operative candidates, who have longer life expectancy, and who are candidates for chemotherapy.

Table 19.1 Technical and clinical success rates after endoscopic colonic stent placement

Author	Year	Country	*N*	Technical success (%)	Clinical success (%)
Khot et al. [28]	2002	UK	598	92	95
Sebastian et al. [27]	2004	International	1198	94	91
Tilney et al [9]	2007	International	451	92.6	
Tominaga et al. [33]	2012	Japan	24	100	83
Kim et al. [11]	2014	Korea	68	97.1	88.2
Gürbulak et al. [31]	2015	Turkey	82	93.9	90.9
Boyle et al. [32]	2015	UK	126	86	70
Bayraktar et al. [34]	2015	Turkey	49	95.9	100

Table 19.2 Overall survival (days) after palliative stenting for obstructing colon cancer

Author	Year	Country	*N*	Median survival
Camunez et al. [35]	2000	Spain	35	103
Lee et al. [36]	2010	USA	46	106
Suh et al. [37]	2010	Korea	55	211
Mackay et al. [38]	2011	UK	71	103

Stenting as "Bridge-to-Surgery"

Endoluminal colonic stenting as "bridge-to-surgery" can be considered in patients with potentially curable colorectal malignancy. Up to 30% of patients with colorectal cancer present with acute colonic obstruction, which would otherwise require surgery. Emergency decompressive surgery carries significant risks of morbidity (30–60%) and mortality (15–35%).

The technical success rate of SEMS with "bridge-to-surgery" intent has been reported between 46.7 and 100% with a clinical success rate ranging from 40 to 100% (Table 19.3). For obstructed patients without proper cancer staging and in the setting of malnutrition, SEMS is an attractive option. Endoluminal decompression with a stent also allows for preoperative medical evaluation and optimization. Emergency decompression with SEMS can also allow for bowel preparation and increases the likelihood of single-stage elective resection. A systematic review by Brehant et al. comparing emergency surgery with SEMS insertion as a bridge to surgery showed a higher primary anastomosis rate, shorter hospital stay, and a lower colostomy rate in the SEMS group [8]. Another meta-analysis by Tilney et al. comparing colorectal stenting with surgery showed similar results with fewer medical complications in the bridge-to-surgery group [9]. Similarly, Tan and colleagues reviewed controlled and randomized trials and reported a higher primary anastomosis rate and lower stoma formation rate in patients undergoing SEMS [10]. However, the permanent stoma rate, morbidity and mortality rates were not significantly different between patients undergoing SEMS compared to those treated surgically.

The possible impact of SEMS on oncologic outcome has been questioned in several studies where the long-term oncologic outcome of stent insertion as a bridge to surgery was associated with a higher recurrence rate compared to emergency resection. In a study by Kim et al., multiple stent insertions were identified as a risk factor for subsequent surgical failure [11]. Perhaps most concerning, stent perforation can lead to peritoneal tumor seeding that upstages the patient and changes a potentially curable situation into an incurable one, as shown in several studies.

While the overall survival rates in several studies did not show significant differences between groups of patients treated with stenting or surgery, the recent guidelines by the European Society of Gastrointestinal Endoscopy do not recommend the use of metallic stents as bridge to surgery because of concerns about oncological safety [12]. This recommendation was endorsed by the Governing Board of the American Society for Gastrointestinal Endoscopy. Thus, emergency stenting in left-sided and potentially curable malignant obstruction can be considered as an alternative to emergency surgery in high-risk patients with increased risk of postoperative mortality. In right-sided colonic obstruction, resection with a primary anastomosis without the need for a diverting stoma is usually possible. Emergency surgery is preferable instead of stent insertion as a bridge to surgery in such subgroup of patients.

The optimal timing for surgical intervention following SEMS depends on several patient factors like the degree or

Table 19.3 Comparison of metallic stent as bridge-to-surgery versus emergency surgery in acute malignant left colon obstruction

Author	Year	Country	*N*	Centers	Technical success (SEMS) (%)	Clinical success (SEMS) (%)	Primary anastomosis (SEMS vs. emergency surgery)	Anastomotic leakage (SEMS vs. emergency surgery)	Overall postoperative complications (SEMS vs. emergency surgery)	Hospital stay (Days)	Favorable outcomes
Cheung et al. [39]	2009	China	48	1	83.3	83.3	83.6% vs. 54%	0% vs. 8.3%	8.3% vs. 70.8%	13.5 vs. 14	SEMS
Van Hooft et al. [12]	2011	Netherlands	98	25	70.2	70.2	44.7% vs. 23.5%	10.6% vs. 1.9%	25% vs. 23%	NA	Emergency surgery
White et al. [40]	2011	Australia	56	1	96.7	90	100% vs. 13.8%	0% vs. 26.9%	6.6% vs. 23.1%	8.5 vs. 17.7	SEMS
Pirlet et al. [41]	2011	France	60	9	46.7	40	73.3% vs. 46.7%	6.6% vs. 6.6%	26.7% vs. 33.3%	23 vs. 17	Emergency surgery
Alcántara et al. [42]	2011	Spain	28	1	100	100	100% vs. 100%	5% vs. 30.7%	13.3% vs. 53.8%	13 vs. 10	SEMS
Guo et al. [43]	2011	China	92	1	91.2	91.2	79% vs. 47%	2.9% vs. 5.2%	Similar	19 vs. 14	SEMS
Ho et al. [44]	2012	Singapore	39	1	75	70	75% vs. 70%	5% vs. 0%	35% vs. 58%	14 vs. 13	SEMS

success of decompression and the need for medical optimization and cancer staging. A significant delay between stenting and surgery should be avoided as this can potentially increase the risk of stent-related complications. A study by Sirikurnpiboon et al. suggested that the optimal bridging time to surgery should be within 5 days and other studies recommend resection 5 to 10 days after stent insertion [13]. Patients with unique factors and patients with locally advanced rectal cancer who undergo neoadjuvant chemoradiation require a longer interval and surgery may be delayed for several weeks.

Stenting of Extrinsic Colonic Obstruction

Most cases of the colonic obstruction are due to intrinsic occlusion by colorectal malignancy, benign stenosis due to an inflammatory process such as diverticulitis or anastomotic stricture. However, extra-colonic conditions can also cause extrinsic compression resulting in obstruction. In such patients, SEMS may be considered as an alternative to surgical intervention; however, the technical success rate of stenting for colorectal obstruction due to extrinsic malignancy ranges from 42 to 100% with a reported clinical success rate of 25–87% [14, 15].

Luigiano et al. showed a lower patency rate in patients with extrinsic obstruction compared to intrinsic malignancy [16]. Trompetas et al. reported 12 stent procedures carried out in 11 patients with colonic obstruction from extra-colonic malignancy with technical and clinical success rates of 42 and 25%, respectively [17]. Importantly, in this study, the 30-day mortality was 36%, the colostomy formation rate was 45%, and the median survival rate was only 2 months. The clinical outcomes of stent placement in patients with extra-colonic causes of the colonic obstruction are less favorable compared to patients with intrinsic obstruction from colorectal cancer. Nonetheless, SEMS should be considered in such patients if technically feasible due to the limited life expectancy of patients with metastatic cancer causing extrinsic compression.

Stenting of Benign Colonic Strictures, Fistulas, and Anastomotic Complications

Most of the available data on the use of SEMS in the setting of benign colonic strictures is derived from case reports or case series. Etiologies of benign strictures include diverticulitis, strictures after pelvic abscesses, radiation-related strictures, inflammatory bowel disease strictures, and ischemia. Stenting has also been described for treating colonic fistulas and anastomotic complications.

A case series of benign colorectal strictures treated with SEMS by Small et al. demonstrated a technical success rate of 95% but the major complication rate was 38% and included stent migration, obstruction, and perforation [18]. Another case series by Keränen et al. reported outcome of SEMS used for anastomotic stricture, diverticular disease, and radiation-induced stricture and documented a clinical success rate of 76% with a 43% complication rate [15]. Most of the complications occurred in patients with diverticular disease. A retrospective review by Pommergaard et al. reported results of SEMS in both malignant and benign colonic obstructions [19]. In this study, the technical success rate was 97%, the complication rate was 21%, and the mortality rate was 2.6% in patients with malignant stricture while in the benign group, the technical success rate was 86%, complications occurred in 71% of patients, and the mortality rate was 28%.

Colovesical fistulas are most often treated surgically; however, in high-risk patients, the placement of a covered stent may provide symptomatic control. Ahmad et al. reported a case of colovesical fistula secondary to malignancy, which was successfully treated with SEMS [20]. Similarly, the technique of SEMS placement in patients with colovaginal fistula has been described.

Anastomotic leak and complications after colorectal resection are challenging clinical problems that often require reintervention and the potential need for diverting stoma formation. There is a paucity of data on the use of colonic stenting for such indications. Abbas first described the use of a covered stent in two patients with anastomotic complications [21]. More recently, Lamazza et al. reported the long-term results after stent placement in 22 patients with symptomatic anastomotic leak after colorectal resection [22]. The technical success rate was 100%, 15 patients (62%) required diverting ileostomy, and the anastomotic leak healed in 19 patients (86%). In two patients with recurrent rectovaginal fistula, stent placement controlled the symptoms of the leak allowing for a subsequent successful surgery with advancement flap and only one patient required a permanent stoma.

Stent Types

Modern colorectal stents such as SEMS are made of radiopaque, woven, uncovered metal mesh and have a cylindrical shape that result in self-expanding forces. There are two major SEMS delivery systems, through-the-scope stents (TTS) and over-the-wire stents (OTW). TTS stents are small enough to fit through the working channel of an adult endoscope and OTW stents are passed alongside the endoscope. After deployment, stents continue to expand and reach their

full expansion diameter within a couple of days. Stent specifications include length, diameter, and proximal flare. The most common lengths used vary from 8 to 11 cm, the most common diameters used are between 18 and 25 mm, and the maximum proximal flare is 30 mm. Partially covered or fully covered colonic stents are not currently available in the United States.

Metal Stents

The most widely used stents today are nitinol based, which is an alloy of nickel and titanium that has a characteristic shape memory and super-elasticity. This material is more flexible than stainless steel or other alloy-based stents. Elgiloy stents are made of an alloy of cobalt, chromium, and nickel, are magnetic resonance imaging (MRI) compatible. The wires can be made very thin, the stent has good elasticity and flexibility.

Biodegradable Stents

Recently, there has been increasing interest in developing biodegradable stents made of polymers and biodegradable metals (magnesium alloys). While these stents can be deployed to address luminal pathology and do not require resection or retrieval, existing data in this field remains limited. Rejchrt et al. published a series of three patients with Crohn's stricture treated with a biodegradable stent after balloon dilatation of the stenosis [23]. All three stents were successfully inserted, the mean time until stent degradation was 4 months, and no major complications were noted. Rodrigues et al. reported a case of a colonic Crohn's stricture which was not amenable to balloon dilation because of the extent of the stricture [24]. Complete stent degradation was confirmed by a plain abdominal radiograph 4 months later and no recurrence of obstructive symptoms occurred during a follow-up of 16 months.

While biodegradable polymer stents have been successfully employed in the treatment of esophageal benign and malignant strictures, perforations, and anastomotic leaks, the use of this type of stent in the lower gastrointestinal tract has been limited. A few case series have reported the outcomes of biodegradable stents in patients with postoperative colonic strictures and fistulas with promising preliminary results with clinical success in up to 50% of patients and stent migration rates of 0–30%. The development of biodegradable stents is still in its infancy and stents with improved designs and reduced migration are expected in the future.

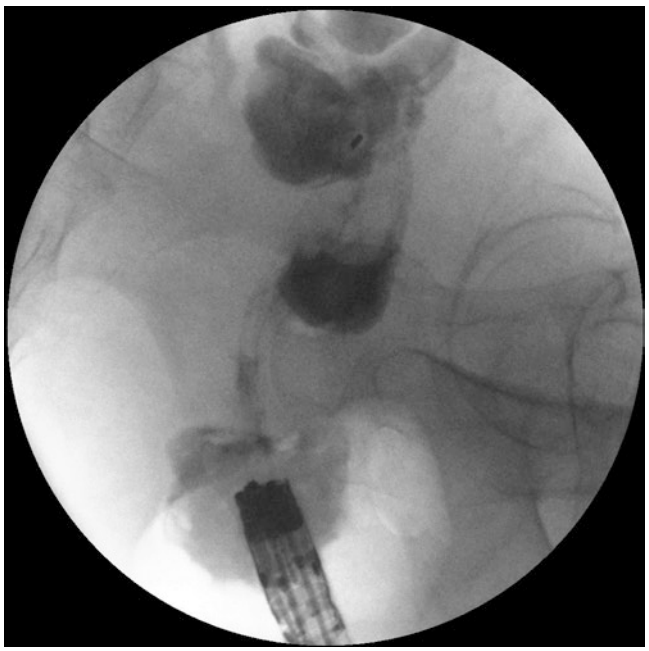

Fig. 19.2 Water-soluble contrast injected through the stricture to confirm tumor characteristics

Drug-Eluting Stents

Drug-eluting stents, routinely used in coronary arteries, may be useful in the gastrointestinal tract by possibly decreasing stent occlusion from tumor ingrowth. Drug-eluting stents are currently in development and the majority of the available data is from animal studies. Drug-eluting lower gastrointestinal stents may expand the indications for stent placement and may potentially improve clinical outcomes.

Preparation and Technical Steps for Stent Deployment Patient Preparation

Successful stenting of a colorectal tumor requires adequate visualization of the distal aspect of the tumor and cannulation of the obstructed lumen. A pre-procedural assessment of the location and morphology of the malignant stricture can be very helpful (Fig. 19.2). A retrograde water-soluble contrast enema examination can assess the lesion and is helpful to evaluate the presence of proximal synchronous tumors. Patients with complete obstruction, especially those with left-sided distal obstruction, usually have evacuated any rectal contents prior to the stenting procedure. In patients whose obstruction is more proximal, the distal colon can be obscured by stool that can hinder stent placement. A water-soluble contrast enema, in addition to delineating the anatomy,

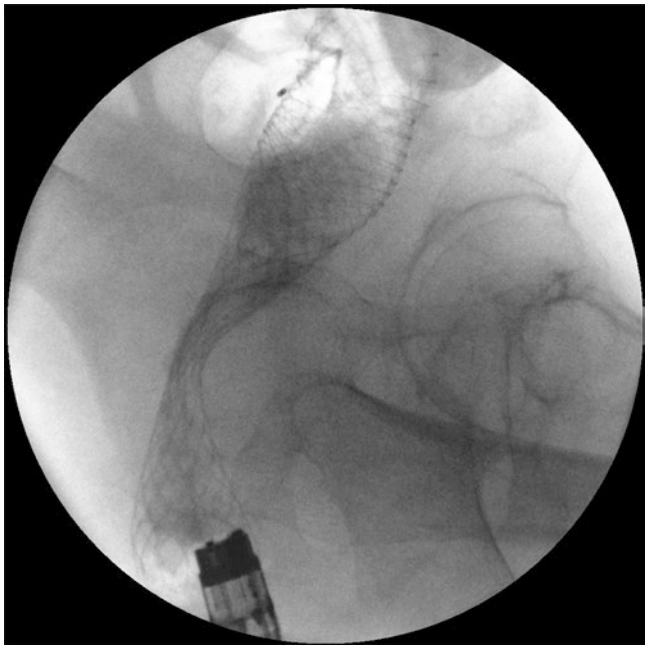

Fig. 19.3 Fluoroscopic view of a deployed stent

can also evacuate the retained luminal contents. Alternatively, one or two cleansing enemas can prepare the distal colon. Oral mechanical bowel preparation is typically contraindicated in patients with colonic obstruction and should be avoided.

Prophylactic intravenous antibiotics are not routinely administered but can be considered in patients with complete obstruction with dilated colon proximal to the obstruction because insufflation during the procedure may cause microperforation and bacteremia. Patients are typically placed in the left lateral position until the obstruction is reached. Rotating patients into the supine position before stent placement allows for a better view under fluoroscopy (Fig. 19.3) but the same view can be achieved with a rotating fluoroscope. The procedure is typically performed under intravenous sedation either in the endoscopy suite or the operating room.

Description of the Procedure

Colorectal stenting can be performed under endoscopic visualization, fluoroscopic guidance, or both. Combining fluoroscopy with endoscopy is considered the preferable approach to stenting (Fig. 19.4). TTS stents are usually used for more proximal obstructions and OTW stents may be utilized for more distal lesions. Dilation of the stricture should be avoided before stenting since dilation increases the risks of perforation [25]. Dilation of the distal aspect of a lesion may be considered to try to identify the lumen in cases where initial wire cannulation of the lesion is unsuccessful.

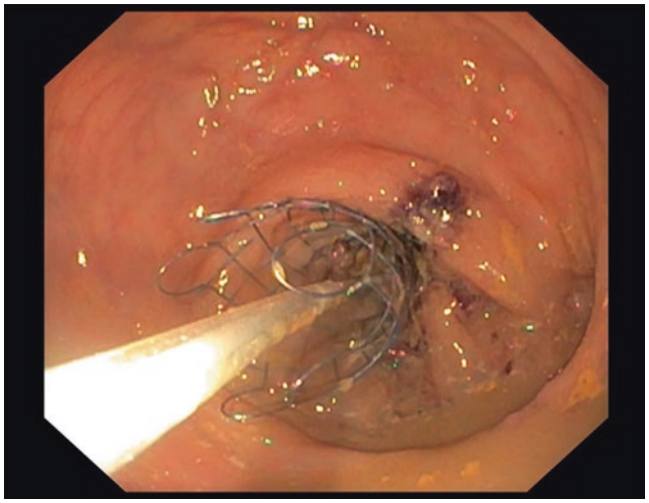

Fig. 19.4 Endoscopic view of a deployed stent

Endoscopic Stent Placement Without Fluoroscopy

This method can be used if the distal aperture of the stricture is wide enough to allow passage of the endoscope. A smaller diameter gastroscope can be used, as needed. This approach, given its limitations, is most applicable to distal left-sided lesions.

TTS Stent Placement

After the scope passes into the distal aspect of the stricture, a guidewire is placed through the endoscope and additional wire length is passed proximal to lesion. It is helpful to estimate the length of the stricture based on the pre-procedure water-soluble contrast enema study. The stent is passed through the endoscope channel, the endoscope is withdrawn to the level of the distal end of the stricture, and then the stent is deployed under direct visual guidance ensuring adequate proximal and distal overlap of the lesion.

OTW Stent Placement

With the scope at the distal end of the stricture, a guidewire is placed through the endoscope and the wire is advanced through and proximal to the lesion. The endoscope is withdrawn while the guidewire is kept in place. The scope is reinserted beside the guidewire and is used to observe the stent delivery system being passed over the guidewire and across the stricture. Under direct visualization the stent is deployed while maintaining at least 1–2 cm of stent length distal to lesion.

Fluoroscopic Stent Placement Without Endoscopy

One of the concerns with radiologic stent placement is the radiation exposure for both the patient and the operator; adequate training and careful use of fluoroscopy are important to minimize such exposure. Studies comparing fluoroscopy and combined fluoroscopic-endoscopic techniques report similar technical and clinical success rates; however, the fluoroscopic-endoscopic technique usually reduces the overall dose of radiation exposure.

In the more distal colon, stent deployment can be performed under fluoroscopic guidance alone. In the proximal colon, combined fluoroscopic-endoscopic or endoscopic alone approaches to stent placement are preferable due to the redundant nature of the more proximal colon which makes fluoroscopy alone a cumbersome technique. Distal bowel preparation, which may be helpful in endoscopic stent deployment, is not always necessary in the fluoroscopic approach.

A water-soluble contrast enema performed prior to the procedure or on the table localizes the stricture and assesses its length. An angiography catheter is advanced over a guidewire proximal to the obstruction under fluoroscopic guidance and water-soluble contrast is injected to evaluate the stricture real-time and to rule out perforation. The angiocatheter is withdrawn over the guidewire and an appropriately sized stent is thereafter advanced over the guidewire and deployed across the obstructing lesion. Fluoroscopy is used throughout the procedure. After stent placement, the water-soluble enema can be repeated to evaluate stent patency and positioning.

Endoscopic-Fluoroscopic Stent Placement

Combined endoscopic-fluoroscopic guided stent placement is the preferred stenting technique. A hydrophilic, soft-tipped guidewire loaded through an ERCP catheter is used to cannulate and traverse the stricture. Once the guidewire crosses the stricture, positioning can be assessed fluoroscopically. The ERCP catheter is advanced over the wire through the stricture and water-soluble contrast is injected to confirm positioning (Fig. 19.6). By injecting contrast proximally and at the level of the stricture, the length of the lesion can be visualized and a proper stent length is chosen. At this point, the ERCP catheter is removed and a colonic through-the-scope stent delivery system is passed over the guidewire and through the lesion under both endoscopic and fluoroscopic guidance. It is important to use a stent with the proper length. The stent should be long enough to cover the entire obstructed segment, and extend by at least 1–2 cm beyond the proximal and distal margins of the lesion (Fig. 19.7). More symmetrically placed stents are associated with higher clinical success rates as demonstrated by a retrospective study of 82 patients [26]. If stent coverage is inadequate, an additional stent can be deployed in series to completely cover the lesion and both proximal and distal aspects ("piggybacking"). It is important to keep the guidewire in place until the stent position is assessed as introducing the guidewire again through a newly deployed stent is technically difficult and risks perforation.

Table 19.4 Short- and long-term complications after colonic stenting

Short-term complications		
Abdominal pain		
Bleeding		
Perforation		
	Intraprocedural	
	Post-procedural	
		Symptomatic
		Silent
Incomplete expansion		
Long-term complications		
Stent occlusion		
	Ingrowth	
	Overgrowth	
	Stool impaction	
Stent migration		
Stent fracture		
Fistulization		
Perforation (bevacizumab treatment)		

Procedure-Related Complications

Complications during colonic stenting occur in 5–7% of cases (Table 19.4). Late complications are more common than early complications and occur in up to 20% of cases. In a study by Sebastian et al. [27]' examining SEMS safety, the overall complication rate was 25%.

Early Complications

The most common early complications are bleeding and perforation. Bleeding is often self-limited and rarely requires intervention. Perforation can occur during the procedure due to wire or catheter misplacement or other trauma, or can occur soon after the procedure due to tumor rupture from the expanding stent or in the cecum due to overdistension from a non-patent stent. Endoscopic treatment of perforation in this setting is very difficult, if not impossible. While patients usually require resection and/or stoma formation, patients with microperforation may be treated initially with bowel rest and antibiotics.

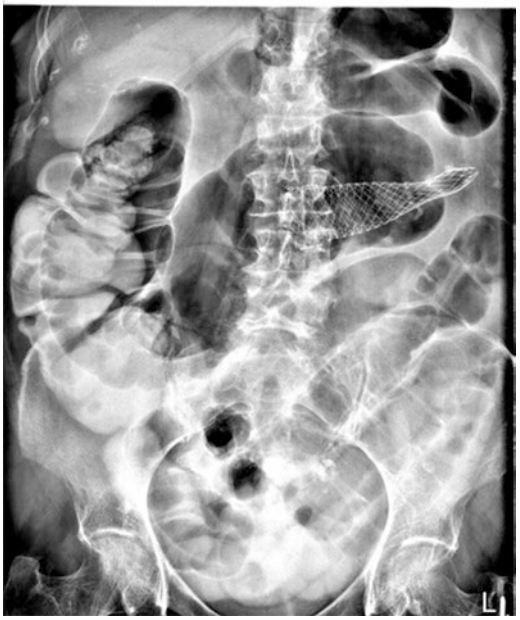

Fig. 19.5 Partial malpositioning of stent in the transverse colon

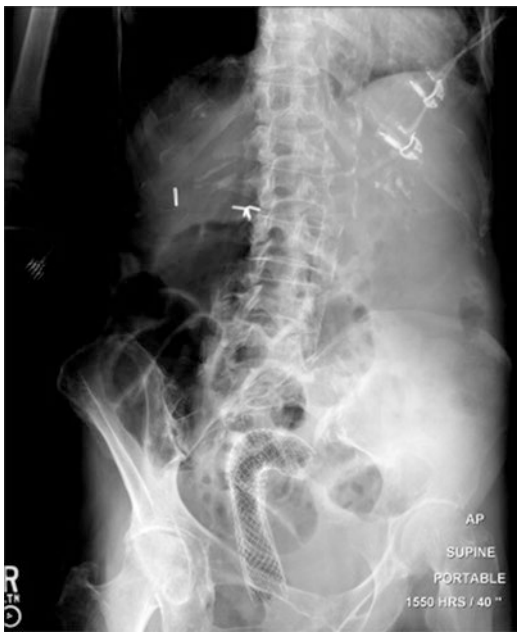

Fig. 19.7 Second stent placement due to occlusion

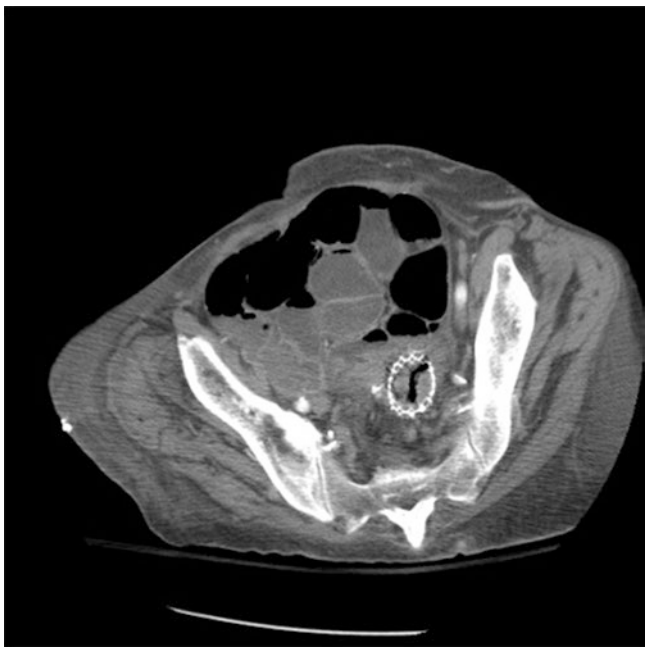

Fig. 19.6 Occluded stent from fecal impaction

A meta-analysis of 86 studies published between 2005 and 2011 revealed an overall perforation rate of 7.4%. Stent design, benign etiology (perforation rate 18.4% compared with 7.5% for malignant strictures), and bevacizumab therapy (perforation rate of 12.5% compared with 7.0% for chemotherapy without bevacizumab) were identified as risk factors for perforation [25]. In a systematic review by Khot et al., the perforation rate was 4% [28]. In a retrospective study of 478 procedures, Samper Wamba et al. reported a technical success rate of 92% with a clinical success rate of 78% [29]. Complications occurred in 18.5% of patients and were more frequent in patients with stainless steel stents rather than nitinol stents.

In some cases, stent placement does not successfully resolve the obstruction, which may be due to failure to stent the entire length of the stricture. Other causes of clinical failure include synchronous colonic obstructions, early stent migration (Fig. 19.5), early fecal impaction (Fig. 19.6), or incomplete stent expansion. Case reports and retrospective studies have described success with placement of a second SEMS after a failed first stent. Placing a second stent can be technically challenging (Fig. 19.7).

Distal rectal stenting (within 5 cm of the anal verge) may cause tenesmus and anorectal pain. These complications are usually transient and can be treated with observation and/or pain medication. In one study, stent deployment within 5 cm of the anal verge caused pain, which spontaneously resolved in three of ten patients while the remaining patients required pain medication. In cases with refractory symptoms, the stent may need to be removed. Incontinence can occur when stents are deployed so close to the anal canal. When possible, the distal end of the stent should be deployed at least 2 cm proximal to the anorectal ring. Early stent migration due to malpositioning of the stent or stenting a non-obstructing lesion can often be managed endoscopically by removing the stent.

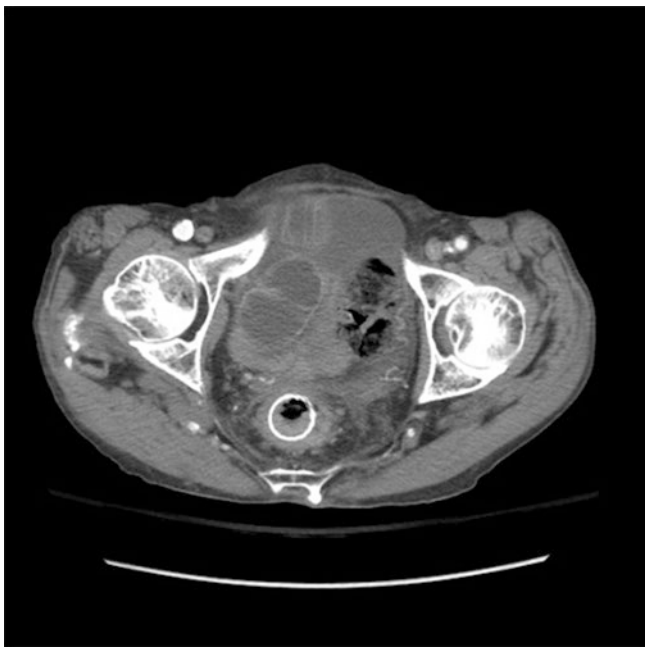

Fig. 19.8 Tumor ingrowth

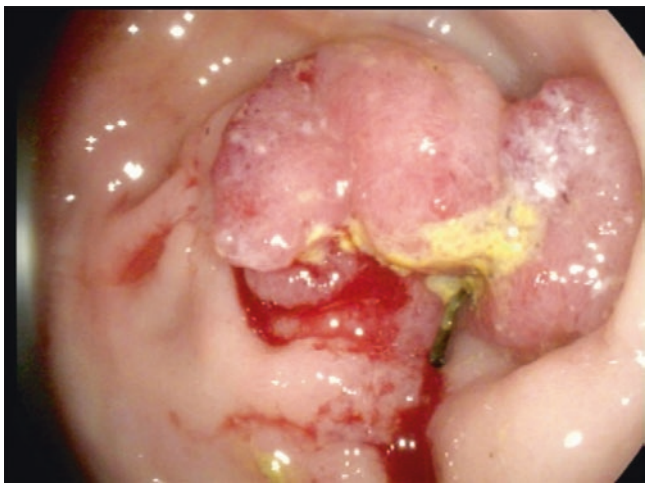

Fig. 19.9 Endoscopic view of tumor ingrowth

Late Complications

The most common late complications are stent migration and stent occlusion by tumor ingrowth (Figs. 19.8 and 19.9) or fecal impaction. In one study, tumor ingrowth after palliative stenting caused stent occlusion in 15% of patients [27]. Putting this into perspective, most patients who have been stented for palliation die from metastatic disease before obstruction from tumor ingrowth occurs. Stent occlusion by tumor ingrowth can often be managed endoscopically by placing another stent through the occluded stent. Impaction can be managed endoluminally or endoscopically

Fig. 19.10 Late distal stent migration

but care should be taken not to displace the stent during the procedure (Fig. 19.10).

