Sherene Shalhub
Anahita Dua
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Editors

Hemodialysis Access

Fundamentals and Advanced Management

Springer

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with contributions from Shahram Aarabi

Springer

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To our patients who inspire us every day with their strength, resilience, and compassion.

Preface

This book is a labor of love for our patients who live with end-stage renal disease on a daily basis. The concept was simple and born 2 years ago when I realized that surgeons in the early years of practice need a comprehensive text to help them navigate the subtleties of care for this patient population. Maintenance hemodialysis became a reality in 1960, and over two million people worldwide currently receive treatment with dialysis to stay alive. Although the role of the surgeon is not especially glamorous, creating a successful hemodialysis access offers a lifeline for a patient with end-stage renal disease.

The book is designed to be a reference for the surgeons, interventionalists, nephrologists, and other providers who care for patients with end-stage renal disease. We wanted to create a multidisciplinary clinical perspective between the various specialties that care for the same patient. By providing a holistic approach to the issues that impact the patients and their providers, it is our hope that this will improve patient care and outcomes.

With this in mind, we divided the book into sections. The first section places the issue of maintenance dialysis in perspective by starting with the history of hemodialysis access highlighting the successes and failures that brought us to today. The current state of dialysis in the United States is then addressed, and we asked our colleagues from Japan and Taiwan to give us another point of view by sharing their own experiences. The section concludes with a discussion of the ethical issues surrounding dialysis, as the inception of formal medical ethics began with the evolution of chronic hemodialysis. The second section addresses hemodialysis access planning with a focus on timing, decision-making, perioperative evaluation, and anesthetic considerations. The third section focuses on the technical aspects, the "how to," for creating hemodialysis access. The fourth section addresses the advanced skill sets required to address hemodialysis access dysfunction. The final section covers alternatives to hemodialysis such as peritoneal dialysis and the criteria for renal transplantation. It also discusses home hemodialysis, wearable hemodialysis devices, and the outpatient approach to hemodialysis access.

We dedicate this book to those who have taken upon themselves the mission of caring for end-stage renal disease patients. It is our sincere hope that you will find the contributions in this book valuable to your practice.

Seattle, WA, USA — Sherene Shalhub, MD, MPH

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Abbreviations

ACR	American College of Radiology
ACS-NSQIP	American College of Surgeons National Surgical Quality Improvement Program
AIUM	American Institute for Ultrasound in Medicine
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
BFR	Blood flow rate
CAPD	Continuous ambulatory peritoneal dialysis
CDUS	Color Doppler ultrasonography
CKD	Chronic renal disease
CMS	Centers for Medicare and Medicaid Services
CPT	Current Procedural Terminology
CQI	Continuous quality improvement
CRBSI	Catheter-related blood stream infections
CVC	Central venous catheter
DAC	Outpatient dialysis access center
DCD	Donation after circulatory death
DOQI	Dialysis Outcomes Quality Initiative
EDV	End diastolic velocity
FFCL	Fistula First Catheter Last
FFI	Fistula First Initiative
JSDT	Japanese Society for Dialysis Therapy
KDOQI	Kidney Disease Outcomes Quality Initiative
KDPI	Kidney Donor Profile Index
MAC	Monitored anesthesia care and sedation
MIPPA	Medicare Improvements for Patients and Providers Act
NAPRTCS	North American Pediatric Renal Trials and Collaborative Studies
NKF	National Kidney Foundation
NVASRS	National VA Surgical Risk Study
PD	Peritoneal dialysis
POC	Point of care
PSV	Peak systolic velocity
QIP	Medicare Quality Incentive Program
RVU	Relative value unit
SRU	Society of Radiologists in Ultrasound
TDC	Tunneled dialysis catheter
USRDS	United States Renal Data System
VQI	Vascular Quality Initiative

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Part I

Historical Perspectives and Current State of End Stage Renal Disease and Hemodialysis

Historical Perspectives on Hemodialysis Access

1

Sherene Shalhub

Introduction

Nearly two centuries ago in 1836, Dr. Richard Bright describes a composite clinical course of end-stage renal disease [1]:

> The patient awakes in the morning with his face swollen, or his ankles puffy, or his hands edematous … already his urine contains a notable quantity of albumin, his pulse is full and hard, his skin dry, he often has headaches, and sometimes a sense of weight or pain across the loins. Under treatment more or less active, or sometimes without treatment, the more obvious and distressing of the symptoms disappear… absolutely forgotten. Nevertheless, from time to time, the countenance becomes bloated; the skin is dry; headaches occur with unusual frequency; or the calls to micturition disturb the nitrous by the repose. After a time the healthy color of the countenance fades; a sense of weakness or pain in the lines increases; headaches often accompanied by vomiting, add greatly to the general want of comfort; and a sense of lassitude, or weariness and of depression, gradually steal over the body and mental frame. Again the patient is resorted to tolerable health; again he enters is active-duty; or he is perhaps less fortunate; the swelling increases, the urine become scanty, the powers of life seem to yield, the lungs become edematous, and in a state of asphyxia or coma, he sinks into the grave; or a sudden effusion of serum into the glottis closes the passages of air, and brings on a more sudden dissolution. Should he however have resumed avocations of life, he is usually subject to constant recurrence of his symptoms; or again, almost dismissing the recollection of his ailment, he is suddenly seized with an acute attack of pericarditis, or with a still more acute attack of peritonitis, which without any renewed warning, deprives him in eight and 40 h, of his life. Should he escape this danger likewise, other perils await him; his headaches have been observed to become more frequent; the stomach more deranged; his vision indistinct; his hearing depraved; he is suddenly seized with a convulsive fit, and becomes blind. He struggles through the attack; but again and again it returns; and before a day or a week has elapsed, worn out by convulsions or overwhelmed by coma, the painful history of his disease is closed.

This background is given here because the clinical course described is rarely seen in these modern days where dialysis is taken for granted. We rarely glimpse into the vivid reality of the deadly clinical illness that dialysis suppresses, and because so we fail to recognize dialysis for the miracle that it is.

The history of hemodialysis access is simply fascinating. It is a story of pioneers in medicine who took a condition that was a once fatal and made it a chronic condition, the story of countless patients who were willing to undergo unproven therapy, and the story of early organ replacement in medicine. While the hemodialysis technology was being developed, the major obstacle to sustainable hemodialysis was the limited accessibility and durability of blood vessels. This chapter offers a historical perspective of the development of dialysis access into the 1980s.

The First Hemodialysis in Humans

The first hemodialysis treatment in humans was performed for 15 min on a boy dying from kidney failure by Georg Haas (Giessen, Germany), in October 1924. He used a glass cannula for arterial and venous access with an inflow from the radial artery and outflow to the cubital vein. This was the first time that a dialysis apparatus and procedure were demonstrated as safe and feasible. He repeated this procedure increasing the treatment intervals for up to 60 min [2].

The treatment intervals were short due to problems with anticoagulation. Initially, he used hirudin. In 1928 heparin became available as an anticoagulant, and he was able to dialyze 400 ml of blood by anticoagulating it and circulating it through the dialyzer for 30 min before returning it to the patient repeating the procedure nine times. The clinical effect of the treatment lasted for 6 days during which the patient clinically improved with resolution of nausea, return of appetite, and a reduction in headaches. This technique did not gain widespread recognition due to its limited efficacy [2, 3].

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Modern Hemodialysis Therapy

Modern hemodialysis therapy started on March 17, 1943, when Willem Kolff, a young Dutch physician in the small hospital of Kampen (the Netherlands), treated a 29-year-old woman suffering from malignant hypertension and "contracted kidneys." He used a "rotating drum kidney" that he constructed with the support of Mr. Berk, the director of the local enamel factory (Fig. 1.1). Arterial and venous access was obtained by venipuncture needles in the femoral artery and vein. Although that patient did not survive, he persevered in his technique. On September 11, 1945, the first of his 17 patients survived, a 67-year-old woman with cholecystitis and sulfonamide nephrotoxicity. Kolff left the Netherlands in 1950 and continued to work in on artificial kidneys in the United States. In the 1950s, the technical devices were available for regular hemodialysis treatments such as Kolff's "twin-coil kidney" [4]. In addition to venipuncture, he performed surgical cutdown of the radial artery, but this was complicated due to severe bleeding during heparinization. In the years that followed, substantial technical developments in dialysis machines followed, but access remained a challenge.