The incidence of stent migration depends on factors like stent type, degree of intrinsic stenosis, flare diameter, and proximal and distal stent clearance. Lack of fixation of a metallic mesh stent to the tumoral tissue can result in stent migration, a phenomenon more common with covered stents where stent interstices do not come into contact with cancer. Migration also occurs more frequently with smaller diameter stents and shorter stents. As narrower stenoses have a lower likelihood of stent migration, shrinking of the tumor after chemo- or radiotherapy can also result in stent migration (Fig. 19.12).

Post-stenting Care and Surveillance

Once patients decompress after stenting, their diet can be advanced as tolerated to a low residue diet. Mild laxatives are helpful to avoid impaction and are commonly continued long-term.

In terms of follow-up, there are no consensus guidelines for surveillance after palliative stenting of obstructing colorectal cancer. According to a prospective study of 49 patients by Im et al., median stent patency lasted 204 days and patency rates at 30, 90, and 180 days were 91.2, 81.0, and 53.3%, respectively [30]. While most patients who have been stented for palliation die from metastatic disease before re-obstructing from tumor ingrowth, in patients whose disease progression is slowed by systemic chemotherapy, endoscopic surveillance of the stent every 4–6 months may be prudent (Fig. 19.11). CT imaging can also be helpful in some cases (Fig. 19.12).

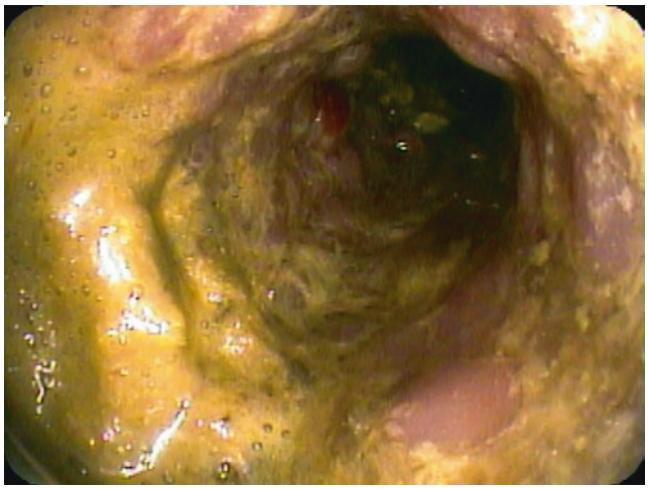

Fig. 19.11 Endoscopic view of stent 4 months after placement

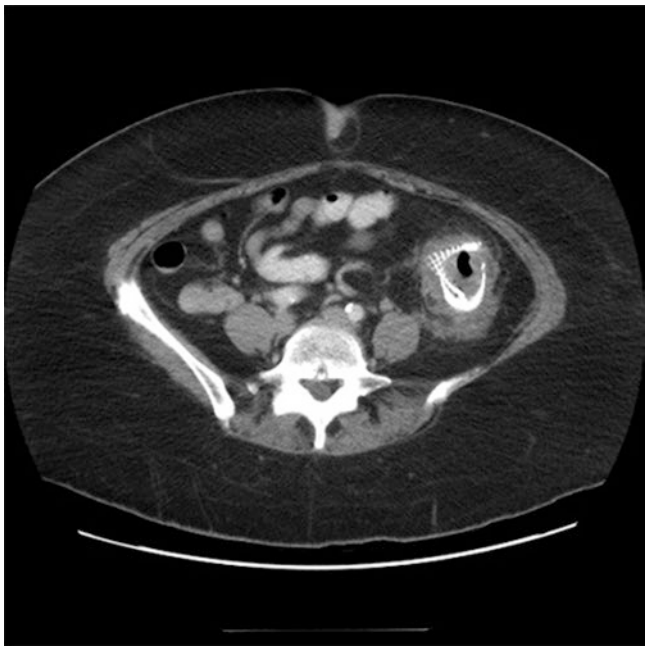

Fig. 19.12 CT 6 months after stent placement

Conclusions

Metallic stents are widely used today for the management of colorectal obstruction, as palliative therapy or bridge-to-surgery. Stenting as bridge-to-surgery provides advantages of higher primary anastomosis rate and lower stoma rate without increasing the risk for postoperative anastomotic leak. The indications for use of colorectal stents will continue to expand to include benign disease, fistulas, anastomotic complications, etc. The future introduction of new stent platforms such as biodegradable and drug-eluting stents may further expand the application of stenting.

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How to Avoid Complications/Treatment of Endoscopic Complications

20

Nicole M. Saur and Joshua I.S. Bleier

Key Points

- There are several techniques to minimize complications from bleeding and postpolypectomy syndrome associated with electrocautery: saline lift, mobilizing the polyp away from the bowel wall, and using short bursts of electrocautery.
- Reducing the loop and avoidance of blind pushing while performing colonoscopy are techniques to decrease the perforation rate of diagnostic colonoscopy.
- Postpolypectomy syndrome is a constellation of symptoms secondary to full-thickness electrocoagulation injury without frank perforation. Imaging is needed to differentiate this syndrome that responds to conservative management from free perforation that may require operative intervention.
- Timing of presentation, health of the colon, and technique of colonoscopy (diagnostic versus therapeutic) should be considered when deciding conservative management versus operative intervention for colonoscopic perforation.
- Patients with fecal peritonitis have increased morbidity, and minimally invasive techniques should be abandoned in favor of conservative operative treatment with diversion.

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How to Avoid Complications

Any discussion of avoidance of complications should begin with the known complications and their relative rates of occurrence. The rate of serious complications or death associated with colonoscopy is low while noting that it is an invasive procedure. Whitlock et al. evaluated 12 studies reporting complications of colonoscopies and showed a rate of serious complications of 2.8/1000 procedures. Serious complications were defined as serious bowel complications, heart complications, or death. In addition, in this analysis, 85% of the complications occurred in colonoscopies with polypectomy [1]. In a study of over two million colonoscopies, Chukmaitov et al. showed a rate of complications requiring hospitalization of 1.98/1000 procedures [2]. In colonoscopy, the mortality rate is 0.007% [3].

Factors that have been shown to increase the rate of complication are patient age and comorbidities, endoscopist volume, complexity of polypectomy, type of sedation, and performance of procedure in an ambulatory unit [2, 4, 5]. Techniques to avoid complications aim to decrease the effect of these factors on the individual procedure. In addition, the techniques are broken down into sections based on the complications discussed later in this chapter: bleeding, postpolypectomy syndrome, and perforation.

How to Avoid Bleeding

Especially in patients on anticoagulant or antiplatelet therapy, cold snare polypectomy is preferred over "hot" snare with electrocoagulation. This is because in approximately 5–7 days, the eschar associated with electrocoagulation will slough off, potentially leaving an exposed vessel that can bleed. Patients typically have restarted their anticoagulants by this time and can have a significant amount of bleeding. As an alternative, the cold snare technique allows for monitoring of hemostasis and placement of one or

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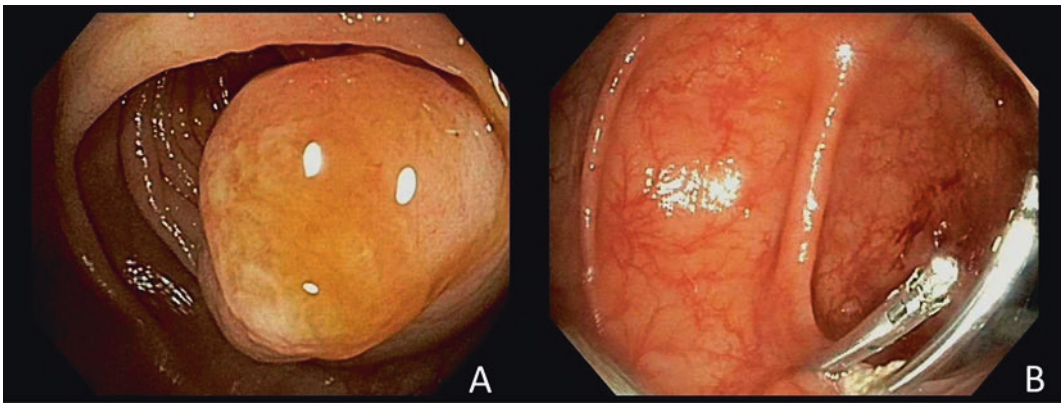

Fig. 20.1 Endoscopic clipping of polypectomy site. (**a**) Large polyp, subsequently removed with snare polypectomy. (**b**) Polyp site after endoscopic clip placement. With permission from the personal library of Manoj Shirodkar, MD

multiple clips if bleeding is noted. Figure 20.1 demonstrates a large polyp (a) that was removed with snare and clipped for hemostasis (b).

How to Avoid Postpolypectomy Syndrome

Full-thickness electrocoagulation can result in postpolypectomy syndrome or perforation, which will be discussed at length later in the chapter. It is not recommended to perform biopsy with "hot" biopsy forceps to avoid thermal spread. In addition, when it is necessary to use a "hot" snare, the polyp should be retracted away from the bowel wall and into the lumen prior to anticoagulation being applied to maximize the distance between the current in the submucosa and the serosa [6]. Additionally, the saline lift technique, during which saline is injected into the submucosa prior to polypectomy, may aid in preventing thermal spread by expanding the submucosal layer [7].

How to Avoid Perforation

Looping of the scope in the colon is a major obstacle to successfully completing colonoscopy and a potential cause of colonic perforation. Looping is caused by a mobile mesentery in the sigmoid and transverse colon. When a loop is formed, paradoxical movement of the scope can occur, which is noted when the tip of the scope moves backward while the endoscopist is pushing the scope forward. There are several techniques to avoid looping and to reduce the loop once one has formed. Initially, during scope insertion, the endoscopist should endeavor to use primarily clockwise rotation. In this fashion, the mobile sigmoid is held against the pelvic sidewall. This minimizes the risk that a medially bent sigmoid can loop with a mobile, narrow-based mesentery. In addition, starting at the second rectal valve, the endoscopist can torque the scope clockwise while applying suction and pulling the scope backward. In doing so, the colon is being intussuscepted onto the colon, and rather than a large omega loop forming, the colon is straightened out onto the scope. This maneuver is repeated every 10–20 cm until the hepatic flexure is reached. A similar maneuver can be used to reduce an already formed loop. The scope is torqued clockwise while applying suction and pulling back until the loop is reduced. When the loop is reduced, paradoxical motion is eliminated, and the scope freely advances forward. There is always a potential to lose ground when attempting to reduce a large loop when the scope regresses further than the loop when pulling back. To avoid this, it is important to reduce the loop as the scope is advanced and avoid making a large loop. Additionally, loops in the scope outside the colon can form and can be addressed by rotating the scope outside the colon.

Another method to decrease looping as the scope is advanced is to irrigate and fill the sigmoid colon with water as the scope is advanced. The colon being weighed down with the water makes it less likely to form a large loop. Abdominal pressure can also be important to stabilize an already formed loop and enable the forward passage of the scope, especially in the right colon. The assistant applies pressure in the left abdomen downward toward the stretcher and the patient's pelvis. This functions by "pinning" the sigmoid colon laterally, preventing torque on a mobile, broad, mesenteric pedicle. Additionally, a second hand can apply pressure upward to stabilize the transverse colon if needed. When a loop forms, it can cause pain or discomfort in the moderately sedated patient. It is important to note this pain and attempt to reduce the loop. Unfortunately, in the heavily sedated patient, this pain is often not apparent, and large loops and painful maneuvers can be underestimated. This underscores the balance of optimizing patient comfort without compromising patient safety and the importance of avoiding over sedation during colonoscopy.

The lumen should be visualized at all times when advancing the scope. There should be no blind pushing of the scope around turns to avoid perforation. When approaching a difficult and tight turn, pulling back on the scope rather than pushing forward can help visualize the lumen and allow the scope to be advanced safely. A pediatric colonoscope can often be advanced around tight turns more easily than a larger colonoscope. Care should be taken to minimize insufflation to avoid barotrauma to the proximal colon while attempting to pass a difficult turn or structure in the distal colon. In addition, difficult turns are often caused by intraabdominal adhesions. Therefore, changing the patient's position can often make passing the turn easier. The patient position can be changed to supine, prone, or right lateral decubitus depending on the portion of the colon in which the difficulty is arising. Difficulty may be encountered when attempting to traverse the hepatic flexure. This may be due to accumulated loops, or simply due to excessive length of scope in the colon, minimizing efficiency of forward movement. The endoscopist should recall that in the most common position, left lateral decubitus, the scope is trying to advance, not only ahead of a significant length of scope but also against gravity, Thus taking advantage of repositioning the patient in the supine position can alleviate one of the factors contributing to the difficulty in navigating the turn. In some cases prone positioning may be employed so as to use the patient's own weight to stabilize loops. It should be noted that if all of the above is attempted, the next step should be to abort the colonoscopy and obtain a CT colonography to evaluate the remainder of the colon rather than make further attempts to pass the scope and increase the possibility of perforation.

Diverticulosis presents a peculiar perforation risk either from pushing the scope through a diverticulum while mistaking the diverticulum lumen for the colonic lumen or mistaking an inverted diverticulum and taking an inadvertent full-thickness biopsy of colonic wall. Special care should be taken to be aware of the challenge of identifying diverticula, and a high level of suspicion should be applied to the lumen or polyp that does not have a typical appearance.

Treatment: Bleeding

Bleeding is more commonly associated with therapeutic colonoscopy and is rare with diagnostic colonoscopy [8]. Bleeding occurs in 1–2% of polypectomies, and this rate increases for polyps that are larger and more difficult to remove [8–12]. The risk of bleeding is also higher in patients with known coagulopathies, history of thrombocytopenia, or patients taking anticoagulant or antiplatelet therapy.

Bleeding complications can be categorized relative to the time of presentation: immediate or delayed. Immediate bleeding can usually be recognized at the time of polypectomy. This occurs secondary to biopsy or snare without the use of cautery or the use of blended current for electrocoagulation. If identified during colonoscopy, bleeding can be treated immediately with epinephrine injection or endoscopic clipping. If recognized in the recovery room or the same day as the procedure, repeat colonoscopy with clipping can be undertaken. Figure 20.2 demonstrates a visible vessel associated with a diverticulum (a) and the vessel after clip placement (b).

Delayed bleeding is typically seen several days to a week after the colonoscopy, but has even presented up to 1 month after the colonoscopy. Delayed bleeding is typically associated with the use of endoscopic electrocoagulation. Approximately 1 week after the use of cautery with polypectomy, the eschar sloughs off and may result in bleeding, especially in those patients who had previously had their anticoagulation prior to the procedure and have since restarted their medication. An alternative mechanism proposed involves delayed thermal injury from the electrocautery with subsequent necrosis and erosion into a nearby

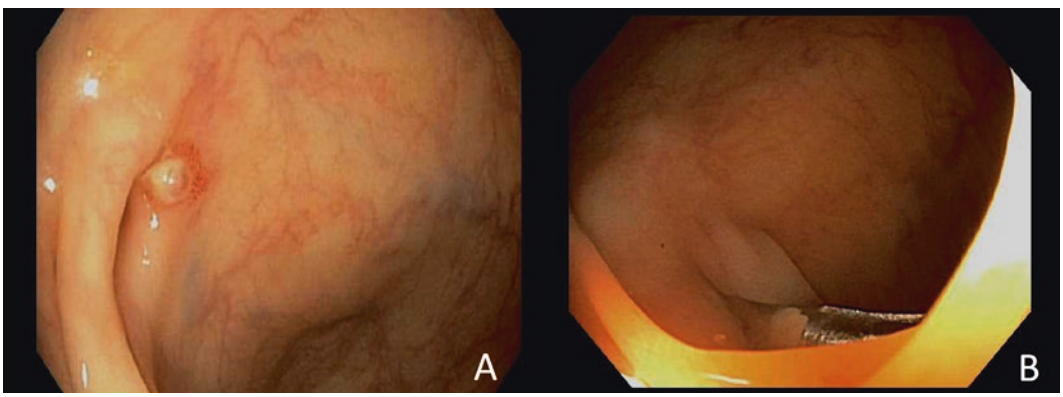

Fig. 20.2 Endoscopic clipping of blood vessel. (**a**) Exposed blood vessel associated with diverticulum. **(b**) Blood vessel after endoscopic clip placement. With permission from the personal library of Manoj Shirodkar, MD

vessel. Patients typically present with hematochezia or melena, but can also present with symptoms from the effects of anemia and hypotension. If the patient is hemodynamically stable and the bleeding appears to have stopped, they can be admitted to the inpatient unit for close monitoring of vital signs, signs of ongoing bleeding, and hemoglobin levels. If the patient is hemodynamically unstable, the patient should be resuscitated prior to any attempt to stop the bleeding. If the patient is hemodynamically stable with signs of ongoing bleeding, colonoscopy can be undertaken with clip placement or epinephrine injection if the site of bleeding can be identified. Unlike the performance of colonoscopy in a patient with bright red blood per rectum from an unknown source, the polypectomy sites should be known to the endoscopist, and special attention to identify the bleeding at biopsy sites can be taken. If significant clot has accumulated in the colon, large-volume irrigation may be necessary to identify the bleeding site [13]. Figure 20.3 displays a treatment algorithm for treatment of postpolypectomy bleeding.

Postpolypectomy Syndrome

Postpolypectomy syndrome (postpolypectomy anticoagulation syndrome) is a constellation of symptoms that may be characterized by abdominal pain, fever, leukocytosis, and localized peritonitis. These symptoms can occur without associated bowel perforation or pneumoperitoneum and occur after polypectomy with electrocoagulation. Because of the overlap with many symptoms of bowel perforation, clinicians should be aware of this syndrome to avoid unnecessary emergent surgery.

The incidence in the literature varies from 0.3 to 50 per 10,000 colonoscopies. As with bleeding, the incidence of postpolypectomy syndrome is increased when larger, more complicated polyps are removed [11, 14–16]. In fact, signs of postpolypectomy syndrome have been reported in up to 40% of cases involving endoscopic submucosal dissection [17, 18].

The pathogenesis of postpolypectomy syndrome involves the spreading of the electrical current applied during electrocoagulation beyond the mucosa and into the muscularis propria and serosa. This full-thickness burn can cause inflammation and peritonitis without perforation [15]. Presentation is typically within 12–24 h, but can occur anytime in the first 5 days [10]. The most typical symptoms are soreness and tenderness in the region of the polypectomy. In addition, tachycardia, focal abdominal tenderness or peritonitis, fever, and/or leukocytosis can be the presenting symptoms, which often overlap with the symptoms of free perforation. Diagnosis is made in the correct clinical context after polypectomy, and postpolypectomy syndrome is differentiated from free perforation with radiological studies. CT scan of the abdomen pelvis with oral and IV contrast is the study of choice. Classic findings in postpolypectomy syndrome include colon wall thickening and pericolonic fat stranding in the absence of pneumoperitoneum or air in the retroperitoneum.

Conservative management is the treatment of choice, including bowel rest, intravenous fluid resuscitation, and antibiotics. In patients with severe symptoms, hospitalization is prudent with close monitoring and intravenous antibiotics. Patients with mild symptoms can be managed as an outpatient with oral antibiotics if they can tolerate a clear liquid diet and stay hydrated. Waye et al. showed a 20% rate of inpatient admission in postpolypectomy syndrome [10].

Treatment: Perforation

There are three potential mechanisms for perforation of the colon during colonoscopy: mechanical trauma secondary to increased pressure applied by the colonoscope such as when blindly pushing by a difficult turn; barotrauma secondary to overdistension of the colon, which is most frequently identified in the cecum; or cautery-induced thermal injury that eventually becomes full thickness. Perforation rates vary widely based on the type of intervention performed during the colonoscopy.

Perforation is the most feared complication of colonoscopy and occurs in 0.016–0.8% of diagnostic colonoscopies and up to 5% of therapeutic colonoscopies [19, 20]. Because in most circumstances the patient has a fully prepped colon, prompt recognition of perforation limits morbidity. As the delay in diagnosis becomes longer, the potential for fecal soiling of the peritoneum and septic complications becomes higher.

Management Based on Diagnostic or Therapeutic Colonoscopy

Just as the etiology of perforation is different for diagnostic and therapeutic colonoscopies, the treatment algorithm is different as well. Figures 20.4 and 20.5 demonstrate a proposed treatment algorithm for the management of perforation after diagnostic and therapeutic colonoscopies.

Perforations during diagnostic colonoscopy are divided into two groups based on the quality of the colon at the time of the perforation. If the colon was unhealthy, as is the case with inflammatory bowel disease or diverticulitis, a trial of conservative management is not warranted, and the patient should be taken to the operating room for exploration and repair versus colectomy with or without diversion. In patients with an otherwise healthy colon, the algorithm is divided based on the presence or absence of peritonitis. In a large

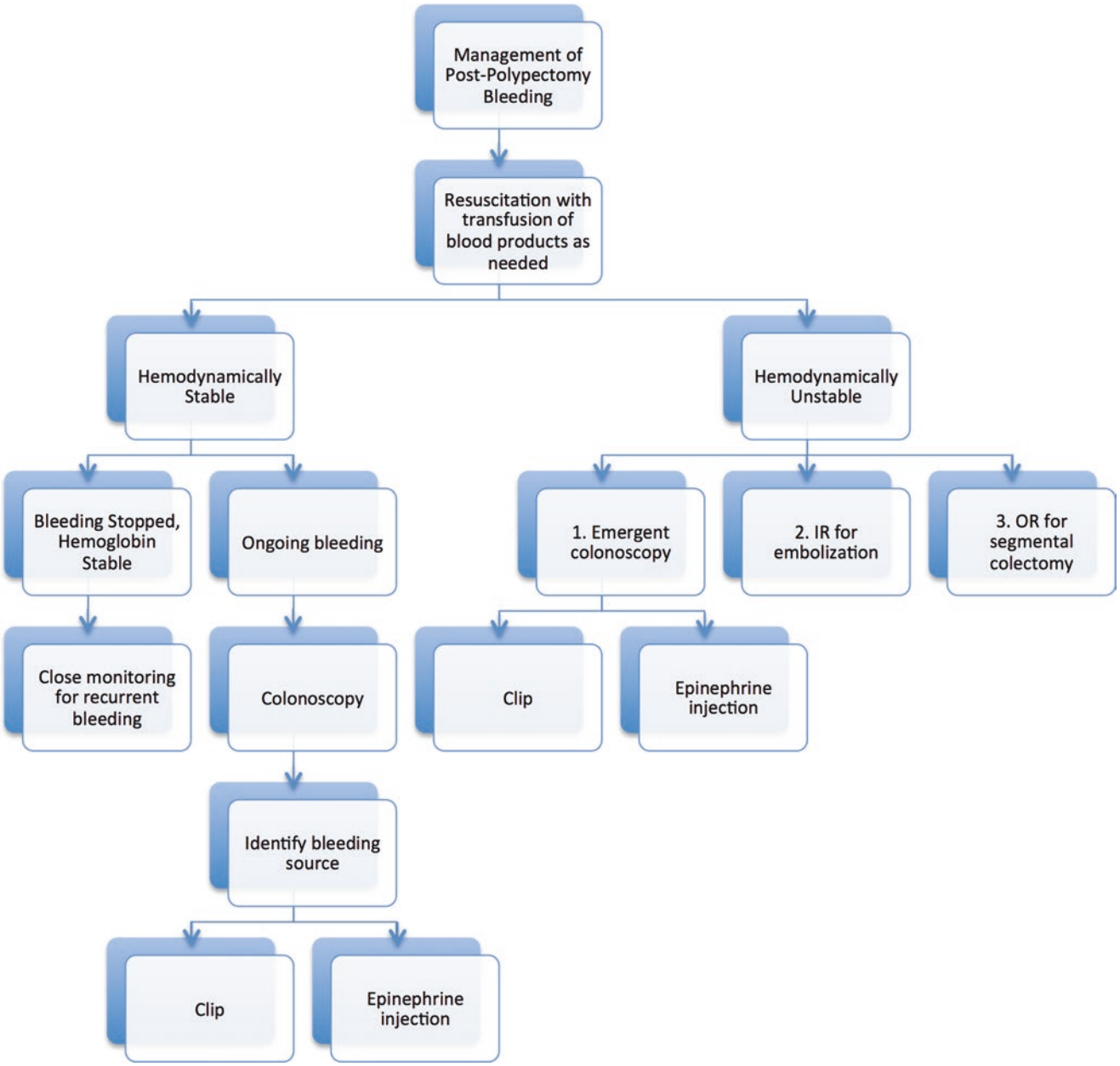

Fig. 20.3 Algorithm for the management of postpolypectomy bleeding. *Note:* For the hemodynamically unstable, the authors recommend interventions in the order listed (1) Emergent colonoscopy, (2) IR for embolization, (3) OR for segmental colectomy. *IR* interventional radiology, *OR* operating room

defect with peritonitis, the patient should be taken to the operating room for exploration with repair versus colectomy with or without stoma. Patients with a healthy colon and without peritonitis are further divided based on the timing of the diagnosis of perforation. If the perforation is identified at the time of the scope by loss of insufflation, identification of the peritoneal contents, or increased abdominal distention, a clip can be placed at the time of the scope. Especially for a small, regular defect, clipping can be effective in controlling the perforation and prevention of sepsis. Patients should be carefully monitored after this management and should be kept on bowel rest with intravenous antibiotics with serial abdominal examinations. In those patients who present after the periprocedure period, but do not have signs of peritonitis, conservative management can also be undertaken with CT scan of the abdomen and pelvis with oral and intravenous contrast and close monitoring, serial abdominal examinations, bowel rest, and intravenous antibiotics.

Perforations during therapeutic colonoscopy are divided according to the timing of presentation. Like with those perforations associated with diagnostic colonoscopy, if the perforation is identified immediately, endoscopic clipping

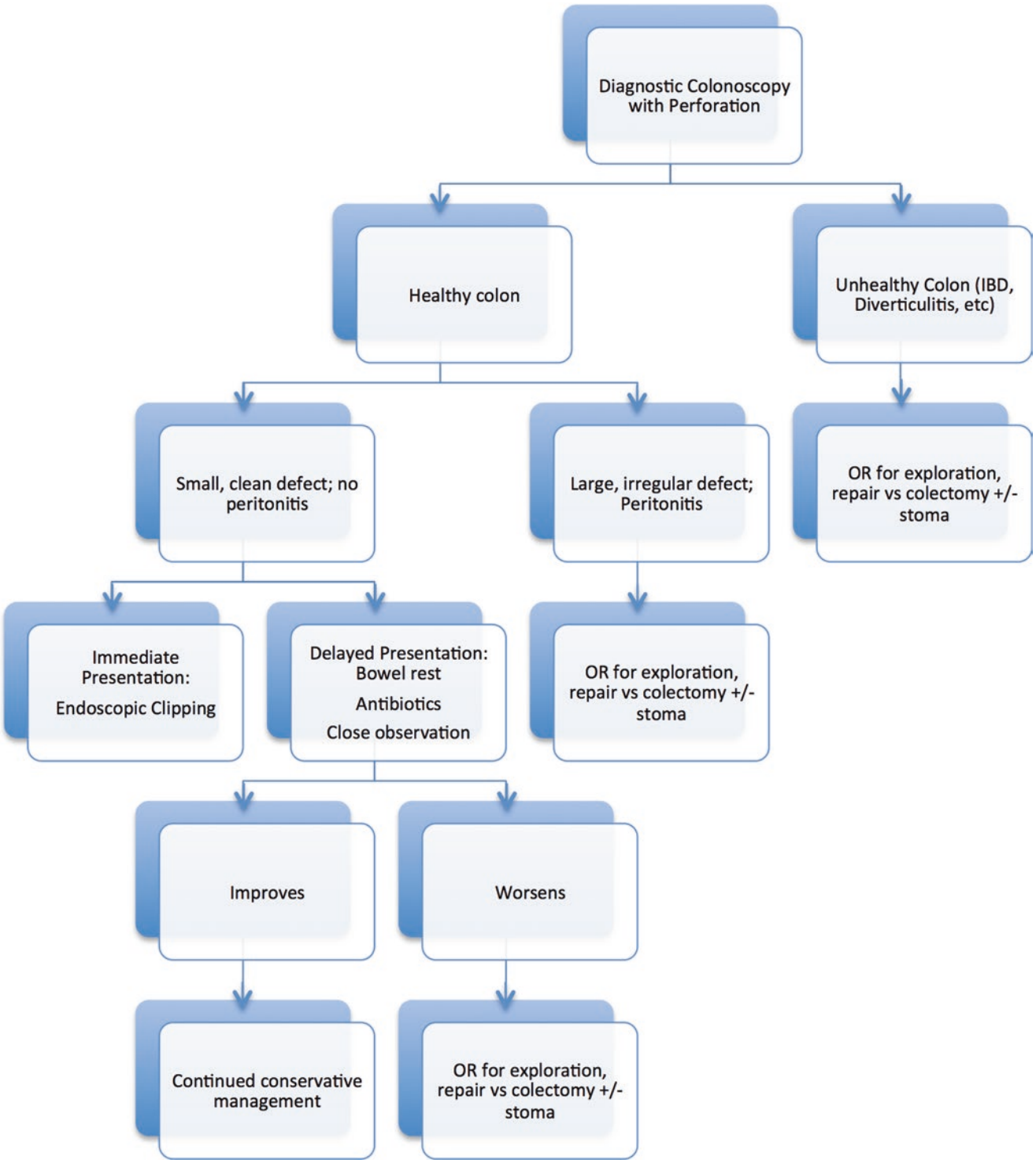

Fig. 20.4 Algorithm for the management of perforation from diagnostic colonoscopy. *IBD* inflammatory bowel disease, *OR* operating room, *vs* versus

can be attempted. If endoscopic clipping is successful, conservative management should follow. If endoscopic clipping is not attempted, but the patient does not develop signs of peritonitis, conservative management can be attempted with close observation for 24 h. If the patient improves or stays stable, continued conservative management is warranted. If the patient worsens or develops peritonitis, operative exploration should be undertaken. If the patient presents in a

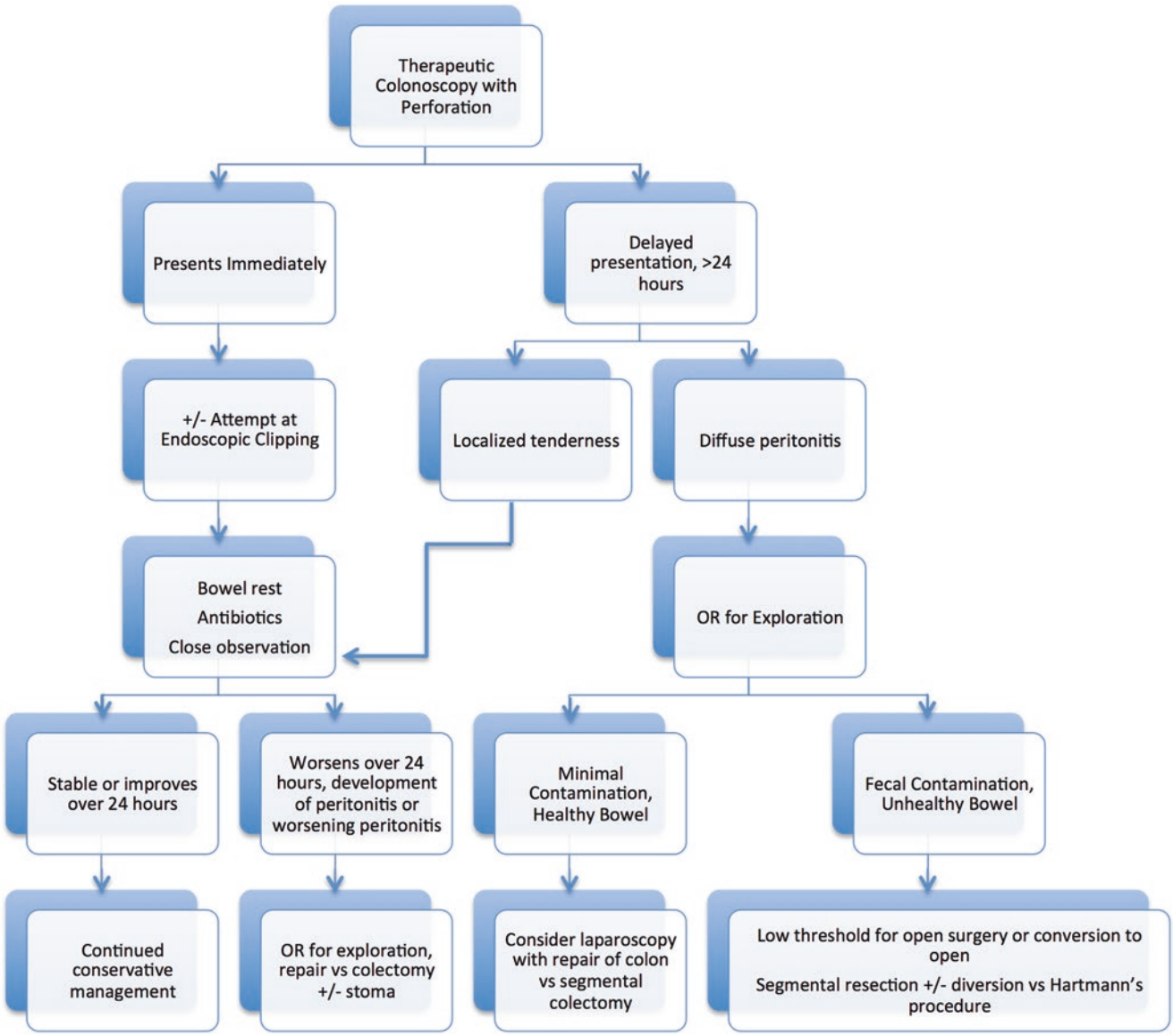

Fig. 20.5 Algorithm for the management of perforation from therapeutic colonoscopy. *vs* versus

delayed fashion with localized tenderness or peritonitis, conservative management can be attempted for 24 h. If the patient presents with signs of peritonitis, operative exploration is warranted.

Criteria for Conservative Management Versus Operation

As discussed in the previous section, patients without diffuse peritonitis and those with an otherwise healthy colon can be managed with short trial of conservative management with bowel rest, intravenous fluids, and intravenous antibiotics. Additionally, patients with extraperitoneal perforations can be managed conservatively. Extraperitoneal perforations have been reported in the mesentery and retroperitoneum, but the air has been reported to track to the mediastinum and pleural cavity with reports of pneumothorax from colonic perforation [13].

Operative Options

Iqbal et al. reviewed 258,248 colonoscopies and identified 180 perforations (0.07% incidence). Of the patients with perforation, 165 underwent surgical intervention. In this series, 29% of patients underwent primary repair, 33% resection with primary anastomosis, and 38% with

fecal diversion. They reported that patients with presentation within 24 h had less fecal contamination of the peritoneum and were more likely to undergo primary repair or resection with anastomosis (64 vs 6 patients, $p = 0.01$). Patients presenting after 24 h were more likely to have fecal contamination (16 vs 4 patients, $p = 0.02$) and were more likely to have a stoma (23 vs 43 patients, $p = 0.02$). They reported a morbidity rate of 36% and demonstrated that blunt injuries, poor bowel preparation, corticosteroid use, and age younger than 67 were associated with increased morbidity. They also reported a mortality rate of 7% percent, but did not identify independent predictors of mortality [21]. This study underscores the treatment algorithm listed in the previous section. In minimal contamination, minimally invasive procedures including laparoscopic primary repair and resection with anastomosis can be performed safely. Haas et al. reported a series of five patients undergoing laparoscopic primary repair of colonoscopic perforations. None of the patients required further surgery and no complications were identified [22]. However, in fecal peritonitis, the safest option is still primary resection with diverting stoma or Hartmann's procedure.

As endoscopic clipping and laparoscopic repair were discussed earlier in the section and combined endoscopic and laparoscopic resection of polyps is a new technique also described in this book, an emerging technology will likely be endoscope-assisted laparoscopic repair of colonoscopic perforations, thus pushing the standard toward minimally invasive surgery and repair of complications. It should be noted again, however, that the minimally invasive approaches should be reserved for those patients who are stable and without fecal contamination of the peritoneum.

Pearls and Pitfalls

- The best way to avoid colonoscopic complications is strict adherence to the techniques described above including attempts to decrease looping as the scope is advanced, avoiding blind advancement of the scope, and paying attention to the patient's pain level with avoidance of oversedation.
- Bleeding is best managed by endoscopic clipping, when available. As with all patients with bleeding, resuscitation should be undertaken immediately and invasive procedures only completed after resuscitation has begun and patient has demonstrated a response.
- Postpolypectomy syndrome is not a free perforation and can be managed conservatively. It should be in the differential diagnosis for patients with local peritonitis after polypectomy with electrocautery.
- Colonoscopic perforation is best managed according to the algorithms in Figs. 20.4 and 20.5. Minimally invasive techniques and conservative management can be undertaken in the absence of fecal peritonitis.

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Alternative Colorectal Imaging

21

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and Gregory D. Kennedy

Key Points

- Bowel preparation is required prior to most imaging techniques for evaluation of the colon. A patient should undergo a thorough history, physical exam, and instructional counseling in order to rule out contraindications specific to the imaging technique.
- Barium enema was historically the most common alternative imaging option to traditional colonoscopy, however required either considerable training in technique or interpretation of images. It has now lost favor among practitioners in the advent of more advanced imaging techniques, such as magnetic resonance colonography, virtual colonoscopy, and colon capsule endoscopy.
- CT and MR colonography have emerged as safe and effective methods for evaluating the colon, such that they have become the investigation of choice among clinicians for carefully selected patients with contraindications to traditional colonoscopy. However, MRC is decreasingly utilized as most radiologists feel that CTC is a more reliable and an overall easier technique to employ.
- Capsule endoscopy is a major technological innovation in small bowel imaging, which has emerged as the investigation of choice for suspected small bowel diseases. Novel applications for colon capsule endoscopy are now broadening indications to the detection of colonic lesions.
- There are several alternatives to traditional colonoscopy. Despite comparable outcomes in diagnostic yield and accuracy, colonoscopy remains the only means for potential diagnosis and therapeutic intervention. Thus, patients are required to undergo follow-up colonoscopy in order to obtain tissue diagnosis.

Introduction

In an era of persistently evolving medical technology, noninvasive diagnostic imaging has expanded to include a wide array of radiologic and endoscopic modalities employed for colorectal imaging. Despite the benefits of therapeutic intervention and tissue biopsy offered by traditional colonoscopy, an increasing number of alternative radiological imaging opportunities present a less-invasive approach to evaluation. Indications for noninvasive imaging are broad, including suspected neoplasm, acute and chronic obstruction, diverticulitis, inflammatory bowel diseases, and interrogation of other conditions suspected to involve the GI tract. In this chapter, we present four principal alternative imaging modalities to colonoscopy while discussing the strengths and weaknesses for each in various clinical circumstances.

Traditional Colonoscopy

The gold standard of care for diagnosis of various colorectal diseases, such as inflammatory bowel disease and neoplasms, require a tissue diagnosis. As such, colonoscopy with biopsy has long been regarded as the gold standard for detection and treatment [1]. Despite widespread acceptance and education among patients, various challenges are commonly encountered with colonoscopy related to the invasiveness of the procedure, poor patient compliance and anxiety, completeness of bowel preparation, and risk of

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bowel perforation [1–4]. Generally speaking, an incomplete colonoscopy is defined as the inability to intubate or visualize the cecum, or an endoscopic procedure limited by inadequate visualization of any part of the colon. As the number of colonoscopies performed annually has increased, so have the number of incomplete colonoscopies that the current reported rate is as high as 25% [5]. Causes of incomplete colonoscopy are vast, including inadequate bowel preparation, obstruction, tortuous colon, severe diverticulosis, stricture, and angulation or fixation colonic loops [6, 7]. Under these circumstances, the endoscopist is then faced with the challenge of offering viable alternative imaging modalities for screening versus repeat colonoscopy. In an updated joint guideline prepared by the American Cancer Society, the Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology, double-contrast barium enema (DCBE), colonoscopy, and computed tomography colonography (CTC) were endorsed as options for CRC screening in the United States and Canada [5]. In this chapter, we describe various imaging alternative for the detection of colorectal lesions.

Virtual Colonoscopy

Virtual colonoscopy (VC), also known as computed tomography colonography (CTC), has been hailed as a less-invasive and feasible alternative to traditional colonoscopy in the detection of colonic lesions, particularly carcinoma. VC is an alternative radiological technique for imaging the large bowel. There are two major roles of virtual colonoscopy, which are screening and diagnosis. VC has been described as an effective, well-tolerated, and cost-effective alternative for colorectal cancer screening in the United States, such that the American Cancer Society (ACS) recommended VC as a reliable alternative screening modality for CRC in 2008 [5, 8]. In general, the benefits of VC are derived from the lack of sedation and invasiveness, in addition to the ability to detect extracolonic lesions, which may offer an explanation for a myriad of symptoms. In contrast, VC may lead to additional investigations that may ultimately bring no clinical benefit to the patient; however, this is also true of colonoscopy. Of note, therapeutic intervention and tissue sampling is not possible with VC. Other drawbacks include unacceptable image quality owing to inadequate colonic distension or inadequate bowel preparation [2].

The technique for VC was first described by Vining and colleagues in 1994, which utilizes advanced imaging software to reformat standard computed tomographic (CT) images of the abdomen into two- and three-dimensional images of the colonic lumen [8]. VC is undertaken following a full bowel preparation, and the patient is then instructed to lie supine and prone in a multi-detector row scanner. Bowel distension is commonly performed by the radiologist, occasionally followed by administration of intravenous muscle relaxants and contrast medium to achieve smooth muscle paralysis and visualization of the bowel wall from luminal contents, respectively [2, 8, 9]. Spiral breath hold scans of the entire abdomen are obtained in the supine and prone positions [2, 9] (Fig. 21.1a–c).

VC may be performed for various indications; however, a cautionary note should be made that VC is not intended to replace colonoscopy as it does not offer the ability to biopsy tissue for definitive diagnosis. It is best suited for individuals who have a history of difficult colonoscopy and poor tolerance and those who have a low risk of a large lesion requiring

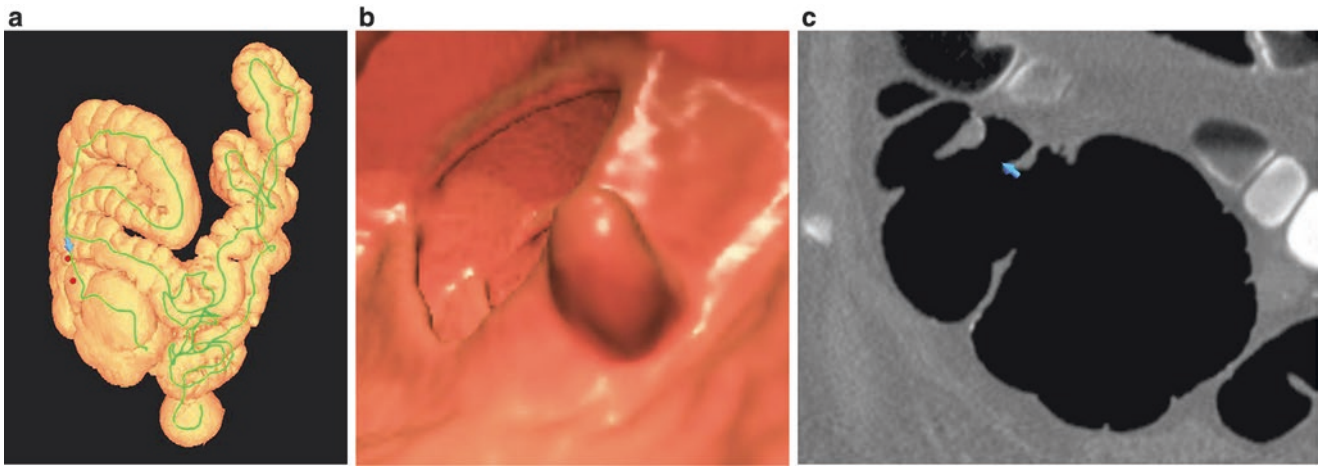

Fig. 21.1 CT colonography (CTC) in a patient with incomplete colonoscopy. (**a**) 3D colon map from CTC shows the colonic anatomy, including marked redundancy and tortuosity. The colon measured 261 cm along the automated centerline. The *two red dots* mark the site of two right-sided polyps identified at CTC. (**b**, **c**) 3D endoluminal (**a**) and 2D transverse (**b**) CTC images show a 10-mm polyp located on the back side of a colonic fold, which is a relative blind spot at optical colonoscopy

colonoscopy [2, 10]. For patients in which a follow-up colonoscopy is likely necessary, a same-day approach to polypectomy following VC avoids the need for subsequent bowel preparation [2]. VC is also possible for screening patients with a slightly higher than average risk, including those with a positive family history of CRC, or personal history of benign polyps. It is also largely of benefit to patients in whom colonoscopy screening is considered high risk, such as those on anticoagulation therapy, with history of adverse effects to sedation or history of difficulty or complicated colonoscopies. A prior incomplete colonoscopy may be considered a major indication for VC. Continually debated applications of VC include screening for nonspecific gastrointestinal complaints such as bleeding and iron-deficiency anemia [11]. For these purposes, VC has been performed in conjunction with fecal occult blood testing, but studies remain inconclusive as to whether VC should be formally recommended for this indication.

Early studies on the diagnostic yield of VC demonstrated variable sensitivities and specificities, which were largely attributed to differences in polyp size [11]. As more clinicians gained interest and formal training in VC assessment, sensitivity rates have seen an improvement such that now, several authors recommend VC as a highly sensitive and specific diagnostic tool for larger polyps (>10 mm), reporting sensitivities similar to that of colonoscopy for CRC detection (as high as 92% to 100%) [1–3, 12–17]. Much variability is seen with the detection of smaller lesions, those less than 10 mm. Sensitivity rates have been reported as low as 48–63% for lesions <10 mm, causing some authors to conclude that VC is inferior to colonoscopy while cautioning the use of VC as the only modality for diagnosis [11, 18]. The overarching trend in the literature implies greater sensitivity and specificity of VC for the diagnosis of CRC and significant polyps with increasing polyp size. In a meta-analysis by Mulhall et al., detecting polyps <6 mm was accomplished with a sensitivity of 48%, which increased to 70% for lesions 6–9 mm, and again to 85% for polyps >9 mm [18]. These data suggest that patient selection, medical history, and risk factors for colonic lesions play a critical role in the success and decision to recommend VC as an initial diagnostic modality.

Subsequent investigations following VC, such as imaging, invasive procedures, or repeat studies, incur additional cost, time, and resources. The inability to obtain tissue biopsies during VC necessarily generates an indication for follow-up investigations; however, this is also true of colonoscopy. A study by Atkin and colleagues identified a significant difference in the rate of additional colonic investigation after VC or colonoscopy for the detection of CRC or large (>10 mm) polyps (30% vs. 8.2%, respectively, $p < 0.001$) [1]. Despite these startling rates, the authors suggest the impetus for additional workup was not adjusted for, revealing greater than 50% of referrals after CTC were for reasons such as small polyps (<10 mm) or clinical uncertainty. Additionally, men were more likely to undergo a second examination due detection of cancer or polyp, whereas women were referred due to incomplete colonoscopy secondary to discomfort [1].

Overall, VC offers several potential advantages over traditional colonoscopy and demonstrates at least comparable outcomes in detection rates for the diagnosis colonic neoplasms in symptomatic and asymptomatic patients. VC may be particularly suitable for patients with low-risk symptoms, who are older, and with multiple comorbidities and those with a higher rate of failed colonoscopy. Widespread use of VC as an alternative to colonoscopy may be implemented for carefully selected patients, under provisions and guidelines of best practice.

Barium Enema

The double-contrast barium enema (DCBE) has existed as a radiologic alternative for CRC screening for decades, but interest has faded in light of the emergence of imaging alternatives yielding improved detection rates, such as VC [6, 10]. Despite its documented value in the detection of colonic polyps, DCBE is widely perceived as time-consuming and technically demanding. Traditional indications for single- and double-contrast barium imaging include diagnoses of large bowel symptoms and the identification of complications such as leak or fistula, as well as intussusception [10].

The contrast agent used in the single-contrast barium enema (SCBE) technique is a solid column of low-density, low-viscosity barium-administered retrograde from the rectum [7]. This is performed under fluoroscopic guidance and requires manual manipulation by the radiologist in order to thin the barium in order to contrast potential lesions as radiolucent defects against barium [7]. This process is rather challenging and requires considerable training and practice. In contrast, DCBE utilizes both a high-density, high-viscosity barium and air or carbon dioxide insufflation to visualize the mucosa [7]. Once both agents are instilled into the rectum, the mucosa is coated by a thin layer of barium against the gas-distended bowel, which creates the double contrast effect. Although this technique has been reported to be technically simpler than SCBE, the entire colon cannot be imaged in a single radiograph due to overlapping colon loops with residual barium pools, thus requiring a series of spot images. Various literature reviews have reported DCBE to be superior to SCBE in routine surveillance and detection of colonic polyps [7].

Some authors have questioned the accuracy of DCBE such that several comparative studies have emerged contrasting the stage and outcome for patients with CRC diagnosed by DCBE versus other imaging modalities and traditional colonoscopy [10, 19–22]. In a study by Kao et al., 22,000

colonoscopies were performed within a year, wherein 67% of patients underwent an incomplete initial colonoscopy and subsequently underwent DCBE [19]. Among those patients who underwent DCBE as a secondary study, 13% of DCBEs were deemed uninterpretable and of suboptimal quality. Furthermore, 50% of patients who underwent a repeat colonoscopy after DCBE demonstrated non-concordant findings [19]. Additionally, the primary reasons for incomplete colonoscopy were largely limited to incomplete bowel preparation or patient discomfort, which the authors believed were amenable causes on subsequent colonoscopy. Various reports have suggested similar findings, with reports of DCBE sensitivities ranging from 33% to up 89.8% for CRC screening and 20–50% for detection of adenoma [20–23]. In a Canadian study by Toma et al., factors associated with missed or new CRC undetected by DCBE included older age, female gender, a positive history of abdominal or pelvic surgery, a history of diverticular disease, and right-sided neoplasm, comprising 22% of the study population [23]. Altogether, various authors have identified significant miss rates for CRC ranging from 15 to 22% [8, 23]. With this data in mind, it is critical to counsel patients on the chances of missing a CRC to be one in five. These figures serve as a greater impetus to reevaluate the role of DCBE in an era of improving imaging modalities with higher sensitivities for disease detection (Fig. 21.2).

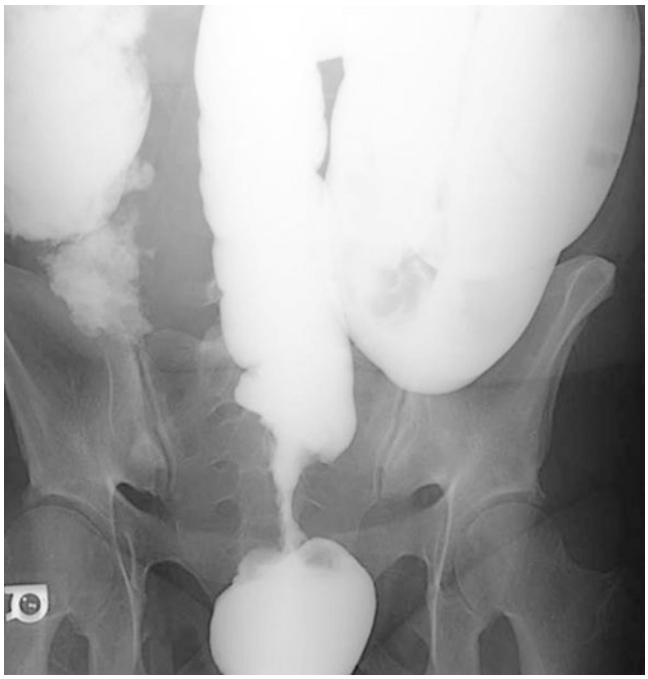

Fig. 21.2 Single-contrast barium enema in a patient with rectal bleeding. Frontal radiograph from barium enema study shows an irregular annular constricting mass in the rectum, which proved to be invasive cancer

Magnetic Resonance Colonography

In an era of increased utilization of medical imaging, the potential risks of future radiation-induced malignancies has led to intensified attractiveness of magnetic resonance imaging (MRI). Magnetic resonance enterography (MRE) has been reported to offer high diagnostic accuracy for detection of distal ileal and colorectal inflammatory conditions (24). Magnetic resonance offers a myriad of benefits and has emerged as a preferred method of noninvasive imaging for inflammatory bowel diseases, using enterography technique. The superiority of MR imaging among other imaging options is well established in revealing superior soft-tissue contrast as well as the absence of ionizing radiation [24]. This is particularly important for patients requiring frequent imaging follow-up in IBD and carcinoma. Advantages of MR imaging include visualization of the entire colon, including intraluminal, extraluminal, and mural definition, permitting detection of complications such as fistulas and abscesses, in addition to the lack of requiring bowel preparation. Magnetic resonance colonography (MRC) utilization, however, has been largely limited to a few centers of excellence, as most radiologists feel that CTC is a more reliable, reproducible, available, and overall easier technique to employ.

There are two principle MR techniques, dark-lumen MRC and bright-lumen MRC [25, 26]. For both approaches, adequate colonic distension is a prerequisite for accurate evaluation. In the dark-lumen approach, colonic distension is achieved with instilling 2 L of normal saline. Alternatively, room air and CO_2 have been utilized with comparable results [25]. Dark-lumen MRC involves the administration of intravenous (IV) gadolinium (Gd) contrast agents, which illuminate the bowel wall, thus differentiating mural abnormalities from stool, which does not enhance [25–27]. In contrast, bright-lumen MRC involves enhancement of the intraluminal space via administration of MRI contrast agents mixed with water enemas [27]. Alternatively, T2-weighted images will also enhance intraluminal content with water enemas (Fig. 21.3a–c). Lauenstein and colleagues contrasted the benefits of dark-lumen to bright-lumen MRC and found the overall cost of dark-lumen MRC to be lower due to smaller amounts of contrast used for IV administration, compared with contrast-enhanced water enemas in bright-lumen MRC [28]. The basis of bright-lumen MRC relies on visualization of filling defects or the presence of mucosal thickening. As a result, air may be confused as defects, whereas dark-lumen imaging relies on directly evaluating mucosal enhancement [27].

Prior to any imaging application, metallic implants or pacemakers should be identified in order to perform MRC successfully. Caution is advised for patients with claustrophobia, and impaired renal function must be identified prior to administration of IV gadolinium, which increases the

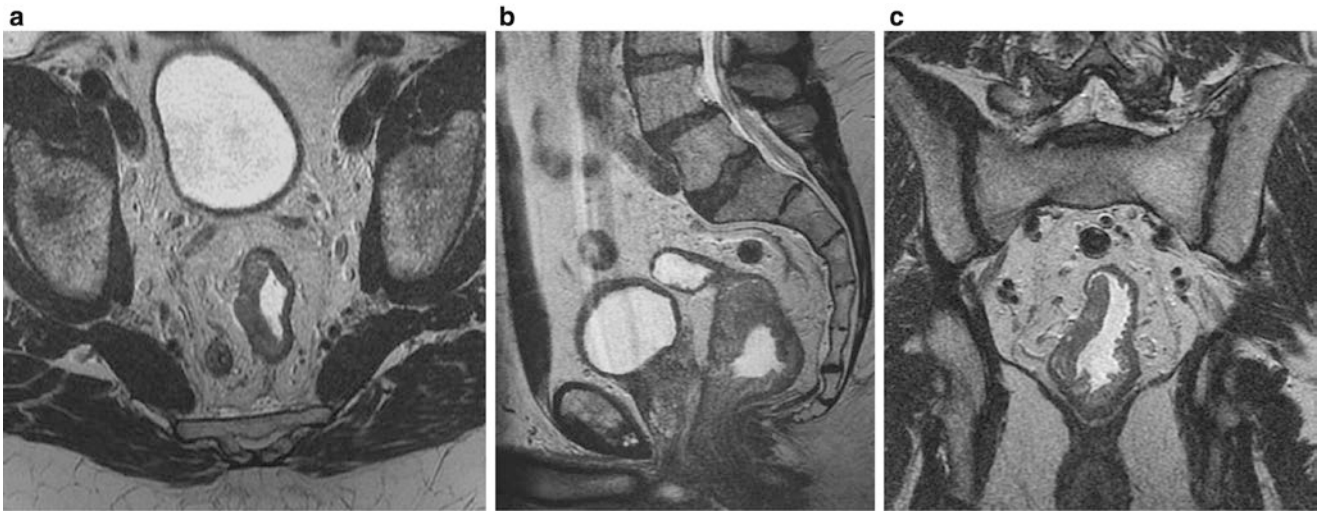

Fig. 21.3 Magnetic resonance (MR) imaging for rectal cancer staging. (**a**–**c**) Axial (**a**), sagittal (**b**), and coronal (**c**) T2-weighted MR images show right-sided rectal wall thickening from a large T2 rectal cancer. Note enlarged heterogenous perirectal lymph node, which upstages the tumor from stage I to stage III. The bright luminal contrast is due to gel placed per rectum immediately prior to imaging

risk of nephrogenic systemic fibrosis [29]. The standard bowel preparation prior to MRC generally mandates the elimination of stool via cathartics. The presence of stool may alter image interpretation leading to increased false-positive rates on bright-lumen MRC, in which stool may appear as filling defects. Conventional bowel-cleansing regimens are consistent with traditional colonoscopy and require ingestion of 2–3 L of polyethylene glycol solution the day prior to evaluation.

The hindrance of stool evidenced on exam has led to the development of various stool-tagging techniques, which deliberately alters the signal of stool so that it becomes no longer visible [30]. Stool-tagging techniques obviate the need for arduous cathartic preparation, and various authors have shown improvements in compliance rates [31, 32]. Tagging is accomplished by ingestion of contrast agents that cause stool to match the signal of the enema, whether bright of dark. Although improvements in false-positive and false rates have been reported, inadequate tagging has also been shown to result in nondiagnostic evaluations [33]. Various tagging agents have been used. The ideal tagging agent will be inexpensive, well tolerated, and robust, generating uniform tagging signals without compromising artifacts. Tagging agents are ingested with low-fiber and low-manganese-containing meals for 2 days priors prior to examination [30]. Manganese-rich foods, such as chocolate and fruits, have the potential to cause bright signal stool artifacts on dark-lumen MRC [27, 34]. A less expensive alternative is barium oral contrast, which renders the stool dark on MRC, hence may be applied in dark-lumen MRC. Ferumoxsil is a dark-lumen agent consisting of small iron particles that may also be used in dark-lumen MRC [27].

The accuracy of detection is of importance as it directly affects therapeutic decisions and patient prognoses in specific clinical scenarios. Numerous studies have evaluated the performance of MRC in contrast to the findings on traditional colonoscopy, surgery, or both with overall sensitivities and specificities to be 91–92.1% and 71.0–72.0%, respectively [24, 35]. Commonly, segment specific detection has been evaluated, which independently evaluates the accuracy of detection at different levels of the colon, including the terminal ileum, ascending colon, descending colon, transverse colon, sigmoid, and rectum. Segment-based sensitivities have been reported to range from 55.1 to 79.1% and specificity of 93.6 to 98.2% [24, 36, 37]. In a study by Jiang and colleagues, MRC identified a greater overall number of fistulas in the distal ileum and associated abscesses among patients with known or suspected IBD, compared to traditional colonoscopy [24]. MRC has been shown to be inferior to colonoscopy under specific conditions, such as low-grade or mild inflammation, and following same-day colonoscopy [36]. These MRC have shown thickened mucosal enhanced with pronounced signal increased on T2-weighted images mimicking active inflammation, which have been attributed to instrumented areas during colonoscopy [24]. As a result, some authors do not recommend performing MRC following colonoscopy on the same day.

MRC is an effective, low-risk, and reliable alternative to standard colonoscopy in the detection of colorectal disease and complications, also serving as a salvage modality following incomplete colonoscopy. Ajaj et al. evaluated 37 patients following incomplete colonoscopies and successfully identified 35 lesions [38]. In another study, investigators identified 51 patients with incomplete colonoscopies

and performed air dark-lumen MRC without fecal tagging and successfully completed 50 cases [38, 39]. Overall, MRC is comparable to that of traditional colonoscopy offering the greatest benefit to patients with elevated risk associated with additional exposure to ionizing radiation and may be considered. Large, prospective, randomized trials are required for definitive recommendations for MRC over traditional colonoscopy in an otherwise symptomatic or asymptomatic patient with suspected colorectal lesions.

Capsule Endoscopy

Capsule endoscopy (CE) is a relatively new technique for imaging for the gastrointestinal tract. First introduced in the United States and Europe in 2000, CE was primarily used for evaluation of the small bowel [40–42]. Fifteen years later, CE is widely used across the world, serving as a highly revolutionized method of direct endoscopic imaging and the first-line investigation for disease of the small bowel [41]. The most common indications for small bowel CE include suspected bleeding, Crohn's disease, celiac disease, and even small bowel tumors [40, 41, 43]. Various capsule endoscopy systems are now available and differ with respect to the field view, dimensions, additional optical enhancements, and image acquisition rates [40, 41]. Examples of small bowel CE devices include PillCam (Given Imaging®; Yoqneam, Israel), EndoCapsule (Olympus; Center Valley, PA, United States), MicroCam (IntroMedic; Seoul, South Korea), OMOM capsule (Jinshan Science and Technology; Chongqing, China), and CapsoCam (CapsoVision; Saratoga; United States) [41]. Several newer generations of small bowel CE have emerged on the market, offering greater versatility in a variety of applications such that its role and application have expanded to detect esophageal and colonic lesions [40–48].

In general, CE is considered a straightforward procedure; however, various safety concerns have been raised such as capsule retention rate, possible obstruction, and perforation. Contraindications to CE include known or suspected strictures, gastroparesis, swallowing disorders, obstruction, and fistulas [41, 49]. There is also a theoretical risk of interference with electromagnetic cardiac devices, which may interfere with video resolution and quality of the video. There is no known association with cardiac events or cardiac device malfunction [46]. Capsule impaction has been reported to be 1.4–2% [43, 49]. In the instance that a capsule is retained, endoscopic or surgical removal is often indicated. As a result, Given Imaging (Yoqneam, Israel) created the "patency capsule" [40, 50]. This is a dissolvable capsule, which is similar in shape and size to the actual camera, and is composed of lactose and barium sulfate surrounded by non-dissolvable cellophane walls [41]. The patient first undergoes a study with the patency capsule which allows the clinician to the verify patency prior to performing the actual CE examination. A radiofrequency identification tag permits localization of a radiofrequency identification tag located within the capsule via radiography or a portable scanner. Once ingested, the capsule body begins to dissolve after 30 h in a fluid-filled environment. When dissolved, the outer cellophane membrane is able to pass through any potential strictures. It is considered safe to continue with CE following excretion of the intact patency capsule of if undetected after 30 h. As with the previously mentioned imaging alternatives, the CE has no therapeutic capability.

Colon Capsule Endoscopy

Colon capsule endoscopy (CCE) is a much more recent and novel, noninvasive technique for imaging the entire colon. There are a limited number of studies that have investigated its utility. Colorectal cancer screening is the most commonly cited application for CCE, particularly given the persistent fraction of noncompliant patients who decline screening due to anxiety [41, 45]. CCE may offer a new avenue for screening and diagnosis in this subset of patients; however, more data is required regarding indications, bowel preparation, and scoring systems prior to providing definitive recommendations.

There are two models of colon capsules available by Given Imaging (Yoqneam, Israel). The earliest of which has been previously described in the literature [46]. The PillCam Colon is an ingestible capsule with dual cameras to allow for image capture from both ends, each offering a 156° visual angle. It is 31 mm by 11 mm in size and equipped with light control options to allow for optimal visualization of the colonic mucosa [41, 45]. A second generation of the PillCam, PCCE-2 (Given Imaging, Yoqneam, Israel), was developed for increased simplicity and sensitivity of the procedure. This model is slightly larger in size, 31.5 mm by 11.6 mm, and works in conjunction with software and a data recorder for video processing. Each camera captures a wider angle of view allowing almost 360° of visualization. An adjunct to the PCCE-2 system is the data recorder, the DR3, which alerts the patient and clinician throughout the study. The DR3 alerts the patient to continue with the bowel preparation protocol and ingest "booster" laxative as it recognizes small bowel mucosa, thus allowing the capsule to progress into the colon. In a series by Adler and colleagues, the DR3 identified the correct time for signaling the ingestion of booster laxative in 98.3% of cases [47].

With no exceptions, patients are required to undergo bowel preparation prior to CCE. Not only does this facilitate visualization but this also encourages progression of the capsule throughout the small intestine into the colon via a "booster" laxative. The CCE functions best in clear liquid under the "submarine view" [41]. Patients are instructed to follow a clear liquid diet one day prior to examination and

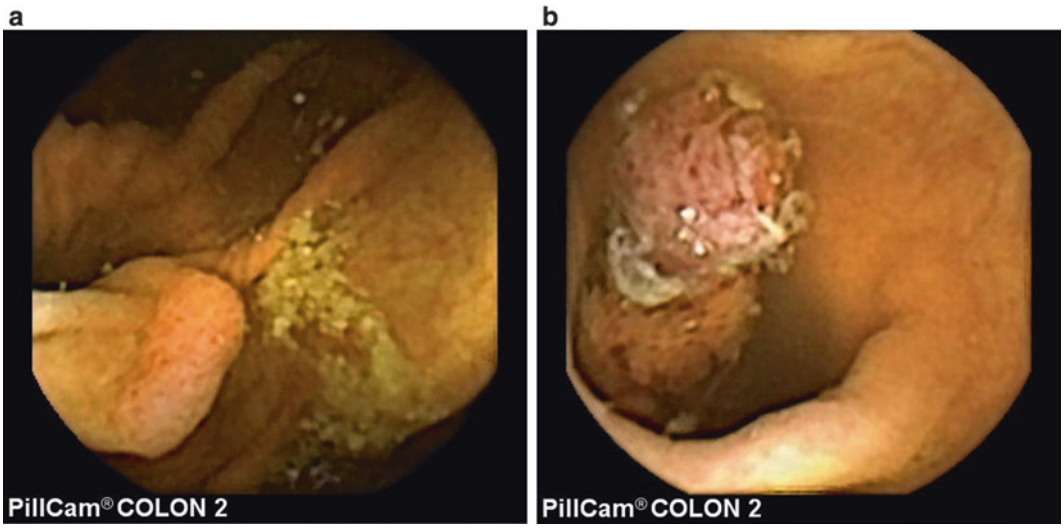

Fig. 21.4 Colon capsule endoscopy in two different patients. (**a**, **b**) Images from two patients undergoing colon capsule endoscopy following vigorous bowel preparation show a diminutive cecal polyp on a fold (**a**) and a 15-mm pedunculated TVA (**b**)

orally ingest 2–3 L of polyethylene glycol (PEG) the evening before. On the morning of the procedure, the patient must ingest another liter of PEG. The patient is administered a dopamine antagonist prior to ingesting the capsule. Two hours later, another 45 mL of sodium phosphate solution is ingested to stimulate capsule progression [41]. Various authors have attempted different variations of bowel preparations so as to decrease the time needed for preparation; however, no significant differences were found between variation protocols [47].

The efficacy and utility of CCE has been investigated in few recent studies. In a prospective, multicenter European study of 328 adults with known or suspected colorectal polyps, successful capsule excretion rate (for first-generation PCCE) was 69% after 6 h of ingestion, which improved to 92.8% by 10 h [48]. In this same study, the sensitivity and specificity of CCE for detecting polyps >6 mm were 64% and 84%, respectively. For larger, advanced adenomas, the sensitivity was slightly better at 73% and specificity was 79% [46]. Another multicenter study investigating the second-generation PCCE-2 was found to have improved sensitivities and specificities for polyps >6 mm at 84% and 88% for polyps >10 mm, along with specificities reported as 64% and 95%, respectively [47]. Similarly, a study by Spada and colleagues reported sensitivities between 84% and 89% for the detection of polyps >6 mm (Fig. 21.4a, b) [51].

The limitations with CCE are attributed to possible device or camera dysfunction, extensive bowel preparation, and time-consuming video assessment. Although CCE reveals great potential as an exciting area in gastroenterology, more extensive research is required in order to elucidate a clear diagnostic and cost-effective benefit over traditional colonoscopy.

Conclusion

There are several alternative testing modalities for the detection of colorectal diseases. In recent years, virtual colonoscopy has emerged as the most comparable modality to traditional colonoscopy, while barium enema has drifted in favor and interest among practitioners. When colonoscopy is not a feasible option for high-risk patients, or when serial imaging is indicated for monitoring disease, magnetic resonance colonography serves as a lower risk and comparably accurate alternative. The role and efficacy of colonic capsule endoscopy will appear as additional comparative studies and novel technological improvements emerge in the future. Patients should therefore be counseled with balance information regarding the potential benefits, risks, and limitations to screening alternatives within the framework of individualized medical risk factors.

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22 Current Endoluminal Approaches: Transanal Endoscopic Microsurgery, Transanal Minimally Invasive Surgery and Transanal Total Mesorectal Excision

Cici Zhang and Patricia Sylla

Key Points

- Current practice in rigid TES (TEM and TEO) is built on over 30 years of experience performing submucosal and full-thickness endoscopic resection of rectal lesions through rigid platforms, where improved visualization and exposure of rectal lesions have resulted in superior local control relative to conventional transanal excision.
- Extensive published data on the long-term oncologic results of local excision for rectal adenocarcinoma including TES has demonstrated that TES with curative intent should only be offered to carefully selected T1 rectal adenocarcinoma with no adverse histopathological features and local recurrence rates equivalent to that of TME, but with substantially lower morbidity.
- TAMIS, which incorporates standard laparoscopic instruments inserted through disposable single ports, has enabled wider adoption of TES and reduced setup and operative time, but has probably not shortened the learning curve for overcoming difficulties of operating within the confined transanal working place, particularly with suturing full-thickness rectal defects associated with peritoneal entry.
- Given the technical and operational challenges of open, laparoscopic, and robotic TME, taTME which combines abdominal and transanal bottoms-up dissection of the rectum and mesorectum has facilitated completion of these complex procedures, particularly for low rectal tumors in obese males.
- The cumulative published experience with taTME based on the largest published series with cohort size ranging from 16 to 140 patients has demonstrated an 89% rate of TME completion with 0–13% incidence of positive circumferential resection margin (CRM). Current ongoing trials are exploring the possibility that taTME might represent a new standard in the surgical management of mid and low rectal cancer.

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The Evolution of Transanal Endoscopic Surgery and Transanal Total Mesorectal Excision

TEM and TEO

Contemporary management of rectal lesions has been transformed by innovation and technology over the past few decades. Until recently, abdominoperineal resection (APR) and low anterior resection (LAR) were considered the standard definitive procedures for benign rectal lesions too large for conventional polypectomy and too proximal for transanal excision (TAE). These radical oncologic resections result in significant and costly morbidity, non-negligible mortality, significant functional disorders including the low anterior rectal syndrome, and the psychologic repercussions of temporary or permanent ostomies. Even when foregoing anastomotic complications and defecatory disturbances, APR still results in a substantial incidence of sexual and urinary dysfunction, as well as abdominal and perineal wound-related complications [1, 2].

Transanal endoscopic microsurgery (TEM, Richard Wolf Company, Tubingen, Germany) was pioneered by Buess in 1983 to perform endoscopic local resection of proximal rectal tumors inaccessible to endoluminal or transanal modalities [3]. TEM and transanal endoscopic operations (TEO, Karl Storz GmbH, Tuttlingen, Germany, Fig. 22.1a, b) are the two rigid metal TES platforms currently commercially available. Both consist in a 4-cm diameter meter beveled

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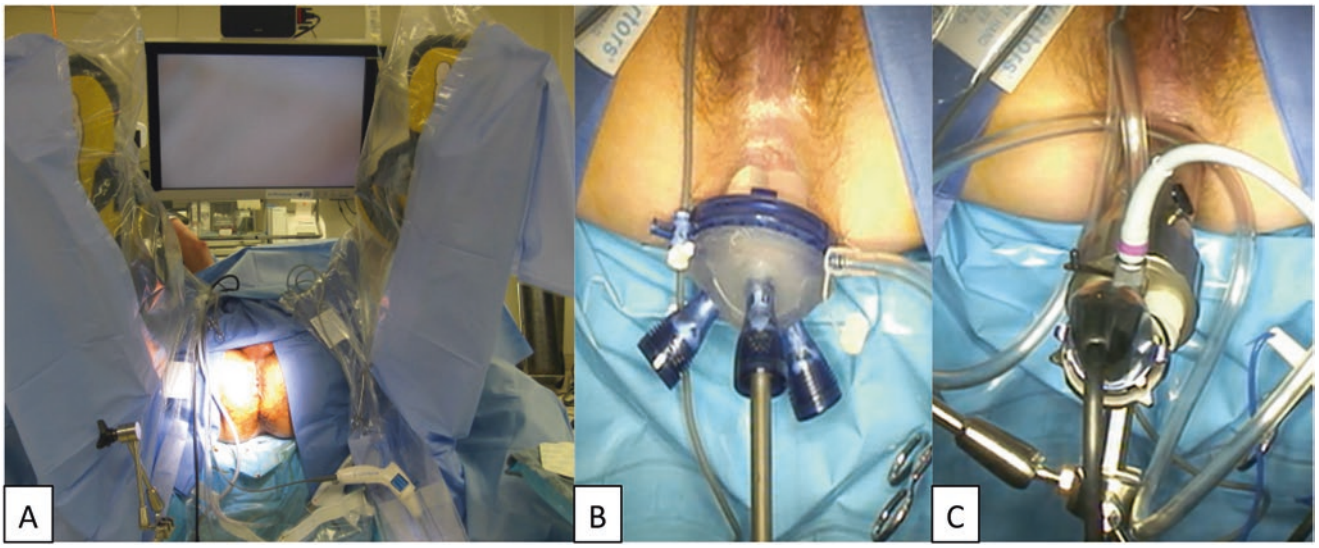

Fig. 22.1 Patient positioning for TES and operative setup. Patients are most commonly placed in high lithotomy position (**a**). The TEO platform is inserted and secured to the operating table using an articulating arm. TEO procedures are performed by a single operator (**b**). Alternatively, a TAMIS platform is inserted which requires an operator and dedicated camera assistant (**c**)

proctoscope sealed by a faceplate that provides multiport access and an airtight seal. The rectoscopes come in a variety of lengths (12, 13.7, and 20 cm for TEM and 7.5, 15, and 20 cm for TEO) to accommodate the location of the pathology with the 20 cm proctoscope providing access to the upper rectum and even the rectosigmoid. TEM and TEO sets include specialized instruments with angled tips, which are designed to improve ergonomics, minimize instrument collision, negotiate difficult angles, and allow for full-thickness dissection and suture closure of rectal defects. The rigid proctoscopes are equipped with a telescope (TEO) and stereoscope (TEM) that are affixed to the platform and provide HD and 3D (TEM) optics. The proctoscopes are in turn mounted onto the operating table by an articulating arm, providing stability of the operative field, and easily piloted by a single operator. TEM and TEO telescopes are compatible with standard laparoscopic cameras which offer the benefits of laparoscopy including HD and even 3D visualization (TEM). The TEM tower is also equipped with an automatic pressure-controlled CO_2 insufflation system that evacuates the smoke generated during dissections while maintaining a stable pneumorectum during transanal dissection.

Relative to radical rectal resections, TEM and TEO are associated with shorter OR time, shorter length of hospital stay and faster recovery, negligible morbidity, and negligible mortality. The cumulative incidence of bleeding, urinary retention, wound dehiscence, and infection ranges from 3 to 23% in the largest TEM series [4–8], with a 4.3–13.3% [6, 9] incidence of peritoneal entry. In a recent meta-analysis by Clancy, six studies encompassing 927 local excisions were compared for oncologic outcomes and postoperative complications [10]. There was no difference between postoperative complication rates (OR, 1.018; 95% CI, 0.658–1.575; $p = 0.937$). TEM had a higher rate of negative microscopic margins in comparison with transanal excision (OR, 5.281; 95% CI, 3.201–8.712; $p < 0.001$). TEM had a reduced rate of specimen fragmentation (OR, 0.096; 95% CI, 0.044–0.209; $p < 0.001$) and lesion recurrence (OR, 0.248; 95% CI, 0.154–0.401; $p < 0.001$) compared with transanal excision [10]. Despite significant heterogeneity in surgeon experience, pathology, and follow-up, the data clearly demonstrated that improvement in visualization and technical precision facilitated by the stable endoscopic TEM and TEO platforms resulted in superior oncologic outcomes when compared to TAE.

TAMIS

Until recently, the utilization of TES has remained largely confined to high-volume and specialized centers. For several decades, widespread adoption of TEM and TEO was hindered by prohibitively high costs of the rigid platforms, scarcity of training, and steep learning curve associated with mastering of techniques. In 2009, during the height of enthusiasm for single-incision laparoscopy, an alternate transanal endoscopic setup using single-incision laparoscopic disposable ports was described named transanal minimally invasive surgery (TAMIS) [11, 12]. TAMIS has rapidly broadened adoption and application of TES for a variety of indications without compromising the benefits of TEM or TEO. Because TAMIS ports are not anchored to the operating table, it

requires the operating surgeon to work side by side with an assistant who holds the bariatric length laparoscope that is recommended for use during these cases. TAMIS can be performed using standard laparoscopic equipment through a variety of single-incision platforms at much lower per-case costs relative to the cost of capital investment in rigid platforms and specialized TEM/TEO equipment [7]. Several commercially available devices have been described for TAMIS, but in the USA, the commercially available devices include the SILS Port (Medtronic, Mansfield, MA, USA) and the GelPOINT Path Transanal Access Platform (Applied Medical, Rancho Santa Margarita, CA, USA, Fig. 22.1c). The Triport (Olympus, Center Valley, PA) and the SSL (single-site laparoscopic access system, Ethicon Endo-Surgery, Cincinnati, OH, USA) have been reported in small series with comparable results mostly outside the USA [13, 14]. Flexible laparoscopes such as the Endoeye Flex (Olympus) and standard colonoscopes have been used through TAMIS platforms in order to reach higher up in the rectum and overcome the instrument collision. Interestingly, the use of automated suturing devices and self-retained barbed sutures, as well as specialized high flow insufflation and smoke evacuation systems to maintain a stable pneumorectum and a clear surgical field, has increased the per-case costs of TAMIS. High-flow CO_2 insufflation units such as the UHI-4 (intra-abdominal Insufflation Unit, Olympus) and the Airseal Insufflation System (SurgiQuestInc, Milford, CT, USA) have been used in conjunction with TES platforms. The Airseal in particular provides a continuous flow circuit that evacuates CO_2 and smoke and quickly recirculates filtered and high-pressure CO_2, thereby maintaining a stable pneumorectum at all times. The Airseal insufflation system is reminiscent of the TEM automatic pressure-controlled CO_2 insufflation system, but it requires the use of disposable specialized cannulas inserted through the transanal platform. Finally, the use of TAMIS has also been described in conjunction with robotic platforms, harnessing the advantage of magnified 3D optics and greater dexterity of the robotic EndoWrist movements [15].

While the use of conventional laparoscopic equipment with TAMIS can be versatile and cost-saving, it poses significant limitations as well. The maneuverability of straight instruments through a small transanal workspace remains limited, and overcoming instrument collision makes for a steep learning curve in TAMIS [16]. In addition, the shorter TAMIS platforms provide limited access to the proximal rectum, and rectal lesions located behind haustral valves in upper rectum may be more difficult to reach, resect, and rectal defects more difficult to close using TAMIS platforms relative to the longer TEM or TEO platform [17]. The longer rigid platforms facilitate successful transanal closure of these defects by maintaining patency of the rectal lumen, particularly in the event of leakage of CO_2 following peritoneal entry. This is reflected in the relatively low conversion rates to laparoscopy or laparotomy in large TEM and TEO series which range from 0 to 41.6%, but average 10% [4, 5]. On the other hand, peritoneal entry during TAMIS appears to result in high rates of conversion to laparoscopic closure of rectal defects, ranging from 0 to 86%, which likely reflects the difficulties stenting the rectum adequately enough to permit closure of the rectal defects [18–20].

Transanal TME

Recent improvements in the treatment of rectal cancer can be attributed to the standardization of TME technique and the selective use of chemotherapy and radiation therapy [21]. Local recurrence rates have decreased from as high as 45% using traditional techniques to <10% after TME alone, and <6% after TME if performed with negative circumferential radial (CRM) and distal margins, in conjunction with radiation therapy [22, 23]. The introduction of minimally invasive techniques including laparoscopy and robotics has not altered the morbidity or negative impact of open TME on quality of life following sphincter-sparing and non-sphincter sparing TME. Among the largest randomized controlled trials comparing open versus laparoscopic TME such as the COLOR II, ACOSOG, and COREAN trials, wound infection rates have ranged from 5 to 6.5% and anastomotic leaks from 1.2 to 10%, without statistically significant differences between the groups [24–26]. Oncologic equivalence or non-inferiority of laparoscopic TME was demonstrated across all the above trials except for the ACOSOG Z6051and AlaCart trials [24, 27]. The 30–40% incidence of sexual, urinary, and defecatory dysfunction are compounded by the addition of neoadjuvant radiation and have not been lowered with the use of laparoscopic or robotic surgery, despite improved visualization of pelvic nerves during pelvic dissection [25, 26]. However laparoscopic TME is significantly more technically challenging and is associated with a steep learning curve. Laparoscopic TME is particularly challenging during dissection of the lowermost part of the mesorectum, especially in male patients with high body mass index (BMI) and narrow pelvis. While conversion rates have progressively decreased from 30% early on in the laparoscopic TME experience to 16% and 11% in the COLOR II and ACOSOG Z6051 trials, respectively [24, 25, 28], overall adoption of laparoscopic TME has remained at 30% or less.

The recent increase adoption of robotic surgery during TME reflects the superior 3D visualization and enhanced dexterity and ergonomics provided by the da Vinci™ system (Intuitive Surgical, Sunnyvale, CA, USA), which may help overcome some of the challenges of deep pelvic dissection and reduce the steep learning curve [29]. Despite the suggestion that robotic surgery may reduce conversion rate during

TME across several large-case series and comparative studies, the recent ROLARR trial, a prospective, randomized-controlled of robotic-assisted versus laparoscopic TME, has not shown any statistically significant difference in conversion rates or other perioperative outcomes between laparoscopic and robotic TME [30].

In light of the ongoing anatomic and technical challenges of achieving sphincter-preserving TME while achieving a complete mesorectal specimen and negative margins, the concept of transanal Natural Orifice Transluminal Endoscopic Surgery (NOTES) colorectal surgery rapidly evolved from the experimental setting to clinical application [31, 32]. By accessing the rectum and mesorectum from a primarily transanal endoscopic approach, taTME aims to overcome these limitations and facilitate completion of these complex procedures. Since the report of the first case of hybrid laparoscopic-assisted transanal TME in a female patient with a T2 N1 mid-rectal cancer in 2009 using a TEO platform, several small pilot studies subsequently demonstrated the feasibility and safety of this approach [33–35]. These pilot studies were quickly followed by medium-sized series of taTME with the largest cohort size ranging from 16 to 140 patients with taTME performed for benign and malignant indications, in combination with LAR or APR, using a variety of transanal platforms and types of transabdominal assistance (open, multiport, single port and hand-assisted laparoscopy, and robotic). Cumulatively, the series have reported 98% rate of complete and near-complete TME specimens and a CRM-positive CRM ranging 0–13%, which is comparable to historical open and laparoscopic TME outcomes with the benefit of exceedingly low conversion rates

Although the experience with taTME remains preliminary with no long-term oncologic or functional outcomes and no randomized trials, these preliminary results strongly support taTME as an attractive alternative and potential new standard in the surgical treatment of resectable low and mid-rectal cancer.

TES: Indications, Contraindications, and Patient Selection

TEM was initially intended for the management of large adenomas deemed unresectable by standard polypectomy or conventional transanal excision (TAE). Since its inception, TES has become an attractive alternative to standard LAR and APR with data supporting its safety profile, significantly lower postoperative pain, and reduced recovery time [36, 37]. Most importantly, TES provides a much more suitable choice for benign lesions that would otherwise be overtreated with LAR or APR. Indications for local excision using TES have expanded to include large adenomas, incompletely resected adenomas with high-grade dysplasia, small low-risk carcinoids, other benign rectal pathologies, as well as carefully selected T1 rectal tumors and more advanced rectal tumors in the palliative setting.

Rectal Adenoma

TES Versus TAE and EMR

In the largest TEM and TEO retrospective series published to date with cohort size ranging from 91 to 353 patients, resection of ≤3 cm rectal adenomas using either submucosal dissection or full-thickness excision resulted in excellent long-term local control with local recurrence rates (LR) ranging 4–10%, mortality under 1%, and morbidity ranging 3–8% [37–40]. With respect to local control, as with TAE, several large TEM series have shown that the strongest predictor for LR following TEM was margin positivity [37, 38]. Several TEM and TAE comparative series have demonstrated superior local control with TEM, which is likely related to the benefits of rectal distention with CO_2, magnified high definition laparoscopic visualization, and more precise dissection through transanal endoscopic platforms. Clancy et al. recently demonstrated in a meta-analysis of TAE and TEM/TEO series ($N = 927$) that TEM was associated with higher rate of negative margins (OR, 5.281; 95% CI, 3.201–8.712; $p < 0.001$), lower rate of specimen fragmentation (OR, 0.096; 95% CI, 0.044–0.209; $p < 0.001$), and lower recurrence rate (OR, 0.248; 95% CI, 0.154–0.401; $p < 0.001$) compared to TAE for benign and malignant rectal pathologies comparing TEM and TAE [10].

TES is also an important adjunct in centers that do not routinely perform endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Relative to conventional polypectomy and EMR, TES is associated with a lower early adenoma recurrence rate [41]. In addition, TES facilitates en bloc resection of complex adenomas including flat, large, prolapsing adenomatous lesions, or particularly in the setting of extensive mucosal scarring. In a retrospective review of 292 patients undergoing excision of adenomas larger than 2 cm via either TEM or EMR, a higher incidence of incomplete resection after a single EMR intervention resulted in a higher incidence of early recurrences relative to the TEM group (31.0 versus 10.2%, p <0.001) [42]. Of note, when additional endoscopic EMR procedures were performed within 6 months from the original procedure, the long-term efficacy of EMR was equivalent to that of TEM.

Complex Adenomas

Traditionally, adenoma size greater than 3 cm, referred to as giant adenomas, has been considered a relative contraindication for TES due to the higher incidence of positive margins and LR. Other relative contraindications to TES include circumferential and near-completely circumferential adenomas,

where, in addition to the increased risk of R1 resection, there is an increased risk of an underlying malignancy, and full-thickness closure of near-circumferential rectal wall defects can be exceedingly difficult, with a high risk for conversion, particularly early during the operator's learning curve. Several groups with extensive TEM experience and expertise have reported their results with TEM performed for rectal tumors larger than 5 cm. In a retrospective review of 233 rectal adenomas with median diameter of 5 cm (1–12 cm) resected full-thickness using TEM, Allaix et al. reported an 11.1% positive margin rate and a 5.6% overall LR rate at a median follow-up of 110 months [38]. However, the rate of positive margins was 8.9% for lesions <5 cm versus 20.9% for lesions ≥ 5 cm ($p = 0.047$). Overall these findings support the use of TES to resect large rectal adenomas as an alternative minimally invasive strategy to avoid proctectomy; however, this is at the cost of an increased risk of an underlying invasive cancer, increased LR, and higher chance of conversion due to the technical difficulty of closing large full-thickness rectal wall defects associated with large rectal lesions [38, 43, 44].

To date, the published TAMIS experience with rectal adenomas is still limited but growing quickly. Among a total of 350 cases from 15 TAMIS series published between 2010 and 2015, 163 consisted in adenomas (Table 22.1) [7, 11, 12, 16, 17, 19, 20, 45–53]. The overall R1 resection rate for benign and malignant lesions ranged 0–17%, but was below 10% among the largest TAMIS series. Morbidity was similar to historical TEM/TEO rates and ranged from 0 to 25%. Noticeable among TAMIS series is the fact that there is limited to no data on resection of larger rectal lesions (>3 cm) and limited data on resection of lesions in the upper third rectum [7, 11, 12, 16, 17, 19, 20, 45–53]. The scant TAMIS experience with full-thickness resection of larger and upper third rectal lesions may reflect the intrinsic limitations of shorter disposable transanal platforms to safely reach, expose, and permit dissection of lesions that lie behind rectal folds and maintain rectal distention in the face of critical loss of pneumorectum during peritoneal entry [54].

T1 Rectal Cancer

The use of TES alone in the curative treatment of rectal cancer remains controversial. Although earlier TEM cohort studies demonstrated unacceptably high rates of LR for unselected T1 (range, 0–26%) relative to a ≤6% LR rate for T1 tumors treated with radical proctectomy [55], more contemporary series have demonstrated its curative potential for carefully selected T1 rectal cancers with low-risk histopathological features [56]. The risk of locoregional recurrence following local excision of T1 rectal cancer is directly correlated to the risk of associated lymph node metastasis, which is not addressed by any of the local excision techniques. While standard preoperative staging of rectal cancer with CEA, stating CT scans and pelvic MRI and/or endorectal ultrasound (ERUS) can exclude patients with T2 and more advanced rectal tumors, the challenge resides in selecting T1 tumors associated with the lowest risk of lymph node metastasis and that will likely be cured with R0 local resection alone.

Histopathologic factors associated with increased risk for local recurrence following local excision of T1 rectal tumors include depth of submucosal involvement, poor differentiation grade, lymphovascular invasion (LVI), positive resection margins (R1 resection), large tumor size, and the presence of tumor budding [57–59]. One of the most important independent predictor for local recurrence following local excision of T1 rectal cancer is the extent of submucosal invasion. In a longitudinal cohort study of 182 patients with adenocarcinoma, Kikuchi et al. determined that the level of tumor invasion into the submucosa is predictive of LR following TEM for T1 tumors. Submucosal invasion was further classified as sm1, sm2, and sm3 representing invasion into the upper, middle, and deepest third, respectively, with deeper submucosal invasion correlating with increased risk of LVI and lymph node metastasis [60]. Kikuchi and Nascimbeni independently determined from large cohorts of T1 colorectal cancers undergoing radical resection that sm1, sm2, and sm3 depth of tumor invasion was associated with a 0–3%, 8–10%, and 23–25% risk of lymph node metastasis, respectively [59, 60]. As a result, local excision alone for sm3 and high-risk sm2 lesions is associated with higher risk of lymph node metastasis and local recurrence.

Another adverse prognostic factor associated with local recurrence and metastases, as well as significantly worse overall and disease-free survival in colorectal cancer, is the presence of tumor budding [55, 61, 62]. Tumor budding refers to the presence of single malignant cells or a small clusters of tumor cells (less than 5 cells) at the invasive tumor margin [63]. Ueno et al. demonstrated that in T1 colorectal carcinoma, high tumor grade, LVI, and tumor budding are all independently associated with lymph node metastases. Patients without any of these three features showed low rates of lymph node metastases (1%, 1/138); in the presence of one risk factor, the rate of nodal metastases increased to 21% (12/58), and when two or three factors were present, the risk was 36% (20/55), suggesting that local excision with TEM with negative resection margins would be sufficient treatment for early T1 colorectal carcinoma [64].

Based on the National Comprehensive Cancer Network (NCCN) guidelines, indications for transanal excision of rectal cancer include T1 tumors less than 3 cm in size, with no radiographic evidence of lymphovascular or perineural invasion. Unfavorable histopathologic features include >3 cm in size, LVI, positive margin, or sm3 depth of tumor invasion (Table 22.2).

Table 22.1 Published TAMIS series

Series	Sex (M, F)	*N*	BMI	OR time (min)	Port	Conversion	Final cancer stage	Positive margin	Distance from anal verge (cm)	Morbidity (%)
Atallah [12]	6, 0	6	–	86	SILS	0	Adenoma (3) pTis (1) pT1 (1) Carcinoid (1)	17	–	0
Van den Boezen [45]	5, 7	12	28	55	SILS	2	Adenoma (9) pT1 (1) pT2 (2)	0	7 (3–20)	8.3 (2 converted to TAE)
Barendse [7]	7, 8	15	–	57	SSL	2 (TEM)	Adenoma (7) pT1 (1) pT2 (3) Carcinoid (1) Fibrosis (1)	13	6 ± 4.5	7.7
Lim [46]	12, 4	16	24	86	SILS	0	pT1 (3) pT2–3 (8) Mucocele (1) Carcinoid (4)	0	7.5	0
Ragupathi [47]	10, 10	20	28.2	79.8	SILS	0	Adenoma (14) Unspecified malignant (6)	5	10.6	5
Albert [11]	33, 17	50	27.4	74.9	SILS/Gelpoint	0	Adenoma (25) Hyperplastic (2) pTis (1) pT1 (16) pT2 (3) pT3 (3)	6	8.2 (3–14)	6
Seva-Periera [20]	4, 1	5	–	52	SSL	1	pTis (2) pT2 1) Fibrosis (1)	0	4	25 (1 converted to LAR)
Bridoux [48]	8, 6	14	25	60	Endorec	0	Adenoma (10) pT1 (3) pT2 (1)	7.1	10 (5–17)	21
Lee [16]	17, 8	25	22.7	45	SILS	0	Adenoma (6) pT1 (9) Carcinoid (9) GIST (1)	0	9 (6–17)	0
Schiphorst [19]	18, 19	37	–	64	SILS	1	Adenoma (23) pTis (7) pT1 (4) pT2–3 (2)	16	7 (from dentate)	8 (1 converted to LAR)

McLemore [17]	18, 14	32	28	132	Gelpoint/SILS	0	Adenoma (10) pTis (1) pT1 (6) pT2 (4) Carcinoid (2) Fibrosis (9)	3	4 +/− 3	25
Gorgun [49]	10, 2	12	28.8	79	Gelpoint	0	Adenoma (10) pT2 (1) Carcinoid (1)	0	8 (5–12)	25
Hompes [18]	8, 8	16	26	108	Transanal glove port, Davinci robot	1	Adenoma (6) pT1 (2) pT2 (1) pT3 (1) Fibrosis (5)	13	8 (3–10)	13 (1 conversion to Hartman's)
Hahnloser [51]	51, 24	75	–	77	SILS	0	Adenoma (35) pTis (11) pT1 (13) pT2 (9) pT3 (1) Carcinoid (1) Hamartoma (1)	4	6.4 ± 3	19
Mendes [13]	5, 6	11	–	53.73	[a]SSL	0	Adenoma (4) Carcinoid (3) pT1 (2) Melanoma (1) Fibrosis (1)	0	5.3 (3–9)	9
Maglio [52]	6, 9	15	28	86	Gelpoint	0	Adenoma (5) pT0 (10)[b]	0	7	0

[a]SSL Single-site laparoscopic (SSL™) access system, Ethicon Endo-Surgery, Cincinnati, OH, USA, min (minutes)
[b]Patient had total regression after neoadjuvant chemoradiation therapy

Table 22.2 NCCN guidelines for transanal excision

Criteria	<30% Circumference of bowel
	< 3 cm in size
	Margin clear (>3 mm)
	Mobile, non-fixed
	Within 8 cm of anal verge
	T1 only
	Endoscopically removed polyp with cancer or indeterminate pathology
	No lymphovascular invasion or PNI[a]
	Well to moderately differentiated
	No evidence of lymphadenopathy on pretreatment imaging

[a]Perineural invasion

As described earlier, while LR rates following local excision of unselected T1 rectal cancer were reported to range from 0 to 26%, these outcomes from older series reflected the heterogeneity of cohorts with respect to the type of local excision (TAE or TEM, submucosal dissection or full-thickness), variations in preoperative tumor staging, completeness of resection (R0 or R1, en bloc or fragmented), treatment with neoadjuvant or adjuvant therapy, tumor size, and detailed histopathologic analysis to stratify outcomes based on risk for occult nodal disease [65, 66]. This is contrast to more contemporary TES for T1 rectal cancer series that have demonstrated that with careful preoperative staging and risk stratification based on detailed histopathologic review, local recurrence following TES rates range from 0 to 10%, which is in line with oncologic outcomes from radical proctectomy [67, 68].

T2 and More Advanced Rectal Cancer

It has been established in previous studies that local excision alone with TEM and TEO for T2 and more invasive rectal cancers with curative intent results in unacceptably high rates of LR [67]. Across early TEM series, the reported LR rates for T2 tumors not treated with neoadjuvant therapy ranged from 20 to as high as 36%, reflecting the associated high incidence of lymph node metastasis [69, 70]. In a systematic comparison of TEM versus radical resection with TME for T1 and T2 rectal tumors of performed by Mellgren et al., the 5-year LR rate for T2 tumors was 47% versus 6% after radical resection ($p = 0.001$). While there was no statistical difference in the overall 5-year survival between local resection and radical surgery groups for T1 tumors (72% versus 80%, $p = 0.5$), there was a statistical difference for patients with T2 tumors (65% versus 81%, $p = 0.03$) [69].

Although the standard of care for locally invasive rectal cancer remains radical surgery with TME, there has been an increasing trend towards organ preservation based on evidence that clinically staged T2 and T3 rectal tumors downstaged with neoadjuvant chemoradiation therapy (CRT) may be cured with local excision or observation alone. Several small retrospective cohorts of patients with locally invasive rectal tumors treated primarily with CRT because they either declined radical surgery or were deemed poor surgical candidates demonstrated acceptable long-term oncologic data. A small randomized trial comparing preoperative CRT followed by TEM alone versus laparoscopic TME in patients with T2 rectal tumors found no difference in overall survival between the two groups (72% in CRT + TEM versus 80% in laparoscopic TME, $p = 0.609$). LR rates were also similar between the groups (12% with TEM versus 10% with TME, $p = 0.686$) [71]. With improvement in preoperative staging and more intensive chemoradiation regimens therapy, complete pathologic response rates greater than 20% have been documented with sustained good local control using either local excision or observation alone. The recent prospective multicenter ACOSOG Z6041 phase II trial reported the 3-year oncologic outcomes in 72 T2N0 tumors located in the distal 8 cm of the rectum, treated with capecitabine, oxaliplatin, and 54 Gy of radiation followed by local excision using TAE or TES [72]. The 3-year DFS for the intention-to-treat group was 88.2% and 86.9% for the per-protocol group. Overall, organ preservation could be achieved in 66% of patients, and the authors concluded that neoadjuvant therapy followed by local excision should be reserved for those with clinically staged T2N0 lesions that are not otherwise amenable to TME [72].

Most recently, advocates of organ-preserving strategies have investigated the outcomes of nonoperative management for rectal tumors that have demonstrated complete clinical regression following neoadjuvant therapy. The Habr-Gama group has the largest clinical experience to date with the "watch-and-wait" approach for locally advanced rectal cancer. Their findings in a cohort of 70 patients with preoperatively staged T2–T4, N0–N2 tumors treated with intensive CRT regimens demonstrated a 68% rate of complete clinical response based on reevaluation with imaging, endoscopy, and digital rectal examination (DRE) 10–12 weeks later to confirm the absence of residual tumor or other mucosal irregularity [73]. These 47 patients were subsequently observed, and a sustained complete clinical response was observed in 51% of the entire cohort at 3 years follow-up. The remaining 49% with evidence of recurrent disease underwent immediate or salvage surgery with either TEM or radical surgery. Based on these data, although the possibility of definitive, nonsurgical treatment of rectal cancer with CRT alone remains limited to a subset of biologically responsive tumors, advances in neoadjuvant chemoradiation therapy may potentially spare 50% of patients with T2 rectal tumors from radical surgery. Several European series have corroborated the findings from the Habr-Gama group [74, 75]

and demonstrated that with more aggressive CRT regimens, the rates of complete clinical response can exceed the historical 20–30% rate, although this may be at the cost of increase toxicity, possible overtreatment of early rectal tumors, and delayed local recurrence that may not be surgically salvageable.

Other Indications

TES has also been demonstrated to be effective at treating a variety of other rectal tumors and benign conditions. Local resection using TES has been well established in the management of low-risk rectal carcinoid tumors, particularly when incompletely resected endoscopically. In the absence of histopathological risk factors for lymph node metastasis including size ≤10 mm and absence of LVI, and early stage confirmed by ERUS and CT scans, rectal carcinoids are amenable to local excision [76]. TES may be better suited than EMR, ESD, and TAE for definitive treatment of rectal carcinoids due to the ability to perform full-thickness rectal excision. Two large series on rectal carcinoids treated with TEM either as initial modality or for completion of incomplete endoscopic excision included 24 and 27 patients, respectively, with lesion size ranging from 7.5 to 10.1 mm and located within 9 cm from the anal verge (AV). These studies demonstrated a 100% R0 resection rate with 100% OS and DFS at a 30–70.6 months follow-up [77, 78]. TES has also been described in small case series of carefully selected GIST tumors and benign retrorectal tumors including tail gut cysts and rectal duplication cysts tumors, as a minimally invasive alternative to transcoccygeal resection or radical proctectomy [79, 80]. There have also been a number of recent case reports and case series on the successful use of TES in the management of complex benign conditions such as recurrent rectourethral [81], rectovesical [82], and rectovaginal fistulas [83] that had failed traditional repair. In addition, other miscellaneous use of a transanal endoscopic approach has included strictureplasty and transanal repair of colorectal anastomotic complications including leaks and abscesses [39]. Finally, TES can be used for palliation of bleeding rectal tumors in patients who are medically unfit to undergo other palliative procedures including fecal diversion, stenting, surgical debulking, cryosurgery, embolization, and palliative radiation [84].

Patient Selection for TES

Historically, a relative contraindication for TES included rectal lesions located higher than 8–10 cm from the AV, particularly if anterior, due to the high chance of full-thickness excision resulting in peritoneal entry. That is because peritoneal entry during full-thickness TEM excision was previously considered to be a complication requiring immediate conversion to laparotomy with low anterior resection or fecal diversion in order to mitigate the risk of leak and infection [85]. However, recent publications from experienced centers have demonstrated the feasibility and safety of transanal suture closure of upper rectal full-thickness defects without increased morbidity or adverse oncologic outcomes [86–88]. Based on this experience, it is generally recommended that only lesions within the reach of the 12–20 cm rigid proctoscope, and otherwise amenable to local excision, should be considered for full-thickness TES resection.

At the other extreme end of the rectum, due to their design and location in the anal canal following deployment, TAMIS does not permit access to rectal polyps located within 4 cm of the AV [16]. For lesions partially or entirely located within the distal 4 cm of the anorectal canal, the TEM and TEO platforms can often be pulled back maximally to permit exposure without losing excessive pneumorectum. This is in contrast to TAMIS where resection must be combined with a standard TAE approach for the distal part of the dissection.

With respect to rectal tumor size, nearly obstructing, near-circumferential, and circumferential tumors constitute a contraindication for TES. This is due to the anticipated difficulty in achieving R0 resection and safely closing giant rectal defects using a purely transanal approach, without resulting in rectal stenosis or incomplete closure [89].

With respect to patient safety, TES can be safely performed in the large majority of patients, including high-risk surgical patients, provided they are acceptable candidates for general anesthesia. TES can also be safely performed in patients with morbid obesity (BMI ranging from 35 to 66) as reported in a recent case series, without an increase in adverse events [90, 91].

taTME: Indications, Contraindications, and Patient Selection

Although firm consensus is building that sphincter-preserving LAR for low rectal tumors is the sweet spot for transanal TME, any type of proctectomy, including completion proctectomy, total proctocolectomy, APR, extralevator abdominoperineal excision (ELAPE), restorative proctectomy, or proctocolectomy (RPC) with ileoanal J pouch (IPAA) reconstruction, can be performed using taTME for a variety of benign and malignant etiologies. Based on the preliminary procedural, perioperative, and short-term oncologic data published to date, specific indications and contraindications of taTME with respect to specific pathology and anatomic factors have been described.

Benign Conditions

Completion proctectomy using a primarily transanal endoscopic approach has been described for benign indications including ulcerative colitis (UC) and Crohn's disease (CD), unsalvageable anastomotic complications, refractory fecal incontinence, diversion or radiation proctitis, and large carpeting unresectable distal rectal polyps [92–95]. Transanal endoscopic completion proctectomy can be performed using a pure transanal endoscopic approach when the rectum is short and mostly extraperitoneal, or using a hybrid approach with laparoscopic or robotic assistance. Distally, transanal proctectomy can proceed along the intersphincteric plane and, posteriorly, along the rectal wall, through the mesorectum, or along the TME plane. In restorative cases, transanal proctectomy or proctocolectomy can be combined with rectal mucosectomy followed by hand-sewn IPAA reconstruction as opposed to stapled pouch-to-anal anastomosis. In a total of four published case series reporting on the outcomes of a total of 35 patients who underwent pure or hybrid transanal endoscopic completion proctectomy, there was no mortality, and conversion to open proctectomy was required in one case [95]. The cumulative morbidity rate was 40% (14/35) including delayed perineal wound healing or dehiscence, colocutaneous fistula to the perineum requiring reoperation, incarcerated parastomal hernia, urinary tract infection, and bleeding [92–95]. In addition, three groups have recently reported their experience with transanal endoscopic proctectomy and IPAA, either as part of a 2-stage or 3-stage RPC for refractory UC in a total of 48 patients [96–98]. Abdominal proctectomy or proctocolectomy was performed using single-incision or multiport laparoscopy. Transanally, the proctectomy was performed following (1) rectal mucosectomy in 2 patients with preoperatively identified dysplasia, followed by hand-sewn anastomosis, and (2) without mucosectomy in 46 patients with subsequent stapled pouch-to-anal anastomosis. Conversion to open proctectomy occurred in three cases, and the overall morbidity rate was 29% and included one anastomotic leak, bleeding, hematoma requiring drainage, and pneumonia [96, 98]. These preliminary reports have demonstrated the feasibility and procedural safety of a primarily transanal endoscopic approach to facilitate distal rectal transection in UC, but data on even short-term pouch function is lacking.

Rectal Cancer

The first 2009 report of a laparoscopic-assisted transanal taTME procedure in a female patient with a T2N1 mid-rectal adenocarcinoma using a TEO platform was rapidly followed by a series of small pilot series and case series that confirmed the feasibility and preliminary oncologic safety of this approach for rectal cancer based on the adequacy of the TME specimen, lymph node harvest, and surgical margin clearance [32, 34, 35]. This early experience supported the subsequent rapid adoption of this technique worldwide, with an increasing number of midsize series on preliminary outcomes of this approach for rectal cancer. The major drive behind wide adoption of taTME has been the unanimously agreed upon benefits provided by transanal endoscopic access including (1) improved selection of the distal resection margin through transanal access, which eliminates the need for multiple stapler firings to transect the rectum transabdominally; (2) enhanced exposure of the perirectal and mesorectal dissection planes which facilitates TME completion, particularly in the narrow male pelvis where transabdominal exposure of the distal-most rectum is typically severely impeded; and (3) transanal extraction when feasible, which eliminates the need for an abdominal extraction incision.

Current indications and contraindications for transanal TME are consistent with indications for laparoscopic or robotic TME and based on standard tumor staging and include resectable T1 tumors with high-risk histological features, T2 and T3 tumors. Although early IRB-approved taTME protocols excluded node-positive disease and metastatic disease, indications for taTME have expanded to include node-positive patients and metastatic disease when taTME if performed with curative intent. Current indications for taTME also highlight specific tumor and patient characteristics that are particularly well suited for a primarily transanal approach. While there is no specified upper BMI limit for this approach, taTME has becoming the preferred approach in morbidly obese male patients with resectable rectal tumors. For very low rectal tumors located at or below the dentate line, when not invading the external anal sphincter, taTME can be performed in continuity with rectal mucosectomy and partial or total intersphincteric resection in order to achieve negative distal resection margins, followed by hand-sewn anastomosis. For mid-rectal tumors located >5 cm above the AV and at least 1 cm above the top of the anorectal ring, full-thickness rectal transection can be performed starting just below a purse-string suture placed to occlude the rectum below the tumor, with preservation of the anal sphincters, and followed by stapled colorectal anastomosis. For upper rectal tumors, located ≥10 cm from the AV, taTME is not unanimously believed to confer added benefits to a laparoscopic or robotic approach, with the obvious exception of the obese male. For these tumors, in an effort to preserve rectal function, transanal rectal transection is performed well above the anorectal ring followed by transanal tumor-specific mesorectal excision (TSME) and stapled colorectal anastomosis.

Currently, taTME is contraindicated for T4 disease, and tumors with predicted involved CRM, unless there is evi-

dence of significant downstaging on restaging MRI following neoadjuvant treatment. Transanal TME is also contraindicated for completely or near-completely obstructing rectal tumors. Another relative contraindication includes prior prostatectomy or other complex pelvic resections, prior pelvic radiation for gynecologic or urologic malignancies, and recurrent rectal cancer, particularly by less experienced operators, which substantially complicate identification of the correct dissection planes from the perineal approach and increase the risk of organ injury, particularly of the bladder and urethra [91].

The published experience of taTME to date demonstrates heterogeneity in taTME approach and setups currently used around the world. The same experience however highlights adherence to the same basic principles of TME dissection with high ligation of the IMA and IMV, sharp dissection along the plane between the presacral fascia and the mesorectum, autonomic nerve preservation, and integrity of the mesorectum during transanal, abdominal, hybrid dissection, and during transanal specimen extraction. Variations in taTME approach include differences in operative setup (1-team versus 2-team simultaneous or sequential approach), operative approach (hybrid versus pure taTME), type of abdominal approach if utilized (open, multiport versus hand-assisted versus single-incision laparoscopic or robotic), transanal platform used (rigid reusable versus disposable), and various types of coloanal reconstruction when utilized (hand-sewn or stapled end-end, side-end, coloanal J ouch, or IPAA).

Among 13 taTME series that included a minimum of 15 patients (N = 16–140 patients per series), a total of 574 patients underwent taTME for rectal cancer with 6% performed with APR and 94% with LAR [99–111]. The majority of cases were performed for carefully selected nonobstructing resectable tumors preoperatively staged as T1–T3, N0–N1 tumors and located average of 4–7.6 cm from the AV. The average BMI ranged from 22 to 28. With a few exceptions, the large majority of authors only used taTME for resection of low and mid-rectal tumors, with preferential use of laparoscopic or robotic techniques for upper rectal tumors.

Cumulatively, across all 13 studies, the mesorectum quality was described complete in 89%, near complete in 9%, and incomplete in 2%, with a rate of positive CRM ranging 0–13% (Table 22.3) and an average lymph node harvest ranging from 10 to 23. In addition, conversion rates were <5% (N = 16–140) [99–111]. These results (Table 22.4) demonstrated oncologic outcomes that are preliminarily comparable to historical open and laparoscopic TME outcomes with the benefit of exceedingly low conversion rates [24, 25, 27]. Intraoperative complications were noted in 7% and the conversion rate to laparotomy was 3%. Intraoperative complications were described by authors as occurring early during their learning curve. It was noted that laparoscopic assistance, preferably when combined with transanal TME dissection (i.e., a 2-team approach), helped identify and avoid critical anatomical structures and may reduce operative time. In a cohort of 20 patients undergoing laparoscopic-assisted taTME, Chen et al. reported that a 2-team approach in 8/12 patients significantly shortened the operative time of the 1-team approach (157.5 versus 226 min) [111]. Of note, to date, after Leroy and Zhang described the first two cases of a pure taTME with LAR in 2013 [112, 113], three small series including a total of 23 patients have described pure transanal TME for rectal cancer, which routine attempt is associated with a high conversion rate to abdominal assistance [107, 110, 114]. Across the 13 largest taTME series, the average length of hospital stay (LOS) was 8.1 days (range 4.5–14), with a 30–40% 30-day complication rate. At an average follow-up ranging 5–32 months, 8 of the 13 studies reported local and distal recurrences occurring 5–24 months postoperatively.

The international experience with taTME does not yet include a phase II or III clinical trial comparing taTME with laparoscopic TME. However, five retrospective studies compare outcomes of matched cohorts of patients who underwent transanal versus laparoscopic TME [104, 105, 115–117]. Fernandez-Hevia et al. performed a case-matched comparison of 37 cases of laparoscopic-assisted TME using a 2-team approach, and 37 cases of transanal TME and demonstrated no significant differences with respect to quality of the mesorectal specimen, lymph node harvest, resection margins, or intraoperative complications [116]. Of note, 2-team taTME was associated with significantly shorter mean operative time than laparoscopic TME (215 versus 252 min). A comparable 30-day postoperative complication rate was also observed, but a statistically significant lower readmission rate was noted in the taTME group (2% versus 6%) [116]. Velthuis et al. retrospectively matched 25 cases of laparoscopic-assisted taTME with 25 cases of laparoscopic TME and found that taTME was associated with a significantly higher rate of complete mesorectum than laparoscopic TME (92% versus 72%) [117]. The studies by de'Angelis, Perdawood, and Chen each retrospectively compared laparoscopic-assisted taTME with laparoscopic TME demonstrating shorter operative times and hospital stays with no differences in intraoperative and postoperative complications and oncologic outcomes [104, 105, 115].

Overall, taTME for rectal cancer has thus far been demonstrated to be safe and effective as an alternative oncologic surgical approach in resectable rectal cancer and is particularly well-suited for tumors of the low and mid-rectum, particularly in the obese male patient. Preliminary oncologic data from taTME series, including the analysis of the quality of mesorectal excision, have shown that taTME is associated with a high rate of complete mesorec-

Table 22.3 Largest published taTME case series

Series	Serra-Aracil ([108])	Burke [109]	Kang [107]	Buchs [106]	Perdawood [105]	de'Angelis [104]	Veltcamp [103]	Muratore [102]	Lacy [100]	Chen [111]	Tuech [140]	Chouillard [110]	Rouanet [99]
Sex (M,F)	24,8	30,20	12,8	12,5	19,6	21,11	48,32	16,10	89,51	38,12	41,15	6,10	30,0
N	32	50	20	17	25	32	80	26	140	50	56	16	30
BMI	25	26	22.3	27.1	28	25.1	27.5	26.2	25.2	24.2	27	27.9	26
OR time (min)	240	267	200	315	300	195	204	241	*166	182	270	265	04
Tumor location from anal verge	5–10	4.4	6	2	4–10	2.5–5	1–10	3–6	30% ≤ 5 50% 5.1–10 20% > 10	5.8	0–5	Mid/Low	<5 (20) 5–10 (10)
CRT	Y(16)	Y(43)	Y(6)	Y(6)	Y(7)	Y(27)	Y(26)	Y(19)	Y(90)	Y(50)	Y(47)	–	Y(29)
Final cancer stage	T0(2), T1(7), T2(10), N+(12), M1(1)	Stage T0(12), T1(2), T2(11), T3(21), T4(4), N+(16)	Tis(2), T1-2(9), T3(3), T3(5), N(+7)	T0(4), T2(8), T3(5), N(+7)	T2(8), T3(16), T4(1), N+(11)	T1(3), T2(12), T3(11), T4(2), N+(5)	T0(6), T1(3), T2(29), T3(42), N0 (44), N+(36)	T0(5), T1(7),T2(6), T3(8), N+(7)	T0 (15), stage I (34), stage II (43), stage III (39), stage IV (9)	T0(8). T1/ T2(13), T3/ T4(12), N+(17)	T0(11), T1(7), T2(16), T3(21), T4(1), N+(15)	T0(1), T1(3), T2(3), T3(7), T4(1), N+(5)	T1(1),T2(8), T3(18),T4(3), N+(16)
Complete TME (%)	93.8	72	90	94.1	80	84.4	88.8	88.5	97.1	–	83.9	–	100
Intraoperative complications (*n*)	0	Conversion (1), urethral injury (1), iliac injury (1)	Conversion (4), urethral injury (1), bleed (1)	Conversion (3)	Bleeding (2)	Conversion (1)	Bleed (2), bowel perforation (1)	0	0	Conversion (1), bleed (2), vaginal injury (1)	Conversion (3)	0	Conversion (2), urethral injury (2), air embolism (1)
Positive margin	0	6	0	5.9	4	9.4	2.5	0	6.4	4	5.4	0	13.3
Morbidity	44	62	25	30	60	25	39	23	34.3	26	25	18.8	26.6

CRT chemoradiation therapy

*Performed by 2 experienced rectal cancer surgeons, working simultaneously, intra-abdominally and transanally

Table 22.4 Comparison of taTME published data and international laparoscopic versus open TME trials

	COREAN [26]	COLOR II [25]	ACOSOG [24]	AlaCaRT [27]	taTME (Table 22.1)
N	340	1044	462	473	574
Laparoscopy	170	699	240	238	
Open	170	345	222	235	
Conversion (%)	0	17	11.3	9	2.6 (0–20)
Laparoscopy mesorectal quality (%)					
Complete	72.4	88	73	87	89% (72–100)
Near complete	19.4	9	19	10	9%
Incomplete	4.7	3	8	3	2%
Positive CRM (%)					4.4 (0–13.3)
Open	4.1	10	7.7	3	
Laparoscopic	2.9	10	12.1	7	
Positive distal margin (cm)					
Open	2	3	9.8	3.0	
Laparoscopic	2	3	9.8	2.6	
Lymph node harvest (*n*)					(10–23)
Open	18	14	16.5	N/A	
Laparoscopic	17	13	17.9	N/A	

tal specimens, which may or may not surpass that achieved using laparoscopic TME. Currently, the GRECCAR 11 in France and the international COLOR III trial are underway and will compare standard laparoscopic TME versus transanal TME [118].

Emerging Applications of taTME

Novel indications for a primarily transanal endoscopic rather than a transabdominal approach have been described. Bravo et al. recently described the case of Hartmann's reversal performed using a transanal approach to dissect the rectum in combination with abdominal assistance to fully mobilize the rectal stump, extract the specimen, and perform a stapled colorectal anastomosis [119]. Although T4 rectal cancer and recurrent rectal tumors constitute a relative contraindication to taTME due to concerns about oncologic adequacy of any procedure that does not achieve en bloc resection of the tumor and involved structures, in experience hands, transanal endoscopic strategies have recently been explored in reoperative complex pelvic surgery. In their series of 17 patients with unsalvageable anastomotic complications following LAR for rectal cancer ($N = 10$) or IPAA for UC or familial polyposis coli (FAP, $N = 7$) despite a number of prior surgical interventions, Borstlap et al. described successful redo coloanal anastomosis or redo IPAA in 82% (14/17) using open or laparoscopic-assisted transanal endoscopic dissection through a TAMIS platform [91]. In this series, no mortality occurred, intraoperative organ injury was noted in 1 patient (right hypogastric vein injury), and the overall morbidity rate was 53% (9/17) including 2 anastomotic leaks, 4 pelvic abscesses, and 1 urethral stenosis requiring urinary diversion. Despite the high morbidity rate noted following these complex transanal procedures, intestinal continuity could be ultimately achieved in 71% (10/14) of patients at 6 months following redo transanal coloanal reconstruction using TAMIS.

Preoperative Staging, Assessment, and Preparation

Preoperative Assessment and Staging

Accurate preoperative assessment and staging of rectal tumors is essential to the appropriate selection of patients for local excision or TES versus TME regardless of the specific approach to radical proctectomy. Accurate staging is essential to achieve R0 resections, and potential candidates for TES or taTME must undergo a comprehensive evaluation to localize and stage tumors accurately.

In addition to a complete medical and surgical history, colonoscopy with biopsies should be performed with careful pathology review to locally stage malignant lesions and identify high-risk histopathological features that might preclude local excision. A comprehensive physical exam and rigid or flexible proctoscopy should also be performed to confirm the tumor size, orientation along the rectal wall, distance from the AV, and extent of rectal wall involvement, as well as a digital rectal exam (DRE) to assess baseline anal sphincter tone, tumor fixity, and relationship of the tumor to the anorectal ring and potential tumor invasion of the anal

sphincters. For TES, this assessment is essential to determine the extent and feasibility of the planned resection, anticipate potential operative challenges, optimize patient positioning, obtain the relevant instrumentation, and mitigate intraoperative complications in order to complete TES procedures safely. For taTME, this assessment is also critical to confirm whether a primary transanal approach is indicated and requires partial or complete en bloc internal sphincter resection in order to achieve R0 resection.

Rectal cancer staging also includes assessment of the pretreatment carcinoembryonic antigen (CEA) level; CT scans of the chest, abdomen, and pelvis to rule out distant disease; pelvic MRI; and possibly an ERUS. Pelvic MRI has largely supplanted ERUS as the preferred modality for rectal cancer staging because it provides critical and objective assessment of the CRM, tumor location in relation to anal sphincters, prostate, vagina, and even the peritoneal reflection, all essential for accurate local staging [120]. Patients with locally advanced rectal cancer should undergo neoadjuvant treatment, although in some select cases, short-course radiation or chemotherapy alone may be selected. Assessment of tumor response by pelvic MRI following completion of neoadjuvant treatment may have an impact on the operative plan, i.e., watch and wait if complete clinical response by pelvic MRI, sigmoidoscopy, and DRE is demonstrated versus radical response, with or without sphincter preservation.

With regard to predicting perioperative as well as functional outcomes and quality of life following LAR and APR, preoperative assessment should include patients' baseline activity level, defecatory function, as well as urinary and sexual function. Patients who are candidates for taTME with sphincter preservation should be extensively counseled regarding the need for temporary fecal diversion, and the anticipated high incidence of functional disturbances and quality of life issues from the LAR syndrome, particularly following coloanal anastomoses for very low rectal tumors that require partial or complete intersphincteric resection (ISR).

Preoperative Preparation for TES

Patients typically undergo mechanical bowel preparation, and enemas are also administered to ensure clearance of the rectum. Adequate bowel preparation is important to reduce the risk of pelvic sepsis in the event of peritoneal entry during full-thickness dissection. Standard perioperative parenteral antibiotic and thromboembolic prophylaxis is provided. A Foley catheter is inserted if procedures are anticipated to require longer than 2 h. General anesthesia with paralytics is usually recommended in order to avoid leakage of CO_2 during procedures; however, spinal anesthesia has been demonstrated to be feasible and safe during TAMIS procedures [72]. Regarding intraoperative positioning, patients are either placed in the lithotomy position, prone, or in lateral decubitus position depending on the platform used, distance of the tumor from the AV, and tumor location along the rectum (Fig. 22.1a). TEM and TEO platforms are beveled metal proctoscopes with a built-in 30° angled scope fixed at the superior aspect of the platform, and patients are positioned such that rectal lesions are directly opposite the scope for optimal access (Fig. 22.1b). The majority of experienced operators will perform TEM, TEO, and TAMIS noncomplex cases with patients in lithotomy position regardless of tumor location. TAMIS does require a dedicated assistant for camera control (Fig. 22.1c). One relative indication for placing patients in prone position includes anticipation of peritoneal entry during full-thickness excision of high-risk rectal lesions [4].

Preoperative Preparation for taTME

When performed for rectal cancer, as for any other TME approaches, taTME is typically deferred for 8–12 weeks following completion of neoadjuvant treatment. For restorative procedures including LAR and IPAA, patients undergo full mechanical bowel preparation with or without enemas, with or without oral antibiotic preparation, in addition to standard perioperative parenteral antibiotic and thromboembolic prophylaxis. A Foley catheter is inserted. As with other types of MIS TME, patients are placed in lithotomy position, although completion proctectomy using taTME has been described in cases with limited hip flexion [94]. Rectal lavage with dilute betadine is often performed either prior or immediately following occlusion of the rectum below the tumor with a rectal purse-string suture. The abdomen and perineum are both prepped and draped to allow for sequential or simultaneous abdominal and transanal procedures.

Technical Considerations

Procedural Steps for TES

Prior to insertion of the TES platform, anal blockade with a local anesthetic is performed followed by gentle dilatation of the anus to prevent rectal trauma. The typical CO_2 pressure needed to maintain an adequate pneumorectum ranges 10–15 mmHg, although high pressures might be needed to compensate for CO_2 leakage [103, 108]. In TAMIS, depending on the port used, two or three 5-mm trocars can be inserted into the cannula of the port. In some cases, fixation sutures can be used for better secure the platform and prevent leakage or extrusion [12]. Regardless of the platform used, the same procedural steps are undertaken. The target lesion

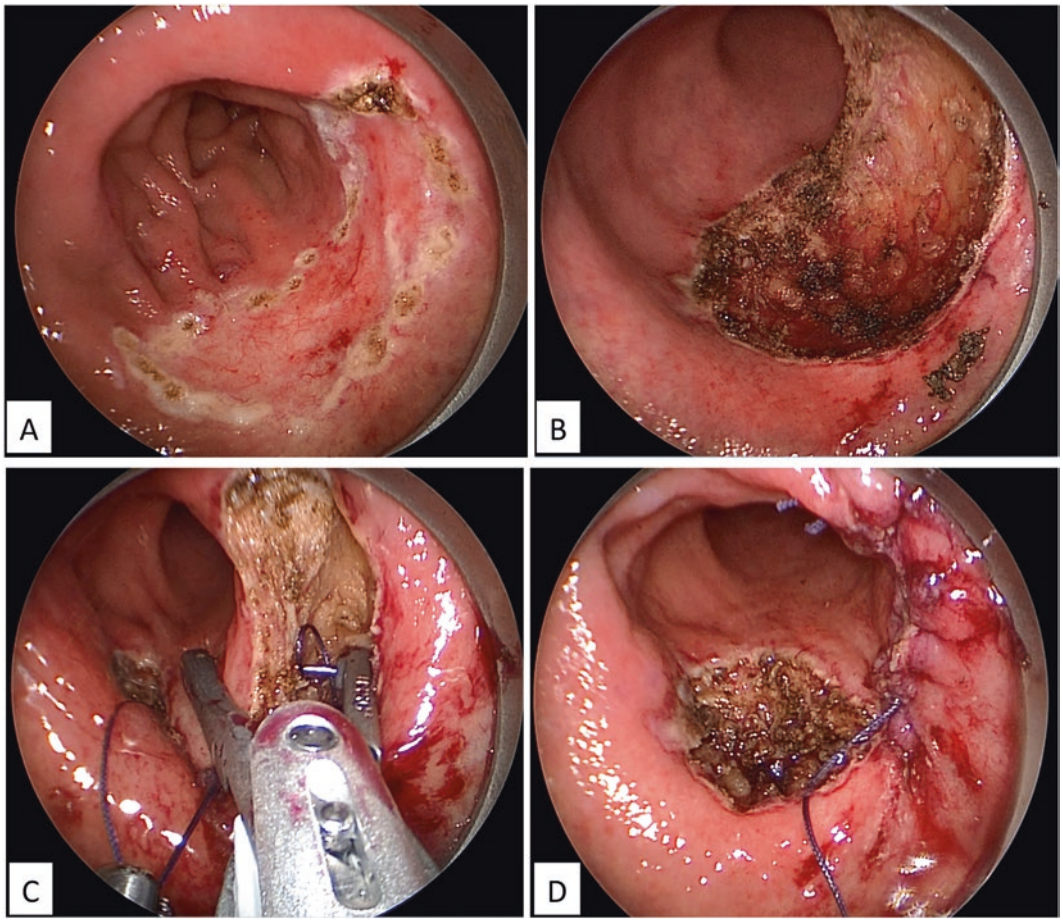

Fig. 22.2 TES full-thickness excision of a residual posterior mid-rectal scar following neoadjuvant treatment of a locally invasive rectal cancer. The mid-rectal scar is scored circumferentially with monopolar cautery with 0.5–1 cm margins (**a**). Full-thickness dissection of the scar is carried out with cautery until the mesorectum is reached (**b**). Following complete excision of the lesion and transanal specimen extraction, the rectal defect is closed using a suturing device (**c**). Full-thickness suture closure of the rectal defect proceeds until the defect is entirely closed (**d**)

is identified, and the rectal mucosa is scored circumferentially with monopolar energy with a 5–10 mm margin (Figs. 22.2a–d and 22.3a, b). Monopolar cautery and/or bipolar device is used for submucosal or full-thickness dissection of the lesion. Submucosal dissection can be used in conjunction with submucosal injection to elevate the pathology from the underlying muscular layer (Fig. 22.3c). Full-thickness dissection is carried out with an energy device through the transanal channel of the TEM/TEO platform or through a standard laparoscopic port in TAMIS. Dissection is continued perpendicular to the mucosal surface, through the entire thickness of the rectal wall, until the perirectal fat or mesorectum is reached (Figs. 22.2b and 22.3b). Of note, the use of CO_2 insufflation units that can evacuate cautery smoke while maintaining a constant high CO_2 flow to maintain a stable pneumorectum greatly enhances the image quality achieved during these procedures and the accuracy of the dissection [121]. Care must be taken if perirectal or mesorectal fat is excised in an attempt to acquire local lymphadenectomy. Wider rectal defects, although may be necessary, not only complicate closure but are also associated with high morbidity such as increase infection, bleeding, and suture line leak [122, 123]. In addition, wider rectal dissection which may be extended to include partial mesorectum may complicate or compromise the quality of salvage TME, if subsequently warranted. Detrimental residual inflammation and fibrosis along the mesorectal plane may be encountered during interval TME up to 3 months after TES [18]. Arolfo et al. also demonstrated that post-TEM perirectal histology demonstrated 62% (24/39) tissue fibrosis after extensive mesorectal dissection which may gravely impact subsequent LAR procedures [123].

Following complete dissection of the rectal lesion, the specimen is extracted through the platform and oriented for pathology as needed. Prior to rectal wall defect closure, particularly in the event of fecal spillage in the rectal wound, the area can be washed out with saline and irrigated with dilute iodine solution. The submucosal or full-thickness defect is

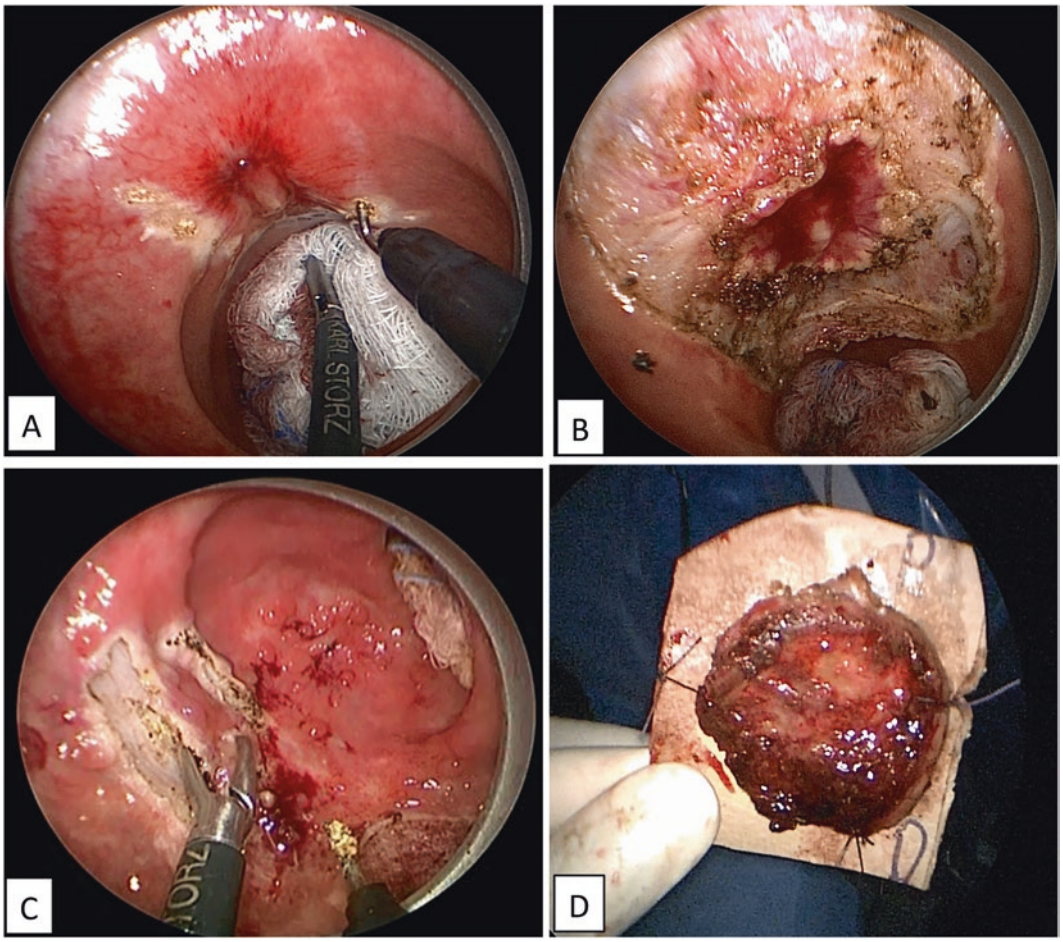

Fig. 22.3 TES full-thickness excision of an anterior mid-rectal wall carcinoid tumor with the patient in lithotomy position (**a**). During full-thickness anterior wall dissection, care is taken not to injure the posterior vaginal wall (**b**). TES submucosal excision of clusters of rectal polyps forms a retained rectal stump in a patient with FAP who underwent prior ileorectal anastomosis (**c**). Following complete TES excision of rectal lesions, the specimen is oriented (proximal and distal margins) for pathology

typically closed with running or interrupted absorbable monofilament sutures (Fig. 22.2c, d). A variety of suture materials are described including glycolide and trimethylene carbonate (Maxon, Codisan S.p.A.), polydioxanone (PDS, Ethicon Inc. Somerville, New Jersey, USA), polyglactin (Vicryl, Medtronic, Mansfield, MA, USA), and the V-loc barbed absorbable suture (Medtronic) which is a self-retaining suture that does not require a knot. In addition a variety of sutures and suturing devices are commercially available to overcome the technical challenges of laparoscopic suturing through transanal platforms. These include extracorporeal knot tiers and disposable automated suturing devices that facilitate knot tying such as the Endo Stitch™ device (Medtronic, Fig. 22.2c) and the Cor-Knot device (LSI Solutions, Victor, NY). In addition, the TEM instruments include an angled needle holder, and sutures can be secured with specialized silver bullets (Richard Wolf).

In the event of peritoneal entry during full-thickness rectal wall dissection, when transanal closure of the rectal wall defect is not technically possible or suspected not to be air-tight, diagnostic laparoscopy should be performed with closure of any residual intraperitoneal rectal defects (Fig. 22.2). The peritoneal cavity defect can also be closed by a combined transanal and laparoscopic approach [17, 51]. Postoperatively, a gastrografin enema can be performed if a leak at the rectal closure site is suspected.

It is worthy to note that there is evidence that leaving rectal wall defects open does not increase the incidence of wound-related complications, as long as the defect is not associated with peritoneal entry [51, 124]. In a recent TAMIS series of 75 patients who underwent partial or full-thickness resection for rectal lesions located an average 6.4 ± 2.3 cm from the AV, the authors found no differences in postoperative complications between the 40 patients whose defects

were left open versus the 35 patients whose defects were suture closed [51]. However, it should be noted that only 6% of the 35 open rectal wall defects were located anteriorly compared to 28% of 38 closed rectal wall defects. Clearly, for larger, full-thickness lesions, and in particular for high-risk lesions where peritoneal entry has occurred or is suspected, closure of rectal defects should be performed to minimize the risk of septic complications.

Procedural Steps for taTME

The large majority of taTME procedures are performed using a hybrid rather than pure transanal endoscopic approach. Abdominal assistance is provided using laparoscopic or open access (multiport, single port, hand-assisted, or robotic). Procedures can either be performed as a 1-team approach (with a single team performing the abdominal and transanal dissection sequentially), or a 2-team approach (with a transanal team and an abdominal team working simultaneously).

Most surgeons using a 1-team approach will start with the abdominal dissection first, with mobilization of the splenic flexure and high ligation of the inferior mesenteric artery and mobilization of the sigmoid and proximal rectum. The extent of subsequent pelvic dissection depends on the surgeon's preference, but is usually carried out until further rectal and mesorectal dissection becomes difficult, at which point the team will transition to transanal dissection. Occasionally, transanal dissection will be initiated first, followed by abdominal access and dissection. Whether a 1-team or 2-team approach is utilized, the steps of transanal dissection are dependent on the exact tumor level, i.e., distance from dentate line and anorectal ring. Following confirmation of the exact location of the tumor by digital and visual inspection with anoscopy, assessment of the required distal margin is made.

For tumors that are >2 cm above the dentate line, or ≥1 cm above the anorectal ring, a purse-string suture is placed at least 0.5 cm below from the rectal tumor either directly through a standard anoscope or endoscopically through the TES platform. In the latter case, the transanal platform is inserted first, followed by purse-string occlusion of the rectum. The purse-string usually consists of 2-0 Prolene or 2-0 Vicryl sutures (Fig. 22.4a). It is essential for the purse-string suture to be airtight to avoid distention of the proximal colon with CO_2 and spillage of fecal material or tumor cells on the operative field. Following insertion of the TES platform and purse-string occlusion of the rectum, pneumodistention with CO_2 is achieved to a pressure of 10–15 mmHg. The rectal mucosa is scored circumferentially with monopolar cautery, followed by full-thickness incision of the rectal wall circumferentially (Fig. 22.4b). Full-thickness rectal and mesorectal mobilization is carried out sequentially using monopolar cautery, with efforts to avoid the use of bipolar energy, which is not usually needed if dissection along the correct planes is carried out. Posterior mesorectal dissection is carried out along the avascular plane between the presacral fascia and the mesorectum (Fig. 22.4c), while anteriorly, dissection is carried between the rectovaginal fascia or rectoprostatic fascia (Fig. 22.4d). Laterally, care must be taken to avoid dissection of the pelvic sidewall during mesorectal mobilization, in order to preserve the nervi erigente. During the anterolateral dissection of the rectum and mesorectum, care must be taken to avoid injury to the neurovascular bundles bilaterally. It also serves as a landmark for the location of the prostate, if difficulties are encountered during anterior mobilization and identification of the posterior aspect of the prostate. Transanal TME dissection is carried out circumferentially and in a sequential pattern, and every effort is made to avoid dissecting too far along any given plan, in order to avoid plane distortion (Fig. 22.5a). Ultimately, anterior dissection is carried out cephalad until the peritoneal reflection is reached (Fig. 22.5b). Posteriorly, depending on the angulation of the sacral promontory, transanal dissection can usually be extended toward S1–S2 levels, and posterior dissection is completed using a combined abdominal and transanal approach in the 2-team approach. Even when using a 1-team approach, abdominal assistance during this step is critical, as it allows 2 teams to work simultaneously to complete mobilization of the rectum and merge the abdominal and transanal planes of dissection. Peritoneal entry is usually performed transanally and under laparoscopic visualization from above (Fig. 22.5b). Following complete mobilization of the TME specimen, the colon is either exteriorized transanally or through an abdominal incision, if the specimen is deemed too bulky to permit transanal extraction. Following transection of the specimen (Fig. 22.5c), colorectal stapled anastomosis can be usually carried out when the rectal transection was initiated well above the dentate line. Double purse-string circular stapled anastomosis technique is used, with either end-end, side-end, coloanal J pouch, or transverse coloplasty, depending on the surgeon's preference [125]. In the large majority of published taTME cases, a protective loop ileostomy is constructed, with the use of closed pelvic drains.

For tumors <2 cm from the dentate line or <1 cm from the top of the anorectal ring, intersphincteric resection, either partial or complete, is performed first in order to achieve negative distal resection margins. ISR is performed first through a Lone Star retractor (Lone Star Medical Products Inc., Houston, TX) and monopolar cautery, which is extended cephalad until the puborectalis muscle and bottom of the mesorectum are identified posteriorly, and the rectovaginal or rectoprostatic plane is visualized anteriorly. The anorectal stump is then closed with a purse-string suture, and the TES platform is inserted with CO_2 insufflation. Further posterior

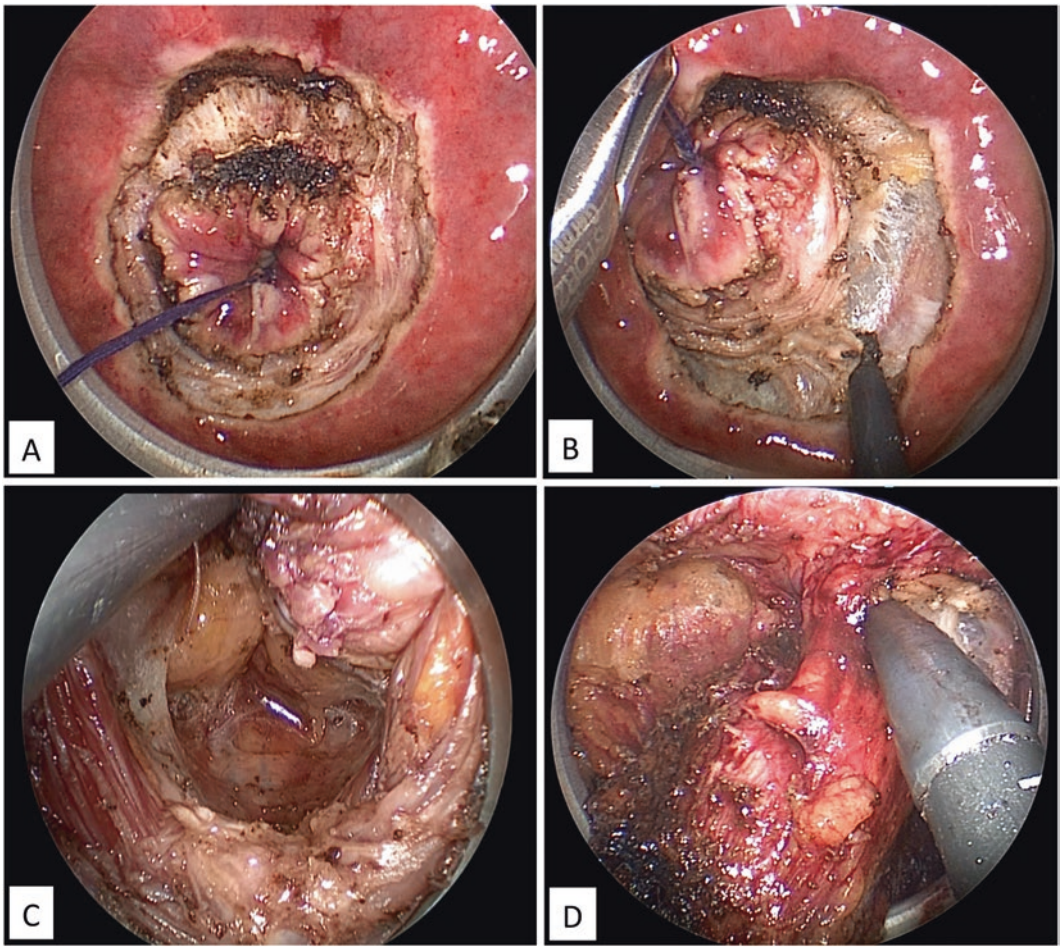

Fig. 22.4 Transanal TME for a mid-rectal rectal cancer in a male patient treated with neoadjuvant treatment. Following purse-string occlusion of the rectal lumen below the tumor, the TEO platform is inserted, and the rectum is distended with CO_2. Full-thickness rectal dissection is carried out with monopolar cautery (**a**). Circumferential rectal and mesorectal dissection proceeds superiorly, until the puborectalis (**b**) and the plane between the presacral fascia and mesorectum (**c**) is identified posterolaterally. Anteriorly, dissection proceeds along the plane between the anterior rectum and the posterior aspect of the prostate (**d**)

dissection is needed posteriorly including division of the anococcygeal raphe in order to access the presacral space. Following identification of the inferior aspect of the mesorectum posteriorly, and the rectovaginal or rectoprostatic plane anteriorly, transanal TME can proceed as described above. Following specimen extraction, hand-sewn coloanal anastomosis is performed using either end-end, side-end, coloanal J pouch or transverse coloplasty with a protective ileostomy.

Alternative taTME Techniques

When transanal restorative proctocolectomy or proctectomy is performed with IPAA in ulcerative colitis of FAP, following laparoscopic mobilization of the colon and/or rectum, transanal procedures are initiated with placement of a Lone Star retractor and circumferential rectal mucosectomy starting at the level of the dentate line. Full-thickness rectal transection is then carried out at the level above the anorectal ring followed by rectal dissection either along the rectal wall or along the mesorectal plane [94]. Alternatively, a purse-string suture is placed transanally 3 cm above the dentate line followed by full-thickness incision of the rectal wall and close rectal dissection. Following specimen extraction, IPAA is performed with a single stapled technique [96].

With transanal endoscopic proctectomy or proctocolectomy with APR, if performed, the colon is mobilized followed by ligation of the inferior mesenteric vessels, and mobilization of the rectosigmoid colon and TME dissection are initiated using an open, laparoscopic, or robotic transabdominal approach. Intersphincteric or standard proctectomy is carried out either simultaneously (2-team) or sequentially with the abdominal dissection (1-team). The anus is suture closed followed by intersphincteric or extrasphincteric proctectomy using a standard perineal instruments. Transanal

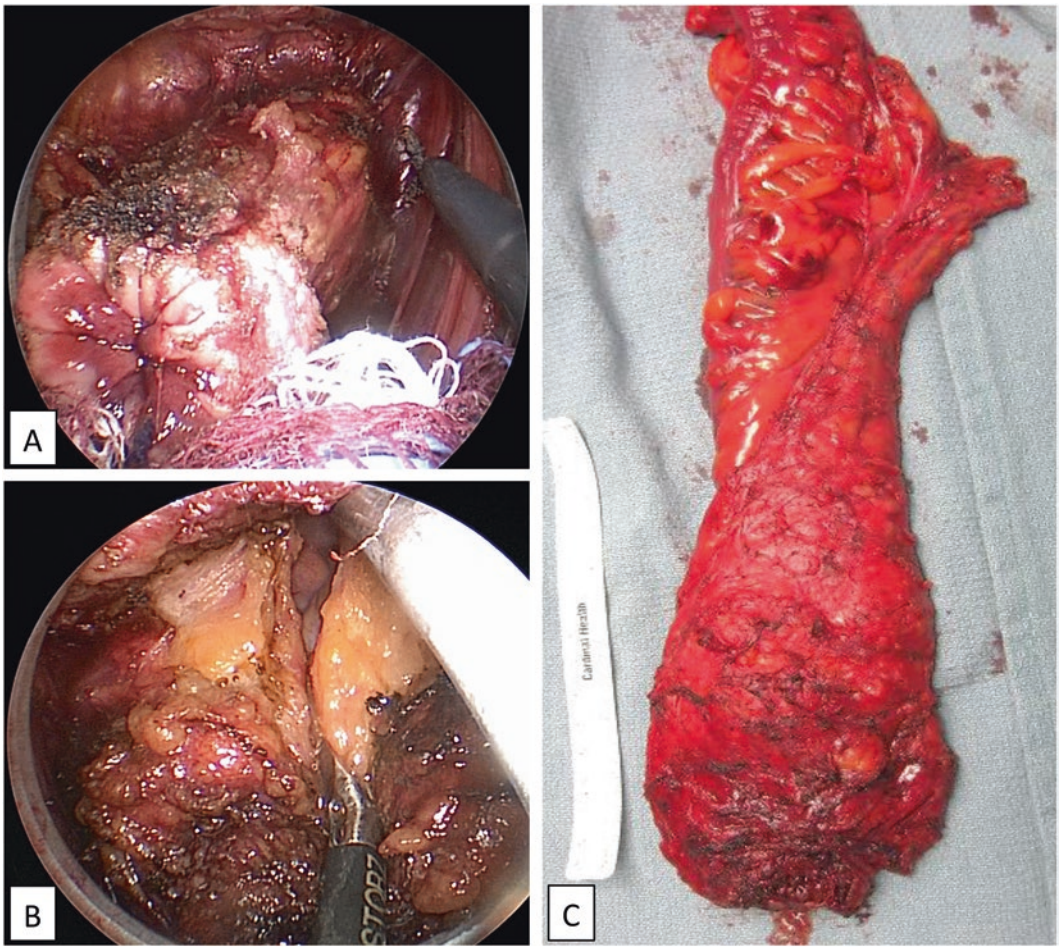

Fig. 22.5 Transanal TME for a mid-rectal rectal cancer in a male treated with neoadjuvant treatment. Circumferential rectal and mesorectal dissection proceeds cephalad toward the peritoneal cavity (**a**). The anterior peritoneal reflection is incised anteriorly under visualization and assistance by the abdominal team in a 2-team approach (**b**). Following completion of the TME using a combined transanal and abdominal approach, the specimen is exteriorized, transected, and sent to pathology for evaluation according to standard TME protocol assessment. Meanwhile, colorectal or coloanal anastomosis is completed

dissection is extended superiorly until the perineal body has been divided and the rectoprostatic or rectovaginal plane is identified. Posteriorly, dissection is carried out until the puborectalis is visualized. The TES platform is then inserted with CO_2 insufflation, and further rectal dissection is carried out endoscopically. Posteriorly, dissection can be carried out either close to the rectal wall, within the mesorectal plane, or along the plane between the mesorectum and presacral fascia, depending on the pathology and surgeon's preference. Following the proctectomy, the specimen is exteriorized followed by perineal wound closure in layers. Another alternative transanal completion proctectomy for benign disease consists in initiating transanal endoscopic full-thickness rectal transection through the TES platform starting well above the dentate line, followed by completion of the rectal dissection and mesorectal dissection, and exteriorization of the specimen. Intersphincteric dissection of the short anorectal stump is then carried out, following by exteriorization of the specimen and perineal wound closure [92].

Specimen Extraction

The specimen can be extracted transanally or transabdominally depending on the size [99]. A wound protector is recommended by most to avoid implantation of tumor cells. Finally, a protective diverting loop ileostomy is recommended by most surgeons. Transanal extraction could result in untoward shearing of the mesentery, namely, the marginal artery with the potential, to seed exfoliated tumor cells. Furthermore, it can result in shear stress on proximal arterial inflow and may result in conduit ischemia compromising the anastomosis when restoring gastrointestinal continuity. To minimize marginal artery injuring during transanal specimen

extraction, the mesentery at the level chosen for proximal division should be performed intracorporeally with division of the marginal artery [126].

Closure of Rectal Defect

The submucosal or full-thickness defect is commonly closed with absorbable sutures. A variety of sutures and suturing devices are commercially available to overcome the technical challenges created by the narrow, rigid platform. A circular staple like the EEA (Medtronic) can be used in establishing the colorectal anastomosis in taTME. It is worthy to note that closing submucosal, posterior, or distal full thickness defects is not associated with increased morbidity [127].

Postoperative Care and Surveillance

Following TES, patients are usually discharged on the same day of surgery, especially if transanal endoscopic resection was submucosal or full-thickness but well below the peritoneal reflection. In patients in whom more complex full-thickness TES was performed, overnight observation is usually recommended, especially if peritoneal entry was clearly visualized and repaired, or suspected based on evidence of pneumoperitoneum at the end of the case. A regular diet can be safely reinstated after surgery, and no additional antibiotics are typically given. Routine imaging is not recommended in the absence of clinical indication. The low postoperative morbidity following TES procedures is reflected in the short hospital stay and minimal postoperative pain requirement. Up to 50% of patients undergoing TEM for rectal cancer are safely discharged on the day of surgery as reported in several recent series [128]. When patients are admitted for observation, length of stay ranges 0–5 days due to management of major medical comorbidities or observation following cases of peritoneal entry [128].

Following routine postoperative follow-up, specific surveillance depends on the final pathology. Patients with completely resected adenomas and other benign pathologies are usually reassessed endoscopically within 6–12 months postoperative to confirm early recurrence. In patients who have undergone complete excision of T1 rectal tumors, in the absence of high-risk pathologic features, patients are observed, and surveillance follows NCCN guidelines with clinical evaluation, CEA, and flexible sigmoidoscopy every 3–4 months for the first 3 years and every 6 months for the following 2 years until year 5 [129]. In addition, yearly CT scans are performed until year 5, and surveillance colonoscopy is performed at 1 year followed by 3 years post-resection. Some physicians have also advocated yearly pelvic MRI for 5 years to assess for locoregional recurrence. In patients who have undergone TES for T1 tumors with positive margins or high-risk histopathological features, completion TME is recommended. In patients who decline radical resection or are poor surgical candidates, adjuvant chemoradiation may be offered.

Patients undergoing taTME are managed using the same enhanced recovery protocols as with any other minimally invasive TME procedures. Removal of the Foley catheter is usually delayed beyond the standard 24–48 h protocols in patients with risk factors for urinary retention, including males with an enlarged prostate, benign prostatic hyperplasia (BPH), and patients who have undergone deep perineal dissection and very low LAR. Additional parenteral antibiotics are given as indicated, and patients are discharged home according to standard protocols once adequate pain control, oral fluid intake, and stoma function have been achieved.

Postoperative oncologic surveillance after taTME follows standard NCCN guidelines for rectal cancer, as outlined above. Ileostomy closure is deferred until completion of adjuvant treatment as indicated.

TES Complications

Perioperative Morbidity and Mortality

Over three decades of published short- and long-term outcomes from large clinical series have consistently demonstrated the exceedingly low mortality and low morbidity associated with TEM and TEO, especially relative to that associated with TME [8, 24, 25, 27, 28]. The largest TEM and TEO series that included 262–693 patients have reported a <1% mortality rate and 5–20% 30-day morbidity rates, with the most common complications including transient urinary retention (5–10%) and postoperative bleeding (1–13%), the latter rarely requiring reoperative intervention [8, 9, 130]. The majority of TES-related complications are relatively minor and transient, with major complications composed of less than 10% [8, 9, 37, 127]. Other reported complications of TES include conversion to TAE or abdominal procedures, suture line dehiscence, which range from minor defects managed conservatively with antibiotics and bowel rest, to major defects with intraperitoneal leakage and sepsis, requiring washout and fecal diversion. In a prospective multicenter study of 588 patients who underwent TEM resection, Guerrieri et al. reported a 5.9% incidence of partial disruption or leak of the suture line that were all successfully managed conservatively with antibiotics [131]. Additional adverse events include infectious complications (urinary tract infections and perirectal and presacral abscess), retrovisceral fistulas, and rectal stenosis. Rare complications include organ injury, with two cases of urethral injury reported following TEM resection of anterior rectal lesions

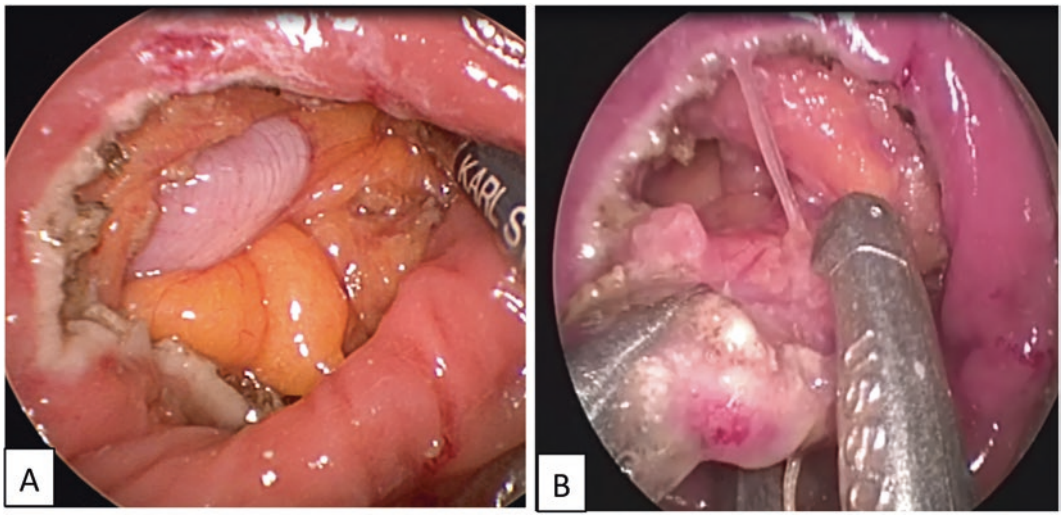

Fig. 22.6 Full-thickness transanal excision of an anterior upper rectal lesion is complicated by peritoneal entry with visualization of the sigmoid colon (**a**). The full-thickness rectal defect was closed transanally with absorbable sutures using a suturing device (**b**)

in a series of 402 TEM cases [132]. In the largest multicenter series published to date, among 693 combined who underwent TEM or TEO procedures, conversion rate to TAE or abdominal procedures was 4.3%, and the 30-day morbidity was 11.1%, with hemorrhage and suture dehiscence being the most common surgical complications [9].

In the more limited literature on TAMIS, the published incidence of postoperative complications ranges 0–25% across series, with bleeding and urinary retention reported as the most common complications (Table 22.1) [129]. A recent review of 16 TAMIS series across a total of 390 patients reported a 10.8% complication rate, including a 2.7% incidence of bleeding and 0.5% incidence of suture dehiscence [129]. There were no deaths, and the conversion rate to either TAE, TEM, or laparoscopy was 2.3%. In the absence of comparative studies evaluating TEM/TEO versus TAMIS approaches, no conclusions can be drawn regarding differences in morbidity, mortality, or length of stay between approaches.

Peritoneal Entry

Peritoneal entry (PE) during TES, either unplanned or anticipated based on location and/or extent of the rectal lesion, often complicates TES procedures and requires careful management. Earlier TEM reports considered PE to be a major complication requiring conversion to laparotomy with lavage, radical resection with or without fecal diversion [85]. From an oncologic standpoint, PE was also thought to increase the risk of tumor cell spillage and peritoneal tumor implants during rectal cancer excision [86]. In TEM series by the most experienced centers with more than 300 included patients, that rate of PE ranges 5 to 10.7% [6]. The studies have demonstrated that PE occurred more commonly during full-thickness resection of lesions located in the upper rectum, anteriorly or laterally along the rectal wall, and during resection of circumferential or near-circumferential rectal lesions [133]. Several studies have reported no increased morbidity relative to TEM cases without PE and no adverse short- or long-term oncologic outcomes in patients in whom peritoneal entry occurred during TEM excision of rectal tumors [68, 88]. As a result, tumor location 10 cm or more from the AV is no longer considered a contraindication to TEM surgery, as long as full-thickness suture closure of rectal defects can be achieved transanally by experienced operators [86, 88]. Entry into the peritoneal cavity during TES procedures can be very challenging to close transanally as a result of collapse of the rectum with leakage of CO_2 into the abdominal cavity, especially if patients are in lithotomy position (Fig. 22.6a, b). Over time however, experienced centers with large TEM and TEO series have demonstrated that conversion rates following peritoneal entry have decreased, with conversion rates ranging from 0 to 40% but averaging 10% or less [68]. Even less has been published regarding the experience of PE during TAMIS. The systematic TAMIS review of 367 procedures reported inadvertent PE in only four cases (1.025%), and the average distance of rectal lesions from the AV was 7.6 cm [129]. All four cases of PE occurred during dissection of upper rectal lesions, and two (50%) could be closed transanally, while the others required abdominal conversion. Only three TAMIS series that include 32–75 patients have reported an incidence of PE ranging from 2 to 9.4% [11, 17, 51]. Among the seven cases of PE during TAMIS across all three studies, six (86%) required conversion to laparoscopy or laparotomy from inability to

effectively close the rectal wall defect. This may reflect the long learning curve required for managing these complex rectal lesions and the currently small experience with TAMIS to date. But it may also reflect technical limitations of shorter TAMIS platforms, which do not always permit adequate retraction and exposure of the proximal rectum [54].

Functional Outcomes

With respect to functional outcomes following TES, anorectal dysfunction ranges from <1 to 4% and is typically transient [5, 8, 130]. In patients with normal anal sphincter function at baseline, transient decrease in resting and squeeze anal sphincter pressures proportional to the duration of procedures have been documented, with complete resolution at 12 months postoperatively and no long-term impact on anorectal function [134, 135]. By virtue of the prolonged stretching of the anal sphincter by 4 cm wide rigid platforms, it has been hypothesized that more pliable disposable transanal platforms may have a less detrimental impact on anorectal function. On the other hand, there is also concern that functional outcomes might be worse as compared to traditional rigid platform TES because of more extreme movements and stretch allowed by the flexible platform. Thus far, although limited, published data on short-term functional outcomes following TAMIS have been comparable to historical TEM reports. One small prospective study conducted by Schiphorst et al. assessed functional outcomes in 37 patients following TAMIS using FISI score collected preoperatively and at 3, 6, 9, and 12 months postoperatively [19]. Among 18 patients with normal fecal continence at baseline, no change in Fecal Incontinence Severity Index (FISI) scores was found in 83%, suggesting preserved long-term anorectal function following TAMIS procedures, while several TEM series demonstrated no significant changes in the Fecal Incontinence Severity Index (FISI) or Fecal Incontinence Quality of Life (FIQL) scores at 6 weeks postoperatively and return to baseline of the colorectal functional outcome (COREFO) at 12 weeks postoperatively [136, 137]. However, two series reported persistent sphincter dysfunction following TEM based on long-term assessment using either St. Mark's or Wexner incontinence scores, with operative time, preoperative radiotherapy, and perioperative complications acting as independent risk factors [138, 139].

Complications of taTME

Cumulatively, across 13 published taTME series with sample size ranging from 16 to 140 patients, conversion to open laparotomy was noted in 3% with an additional 7% incidence of intraoperative complications including hemorrhage, rectal and vaginal perforations, four cases of urethral injuries in males, and one ureteral injury, and prostatic injury, as well as cases of delayed anastomosis due to questionable viability of the colonic conduit (Table 22.3). In two of the four cases of urethral injuries, the injuries were described in taTME cases involving low, anterior, and/or bulky rectal and anterior tumors in males, with difficulties identifying the correct dissection plane and relatively early along the surgeon's learning curve [99]. In one case, the injury was treated nonoperatively, two were repaired intraoperatively, and one required urethroplasty 1 month postoperatively [99, 107, 109]. It was noted that laparoscopic assistance at this stage helped identify and avoid critical anatomical structures. The overall mortality rate across all large taTME series was less than 1%, and the 30-day morbidity rate was 33.7% with major complications including anastomotic leaks (8.6%), pelvic sepsis (<5%), and minor complications including transient urinary retention and urinary tract infection, ileus, obstruction, surgical site infection, and rectal stricture. Of note, transient urinary retention was noted at a rate ranging from 3 to 9% across series, with resolution within 3 months following taTME procedures [99, 102, 116, 140, 141].

Regarding functional outcomes, at a follow-up ranging from 5 to 32 months, 5 of the 13 studies reported fecal incontinence with average Wexner score of 6.9 (3–18). Rouanet and colleagues reported 60% incidence of fecal incontinence at 1-year follow-up with median Wexner score of 11 with gas incontinence of 35% and liquids of 15% [99]. In a series of 56 patients, Tuech reported a 5% incidence of severe incontinence with one patient converted to a colostomy 1 year postoperatively. The median Wexner score was 5 overall [140]. Regarding oncologic outcomes, eight out of the 13 studies reported local and distant recurrence with 45 cases of local or distant recurrences. The time to recurrence ranged from 5 to 24 months.

Pearls and Pitfalls

Management of Peritoneal Entry During TES

Rectal lesion that is particularly high risk for peritoneal entry during full-thickness resection includes anterior and lateral lesions located in the upper rectum or rectosigmoid, as well as circumferential or near-circumferential lesions [86–88]. Depending on the size of the peritoneal defect, rapid accumulation of CO_2 into the abdominal cavity can result in the collapse of the pneumorectum. When patients are positioned in lithotomy, this can significantly complicate closure of the rectal wall defect. Several strategies can be used to mitigate the critical loss of pneumorectum such as placement of an abdominal Veress needle or trocar to decompress the pneu-

moperitoneum and increase in the transanal CO_2 insufflation pressure. Ideally, the rectal defect should be closed, at least partially, as rapidly as possible in order to minimize ongoing loss of pneumorectum (Fig. 22.6a, b). Some operators also recommend placement of stay sutures near high-risk lesions prior to full-thickness rectal dissection, in order to facilitate quick identification of the edges of the rectal defect for rapid closure. Most importantly, preemptive positioning of patients in prone position in anticipation of possible peritoneal entry helps mitigate the degree of CO_2 leakage into the abdominal cavity. The prone position helps tamponade the volume of CO_2 loss and helps maintain a stable pneumorectum to facilitate closure of the full-thickness rectal wall defect [68]. Following closure of the rectal defect, if there is concern that the rectal closure is not entirely airtight, laparoscopy should be performed to evaluate and/or reinforce the closure, and a leak test can also be performed at that time.

taTME Dissection for Very Low Rectal Tumors in a Male Patient

It has been well established among taTME experts that although taTME is best suited for low rectal tumors in obese males in particular, these cases are the most complex cases with the longest learning curve, by virtue of the lack of familiarity of surgeons with the deep perineal anatomy from an endoscopic approach, and [2] variable expertise with rectal mucosectomy or intersphincteric resections, which is a necessary skillset during sphincter-preserving taTME when a negative distal margin must be achieved for very low tumors. When taTME is used for low rectal tumors that require ISR (tumors <2 cm from the dentate line or <1 cm from the top of the anorectal ring), it is recommended to initiate intersphincteric dissection using an open transanal approach using monopolar cautery, until critical structures have been clearly identified, including the puborectalis posteriorly with the inferior aspect of the mesorectum and the posterior aspect of the vagina or prostate anteriorly. Several authors have described having initiated intersphincteric dissection endoscopically, through the transanal platform. Endoscopic dissection is carried out for a few centimeters cephalad followed but purse-string closure of the anorectal stump and completion of endoscopic TME. Early in the operator's learning curve however, endoscopic ISR has been associated with a high risk of erroneous dissection into an incorrect plane anteriorly, where, as in the case of a difficult APR, dissection above the perineal body can result in dissection too close to the prostate, or worse, dissection above the prostate and into the membranous or prostatic urethra. This is primarily related to unfamiliarity of surgeons with this perineal approach and the periprostatic anatomy.

taTME Operative Setup

Based on the taTME reports published to date, procedures can be performed using as 1-team approach, whereby the same operative team performs transanal TME followed by abdominal mobilization of the splenic flexure, inferior mesenteric vessel transection, left colon and rectosigmoid colon mobilization and completion of the TME, or vice versa (abdominal mobilization first followed by transanal dissection). The alternative 2-team approach utilizes 2 surgical teams that work simultaneously from the start by combining abdominal and transanal dissection, or sequentially, where both teams work simultaneously only during the critical taTME portions which include peritoneal entry from the transanal side followed by completion of the TME followed by transanal or transabdominal specimen extraction. Several studies suggest potential advantages of a 2-team simultaneous approach including reduction in operative time [100, 107]. Another potential advantage is avoidance/reduction of intraoperative complications by improving visualization of deep pelvic structures by combining view from the abdominal and transanal sides, which may increase the accuracy of the dissection. A 2-team approach is difficult to organize in many hospitals, with logistical difficulties staffing cases with two attendings for the several hours required for taTME. When a simultaneous 2-team approach is not practical, it is recommended that at the very least, the transanal team employs a second team during the critical time needed for completion of the rectal and mesorectal mobilization following peritoneal entry by the transanal team and during specimen extraction and confirmation of the viability of the colonic conduit prior to anastomosis.

Conclusion

Since the first description of TEM over 30 years ago, the operative management of rectal diseases has evolved from radical proctectomy to minimally invasive abdominal techniques that most recently have incorporated transanal endoscopic approaches. Driven by the need for improved surgical outcomes in patients with rectal cancer, and steady technological and conceptual innovations in the field of minimally invasive surgery, TES had rapidly expanded the range and complexity of minimally invasive colorectal applications that can be performed using a primarily transanal endoscopic approach. The recent development of taTME and its rapid adoption worldwide based on favorable preliminary oncologic results is a reflection of ongoing efforts to facilitate the safe completion of otherwise exceedingly complex pelvic procedures and possibly move the field one step closer to NOTES in minimizing the trauma and limitations of transabdominal incisions and dissection. Several randomized trials

of taTME versus laparoscopic TME are underway to further evaluate the safety and efficacy of taTME, which may become the new standard of care in the surgical management of mid- and low rectal tumors.

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Future Endoscopic Tools and Platforms for Endoluminal Surgery

23

Kiyokazu Nakajima and Jeffrey W. Milsom

Key Points

- The advanced endoscopic intervention has not been widely available for colonic lesions. This is partially due to anatomical peculiarities of the colon (long length, easy expansion, thin wall) but also due to immature current flexible GI endoscopy in gaining exposure, maintaining visualization, and stabilizing working space. In addition to these fundamental elements of endoscopy, the lack of good tools is also responsible for the technical challenge.
- Future endoluminal surgery including advanced colonoscopic intervention will become a reality not by developing "ultrahigh-definition endoscopes" but by reconsidering its fundamentals such as insufflation, evacuation, and stabilization of working space. In addition, truly usable ancillary tools will contribute to overcome each technical difficulty.

Introduction

The advanced endoscopic intervention including endoscopic submucosal dissection (ESD) has not been widely available for colonic lesions. Anatomical peculiarities of the colon that make these procedures more difficult include its long length, easy expansion, numerous convolutions, and very thin wall [1]. Consequently, the *colonoscopic exposure* and working space are often unstable and suboptimal to perform complex procedures. The lack of truly "usable" ancillary tools has also been attributable to the technical difficulties of colonic ESD and other advanced procedures.

The authors have been working on the research and development of necessary devices/tools to improve performance and quality of flexible gastrointestinal (GI) endoscopic intervention. Our efforts have been focused on the improvements of "fundamentals" of endoscopy such as insufflation, smoke evacuation, and stabilization of working space. Our goals are not only to put colonic ESD into daily practice but to go beyond ESD, i.e., to bring "future endoluminal surgery" into reality. In this chapter we describe part of our recent achievements and their possible implications for the future of therapeutic endoscopy.

Improvement of Endoscopic Insufflation

Need for Stable Endoscopic Exposure

The stable visualization/exposure is no doubt a key to success in any aspect of endoscopic diagnoses/procedures [2]. Currently, a gas insufflation is routinely used to gain and maintain the endoscopic exposure. This fundamental technique, however, has not been fully reviewed throughout the history of flexible GI endoscopy [3]. Although carbon dioxide (CO_2) has been increasingly used instead of atmospheric air [4–7], the gas is still supplied through the endoscopic air/water channel in a manual and blind manner [2].

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Consequently, even a highly advanced procedure such as ESD is still a "one-person" process, with the operating endoscopist providing visualization, exposure, and instrument manipulation [2, 7].

The authors believe that a computer-mediated and pressure-regulated automatic insufflation, i.e., "laparoscopy-like" insufflation, will be a standard in current and future endoscopic intervention. With automatic insufflation in the gastrointestinal lumen, endoscopists will be able to focus on the intervention itself, like surgeons can focus on laparoscopic surgery under automatic pneumoperitoneum.

Fig. 23.1 Computer-mediated automatic insufflation unit for flexible GI endoscopy (GW-200, Fujifilm Corporation, Tokyo, Japan)

Space-Pressure-Controlled Endoscopy

Steady pressure automatically controlled endoscopy (SPACE) is a new technology to generate and maintain constant pressure environment inside the GI lumen (Fig. 23.1). [8] shows a fully computer-mediated SPACE insufflation unit for GI use (GW-200, Fujifilm Corporation, Tokyo, Japan). The unit feeds CO_2 into the GI lumen via dedicated overtube and leakproof adapter (Fig. 23.2). Alternatively, a commercially available "snap-on" device for gas insufflation can be used without placing the overtube in the GI tract (Fig. 23.3). The GI lumen is automatically insufflated with CO_2 to the setup intraluminal pressure, which is intermittently monitored by the GW-200 unit. An "add-on" manual insufflation is still possible within the setting range during SPACE; however, neither automatic nor manual insufflation is terminated when actual intraluminal pressure goes above the safety range. Suction can be done on demand, and the lumen is re-insufflated immediately after the endoscopist stops the suction (Video 23.1). Thus, the endoscopist no longer has to control the insufflation during the procedure and therefore becomes free to concentrate on the intervention itself. The endoscopic exposure theoretically becomes more stable and reproducible, as in laparoscopic surgery.

Preclinical Evaluation of Space

We have preclinically evaluated the feasibility and safety of SPACE technology in the upper and lower GI tracts [8–10]. In the esophagus, we successfully demonstrated that SPACE

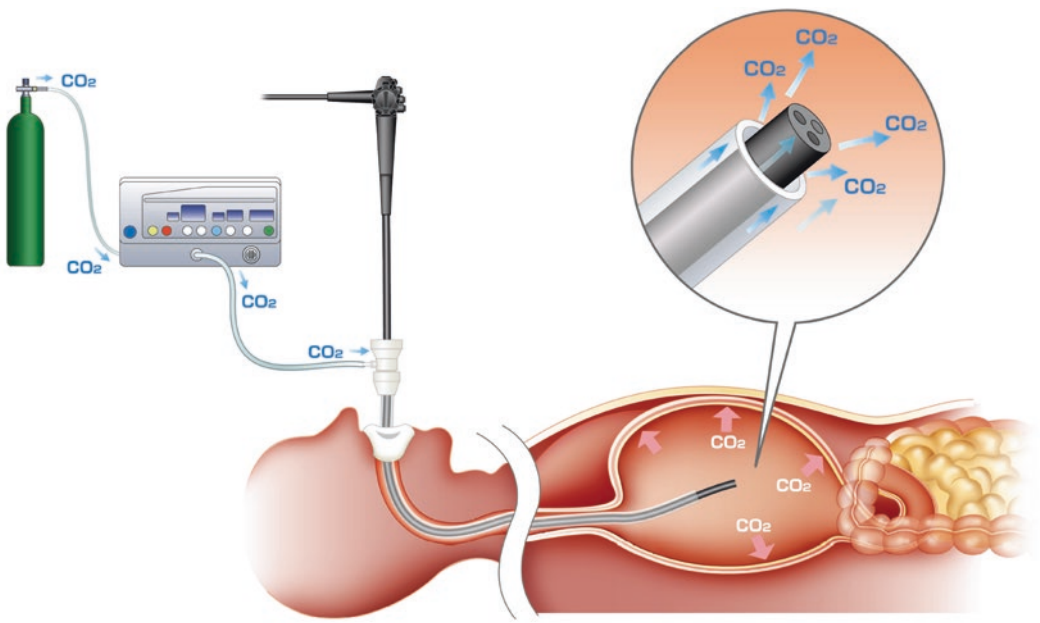

Fig. 23.2 The SPACE system

is feasible and safe in porcine models, without causing massive gas migration into the downstream bowel. In addition, SPACE significantly reduces operating times of esophageal ESD compared to manually insufflating endoscopy, by stabilizing the exposure, providing uniform tissue tension onto the mucosa at cutting, and reducing time to regain exposure after each suction [8]. In the lower GI tract, we also successfully confirmed that SPACE colonoscopy is feasible and safe in canine models [10]. SPACE colonoscopy provides stable and highly reproducible endoscopic exposure without causing massive retrograde gas migration [10]. Interestingly, the gas migration into the upstream bowel was even more significant in conventional (manual) insufflation than in SPACE, when the insufflation pressure is adequately set in advance (Fig. 23.4).

Fig. 23.3 Add-on insufflation line (Impact Shooter, Top Corporation, Tokyo, Japan)

Implication

The clinical feasibility and safety of SPACE using commercially available surgical insufflator (not GW-200) were validated in the esophageal ESD for patients with esophageal cancer [11]. The GW-200 insufflator and related accessory devices gained approval of their manufacture and sale pursuant to the provisions of the Pharmaceutical Affairs Act in Japan in 2015. The system is now under clinical evaluation in Japan and will be officially released in the market soon. Further clinical assessments are needed to apply this new technology to wider range of advanced endoluminal surgery worldwide.

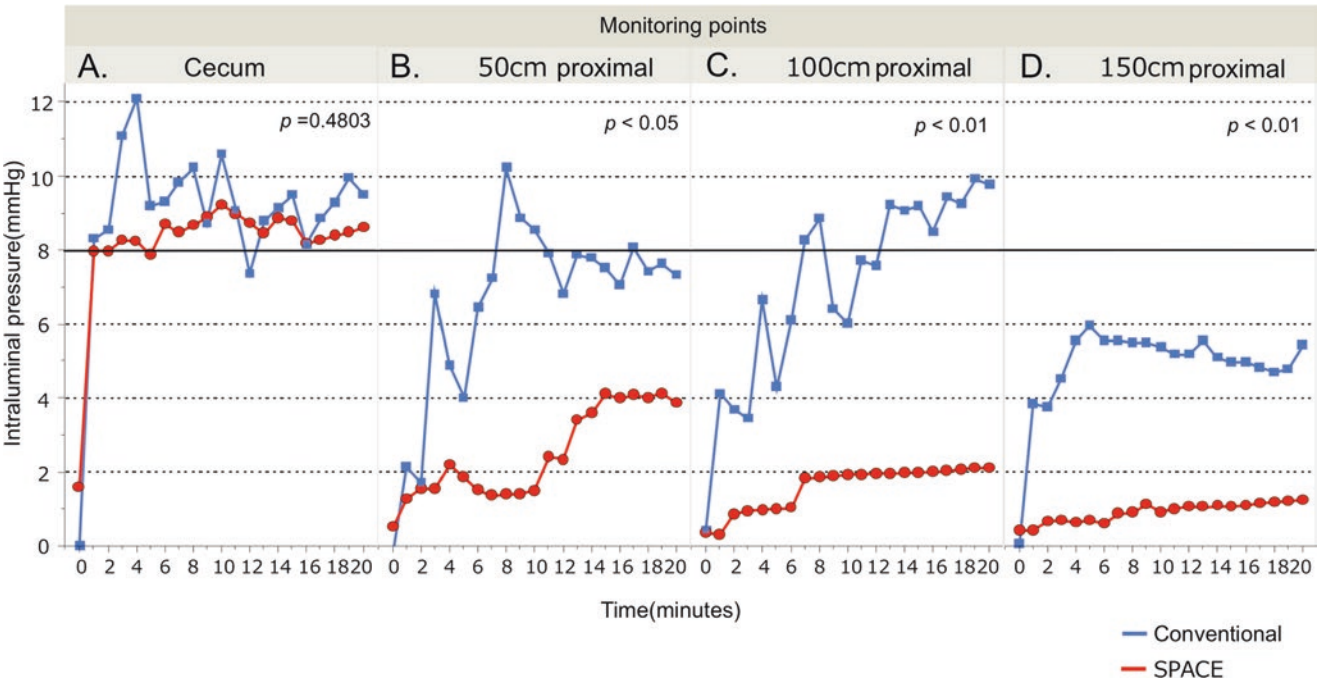

Fig. 23.4 Multipoint pressure monitoring during conventional (*blue squares*) vs. SPACE (*red circles*) colonoscopy at (**a**) insufflation site (cecum), (**b**) 50 cm proximal, (**c**) 100 cm proximal, (**d**) 150 cm proximal bowel, respectively. *Note*: significant pressure elevation (i.e., gas migration) in proximal bowels during manual insufflation whereas minimal or no elevation during SPACE

Improvement of Endoscopic Smoke Evaluation

Potential Hazards of Smoke in the GI Lumen

It is known that the smoke generated by energy devices not only reduces visibility in laparoscopic surgery but also increases chemical/biological hazards to patients, surgeons, and operating room personnel [12, 13]. This fact has led to recent improvement in smoke evacuation system in laparoscopic surgery. However, less has been known about the smoke generated during flexible GI endoscopic intervention. Recently, we have demonstrated that the smoke generated by endoscopic mucosal/submucosal ablation contains harmful substances as well [14]. The effective smoke evacuation system not only may improve performance and quality of endoluminal surgery but also may reduce potential risk of health hazards in patients and medical professionals.

Automatic Smoke Evacuation System

The automatic smoke evacuation in the GI lumen is only possible under automatically pressure-controlled environment; otherwise, each activation of evacuation almost always leads to significant collapse of the pneumoviscera [14]. Our SPACE technology can provide virtually "non-collapsing" exposure as long as the insufflation pressure and evacuation power are optimally set. An evacuation line is dedicated to the standard flexible endoscope, and any kind of automatic smoke evacuator for surgical use, equipped with a smoke absorptive membrane, is connected to the evacuation line (Fig. 23.5). To accomplish effective evacuation in the GI lumen, a simultaneous evacuation and insufflation at a well-balanced power is required. In the above experimental setting, the setup intraluminal pressure was 8 mmHg in SPACE, with the mode of evacuator of 100% power with delay time of 10 sec.

Preclinical Evaluation of Evacuation System

The system was preclinically evaluated in terms of visualization and dense of residual smoke after endoscopic session (mucosal ablation) in a porcine stomach [14]. The endoscopic visualization was significantly clearer in animals with automatic evacuation than that of animals without automatic evacuation (Fig. 23.6). The residual smoke inside the GI lumen was denser in animals without automatic evacuation than that of animals with automatic evacuation [14]. The semi-quantified relative carbon concentration was significantly lower in evacuation group than that of no evacuation group. During the activation of automatic evacuation, the actual fluctuation of intraluminal pressure remained within 6–8 mmHg, and no significant luminal collapse was observed [14].

Implication

Although still in its "POC" phase, the automatic smoke evacuation in the GI lumen has been proven feasible and promising. The data above has encouraged industry to develop ideal automatic smoke evacuators and related peripheral devices for flexible GI endoscopic interventions. Ideally, future endoscopes and/or related platforms should provide dedicated insufflation/evacuation channels.

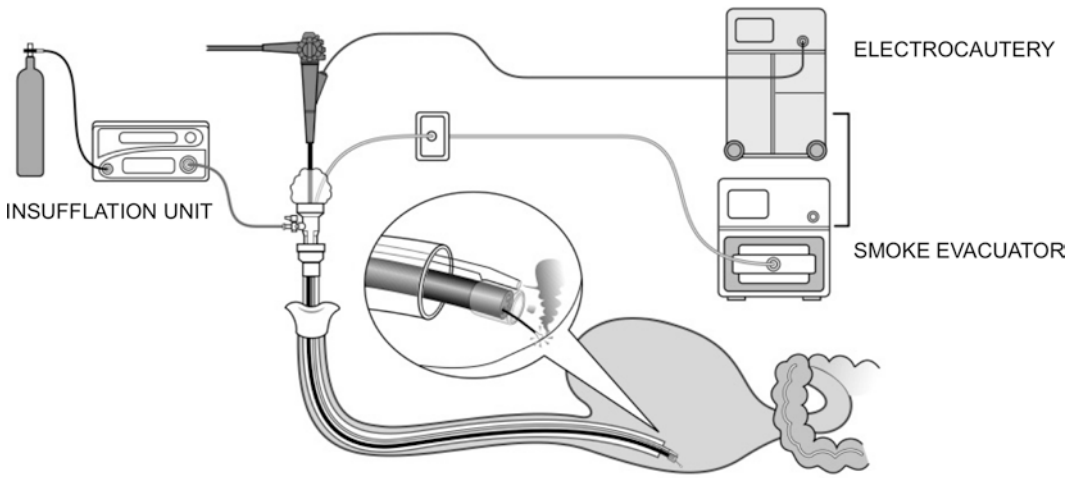

Fig. 23.5 Simultaneous insufflation/evacuation system

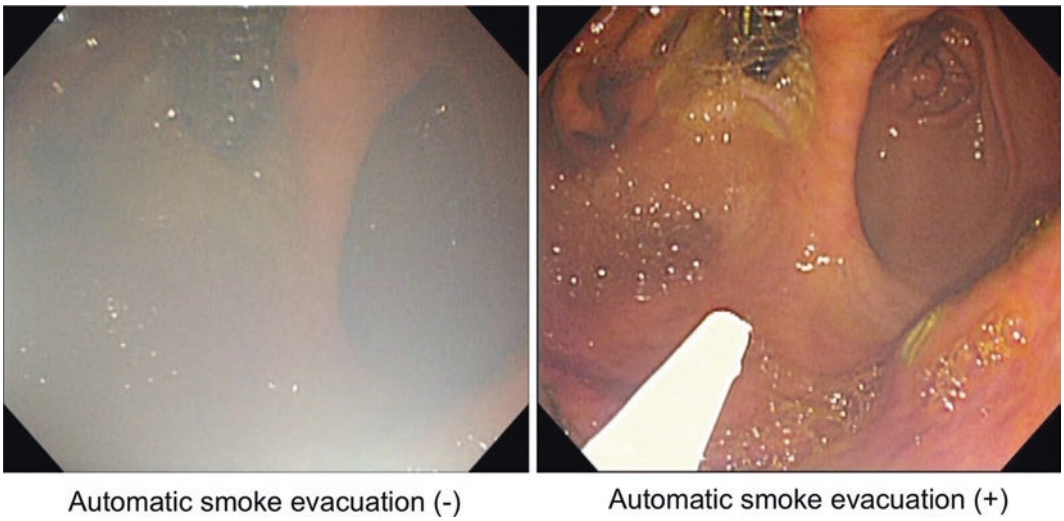

Fig. 23.6 Endoscopic visualization after mucosal ablation with or without automatic smoke evacuation

Improvement of Endoscopic Working Space

Need for Stable Endoscopic Working Space

In addition to stable endoscopic visualization/exposure, the stability of working space is another major factor to the success of advanced endoluminal surgery. Although SPACE technology can provide a stable pneumoviscera, the flexible endoscope is still floating freely inside the GI lumen. It needs to be kept in the correct position by an operating endoscopist or assisting endoscopist. The precise surgical actions needed for advanced endoluminal surgery are technically difficult without fixing/stabilizing both the endoscope and the intestine.

The ESP System

To obtain a stabilized endoscopic working space, various "platforms" have been proposed to date [15]. Some systems are robotic, having integrated optics and independent instrument manipulation function. The other systems are more mechanical, using conventional flexible GI endoscopes for visualization, and instrument manipulation being integrated with the use of a flexible, often lockable, multichannel access device [16]. It is easy to imagine that these platforms have been originally developed for more extreme conditions such as NOTES (natural orifice transluminal endoscopic surgery), where the stabilization of working space is more technically demanding. Each system has then been trickled down as a spin-off for current endoscopic intervention. As a result, most systems, especially robots, are too bulky and complicated to be applied inside the GI lumen.

The endoluminal surgical platform (ESP, Lumendi Ltd., London, UK) is also an endoscopic platform but has several unique features. The system has been designed for colonic use from scratch, as an add-on sleeve over the scope. It has two balloons (fore balloon and after balloon) and can be easily attached on virtually any colonoscope (Fig. 23.7). The ESP is advanced with both balloons not inflated into the colon. At the surgical site, the after balloon is first inflated to stabilize the system; then the fore balloon is pushed out beyond the point of pathology to manipulate the colon and to create an isolated, stable, and workable space called the "therapeutic zone" (Fig. 23.8). The distance between the two balloons may be adjusted, therefore smoothing out folds, straightening the colon between the balloons (by extending the fore balloon), or pulling the wall of the colon more directly in view (by pulling back on the fore balloon) (Fig. 23.9).

Preclinical Evaluation of ESP

Several preclinical evaluations have demonstrated that the use of ESP does not impact the movement and function of colonoscope but does improve the stabilization of surgical site and potentially reduces endoscopist's workload in advanced endoluminal procedures. The system has completed the preclinical experimental stage and has been submitted for approval to the US Food and Drug Administration. We expect clinical trials to begin in late 2016, with the main indication being for assistance in the endoscopic removal of large or difficult to reach colorectal polyps.

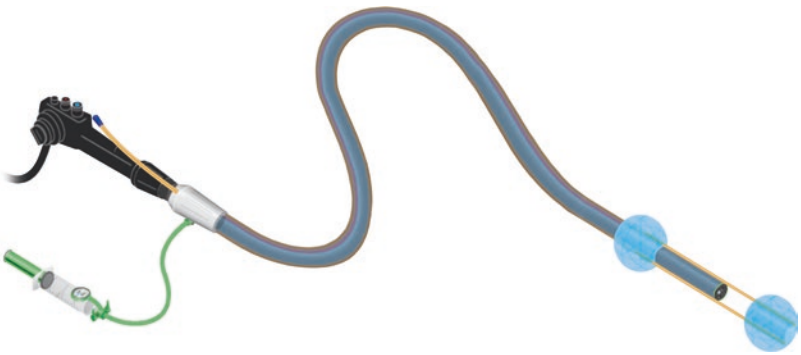

Fig. 23.7 The ESP system

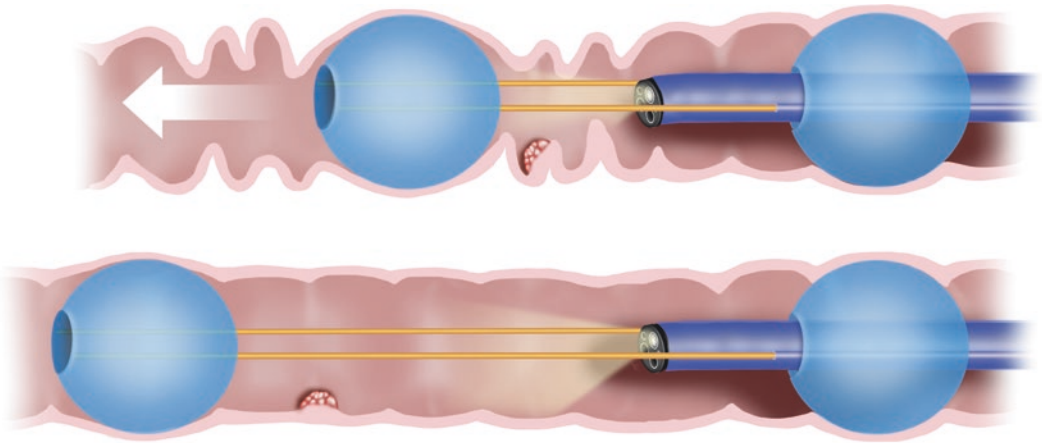

Fig. 23.8 Therapeutic zone between two balloons

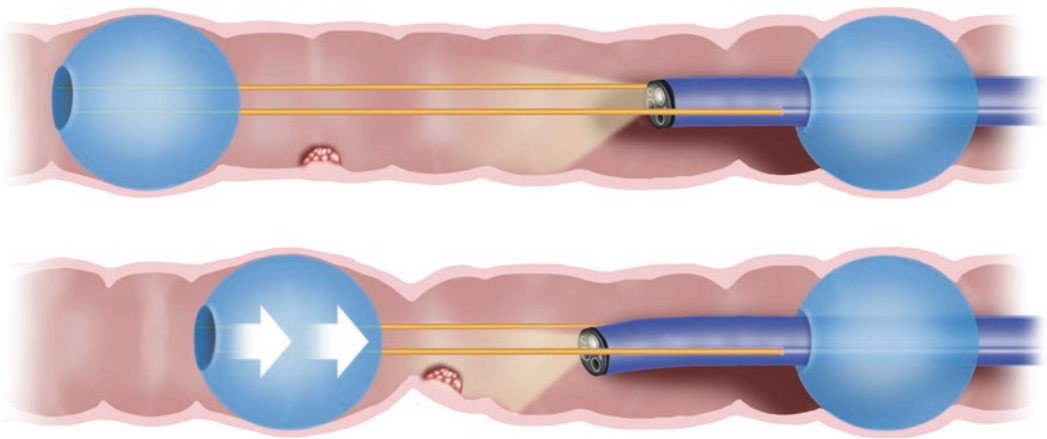

Fig. 23.9 Optimization of view/working angle by pulling back on the fore balloon

Implications: ESP and SPACE

The ESP can be a stand-alone device, but recent collaborative studies have indicated that the use of ESP under SPACE creates a synergy effect, by further optimizing the visualization and working space. With ESP, the colonic segment that needs to be insufflated will be further minimized. With SPACE, the therapeutic zone will be further stabilized even with repeated ablation/suctioning maneuvers during the procedure.

Other Future Improvements

Most flexible tools such as graspers and hemostats available in the current flexible GI endoscopy have lower performance, are less robust, and have a narrower range of variation compared to surgical devices. Some very common surgical tools such as scissors, clips, and staplers are not available in this current environment. In addition to the improvement of "fundamentals" as stated previously, we definitely have to improve each flexible endoscopic tool from the surgical viewpoint and also have to develop truly usable tools from scratch. These future improvements will only be possible with constant technological innovation made by substantial medtech collaboration. Herein we describe some recent examples.

Continuously Rotating Forceps

Virtually no flexible forceps are comparable to rigid laparoscopic instruments in terms of rotation capability. Even the so-called "rotatable" forceps in the market do not show satisfactory performance. This is part due to expense. The use of high-performance (therefore expensive) metallic torque wires is too costly to implement. The main reason, however, is because most current endoscopists have not understood the value of fully rotatable forceps. Instead of rotating the forceps, they have adapted by rotating the endoscope to adjust the direction.

In future endoluminal surgery, the endoscopists will no longer rotate their endoscopes but will fix the horizon inside the GI lumen. Under a stabilized fixed-horizon visualization/working space, endoscopists will soon use fully functioning flexible tools as in laparoscopic surgery. The current technology has already solved the technical problems in incorporating special torque wires with higher conductivity (Fig. 23.10). The cost for high-performance wires will be reduced as the expansion of clinical needs.

Suction/Irrigation Device

Currently, suction is performed via a built-in channel of the colonoscope. The endoscopic visualization is lost during this "tip suction," since the endoscope has to "dive" into the fluid. This temporary loss of visualization has been less of an issue in the GI lumen, but it is unacceptable in laparoscopic surgery, where blind-tip suction may lead to serious complication. In future endoluminal surgery, the endoscopic visualization should be maintained even during the suction procedure. The dedicated endoscopic suction catheter (Endoshower, Yamashina-Seiki, Co., Ltd., Shiga, Japan) has been developed based on such concept. The 2.5 mm flexible catheter, with 24 side holes (0.4 mm in diameter) on its nozzle, accomplishes "laparoscopy-like" irrigation and suction via a standard biopsy channel (Fig. 23.11). The device is now

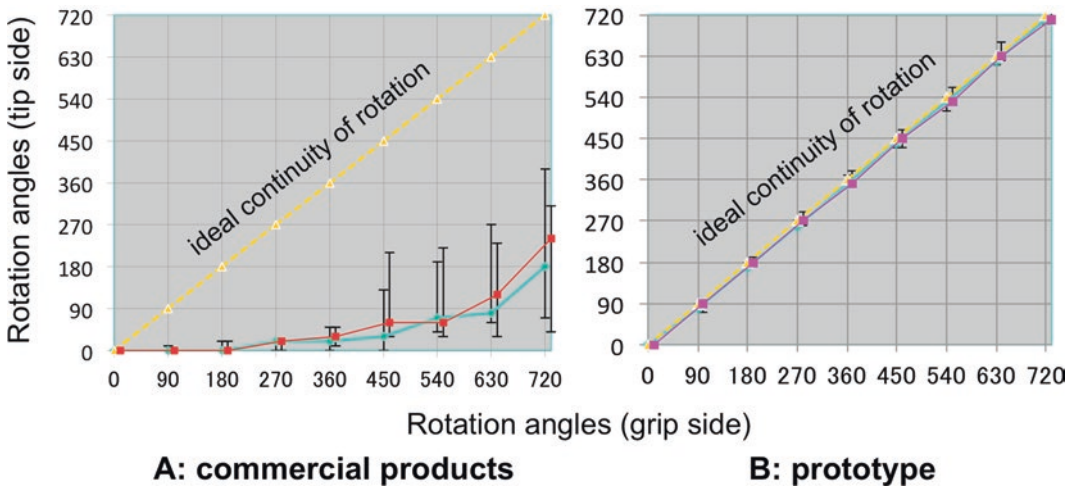

Fig. 23.10 Difference in rotation performance between (**a**) commercially available "rotatable" forceps and (**b**) prototype forceps with high-performance torque wire

gaining clinical acceptance in the Japanese market with satisfactory performance. We expect that its clinical indications will be expanded in the era of future endoscopy, where prior "built-in" functions, e.g., insufflation, suction, and irrigation, will no longer be dependent on the endoscopes.

Countertraction Overture

Some rectal and sigmoid lesions can be approached using another unique platform. The device is an endoscopic overtube with a built-in side channel (Fig. 23.12). The tissue (mucosa) is retracted by grasping forceps that passes through the side channel of the overtube, not through the biopsy channel of the endoscope. The strength and direction of traction are controlled by rotating the overtube (not the endoscope) and by adjusting its depth (Fig. 23.13). [17] This device (Endotornado, Top Corporation, Tokyo, Japan) may change current ESD practice in its accessible segments of the GI tract (Video 23.2). The Endotornado has gained approval of its manufacture and sale pursuant to the provisions of the Pharmaceutical Affairs Act in Japan in 2016, and it is undergoing clinical evaluation. Currently, its indication is limited for esophageal lesions but will be soon expanded to other segments of the GI tracts.

Fig. 23.11 A new endoscopic flexible suction/irrigation catheter (Endoshower, Yamashina-Seiki, Co., Ltd., Shiga, Japan)

Suturing Device

Suturing, not clipping, has been a dream among endoscopists for decades. The development of truly usable endoscopic suturing device is not technically easy, mainly due to size limitation and "in-line" mechanism of flexible endoscopes. Among numerous experimental and/or limitedly released devices, the OverStitch (Apollo Endosurgery, Austin, Texas) is virtually the only device available in the market (Fig. 23.14). This device has been evaluated preclinically and clinically and has now gradually gained clinical acceptance in the field of upper gastrointestinal endoscopy [18, 19]. Since the current version requires a double-channel endoscope with relatively short length, the device is not optimal for use in the colon, especially in deep locations. The industry appears to be developing a next-generation OverStitch with improved ergonomics and broader endoscope compatibility, including compatibility with single-channel diagnostic endoscopes.

Flexible Robot

The concept of NOTES encouraged the researchers/industries to develop various types of flexible multitasking platform, e.g., EndoSamurai (Olympus), ANUBIScope

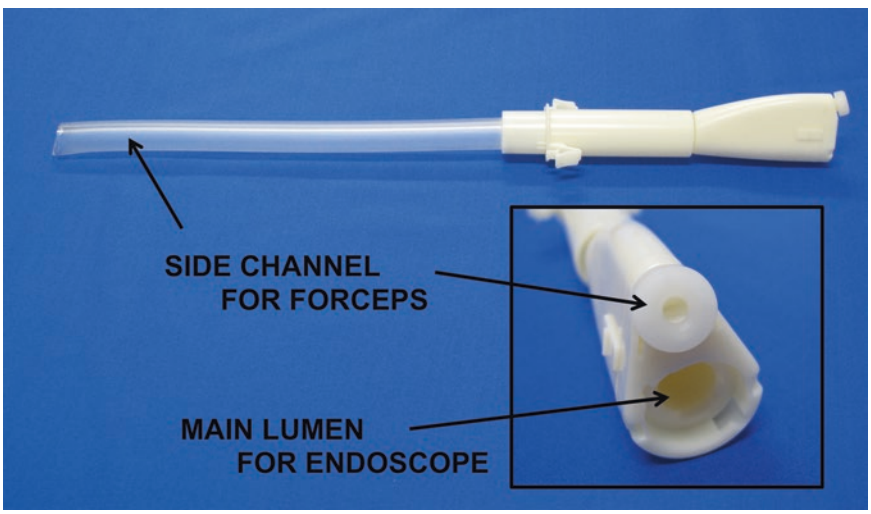

Fig. 23.12 A new overtube with built-in side channel (Endotornado, Top Cooperation, Tokyo, Japan)

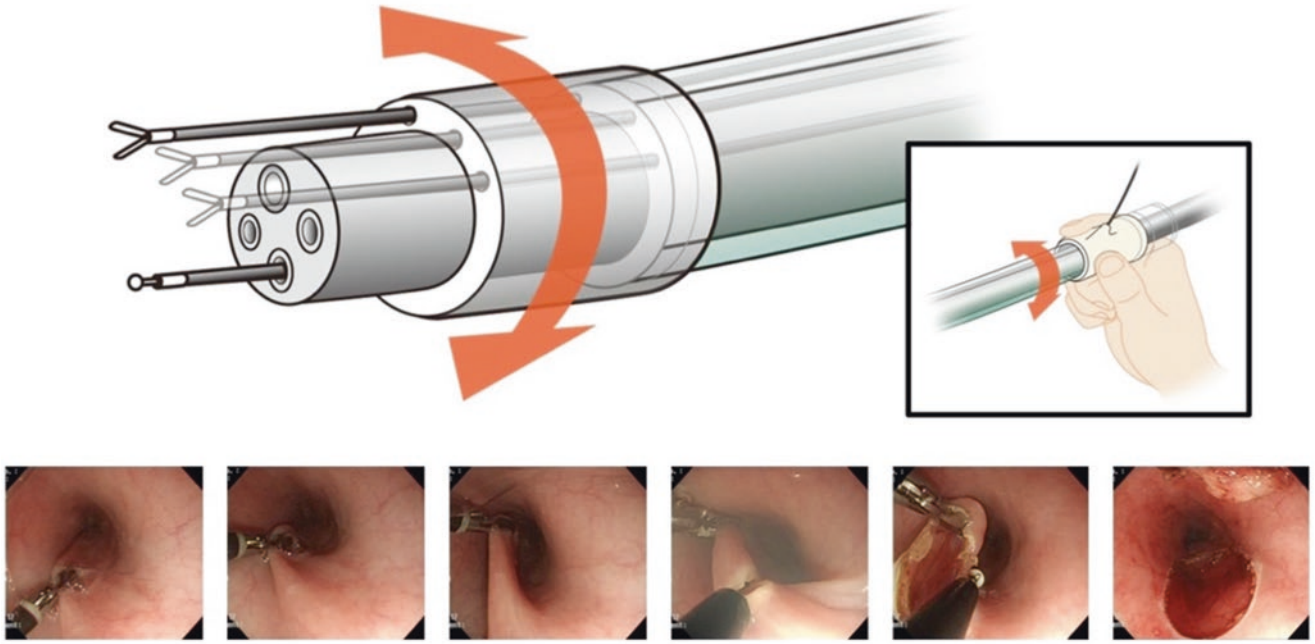

Fig. 23.13 Adjustable tissue traction/countertraction in ESD using Endotornado overtube

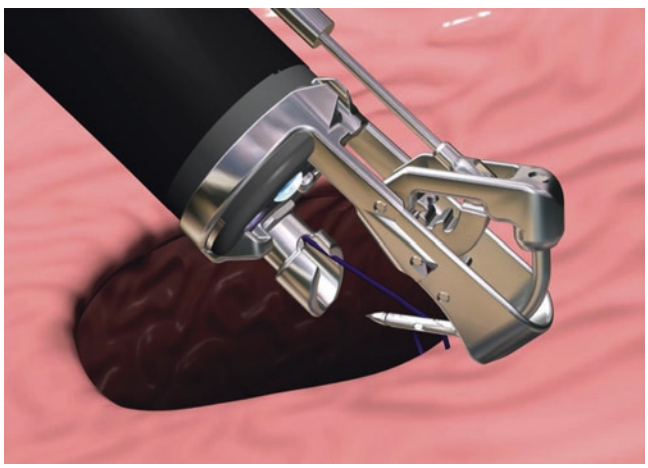

Fig. 23.14 The OverStitch endoscopic suturing system (Apollo Endosurgery, Austin, Texas)

(Karl-Storz), and DDES system (Boston Scientific). Since these "mechanical" systems basically employed traction cables for actuation, they had technical limitations in downsizing and were physically prone to hysteresis [16].

A flexible robot, which does not fully rely on conventional traction cable mechanism, can theoretically overcome above challenges. One example is Master and Slave Transluminal Endoscopic Robot (MASTER), developed by Endomaster Pte Ltd., Singapore. Its first generation showed feasibility of performing gastric ESD in human subjects and rectal ESD in porcine models (Fig. 23.15). The flexible robotic technology is promising but still in its interval phase and therefore requires continuous research/development efforts. However, together with the improvement of "fundamentals," this technology may impact on future GI endoluminal surgery.

Pearls and Pitfalls

Flexible GI endoscopes were originally designed for diagnostic purposes, not for therapeutic purposes. Their basic concept (design and function) has had little change in the past 50 years, one-person procedure using one endoscope. As a result, currently, there are too many functions in a single endoscope and too many tasks for a single endoscopist. Besides research and development of endoscopes/related devices, what is even more important may be a daring innovation in our way of thinking, i.e., a paradigm shift—that treatment of serious lesions of the GI tract may be accomplished endoluminally. We need to discard the notion that almost all surgical therapies involving the intestine require a segmental resection. By adopting this paradigm shift, not only will disease therapies become safer but also LESS expensive!

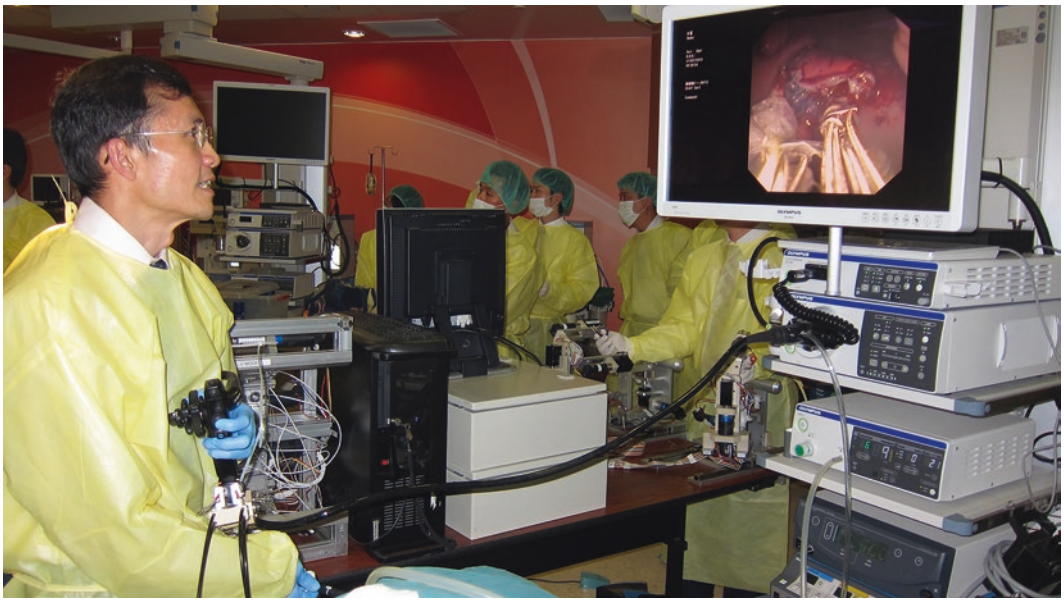

Fig. 23.15 Porcine rectal ESD using MASTER robot system (Endomaster Pte Ltd., Singapore)

Conclusions

The future of GI endoluminal surgery will develop more rapidly and surely by redefining and perfecting the "fundamentals" such as insufflation, evacuation, and stabilization of working space. Truly usable endoluminal tools will also contribute to overcome technical difficulties. An intensive developmental effort will generate lots of spin-offs that will be immediately applicable to current and future flexible endoscopic interventions. There are many reasons to assume that future endoluminal surgery will soon assume an equivalent role to traditional laparoscopic surgery and eventually surpass it in many disease therapies of the digestive tract.

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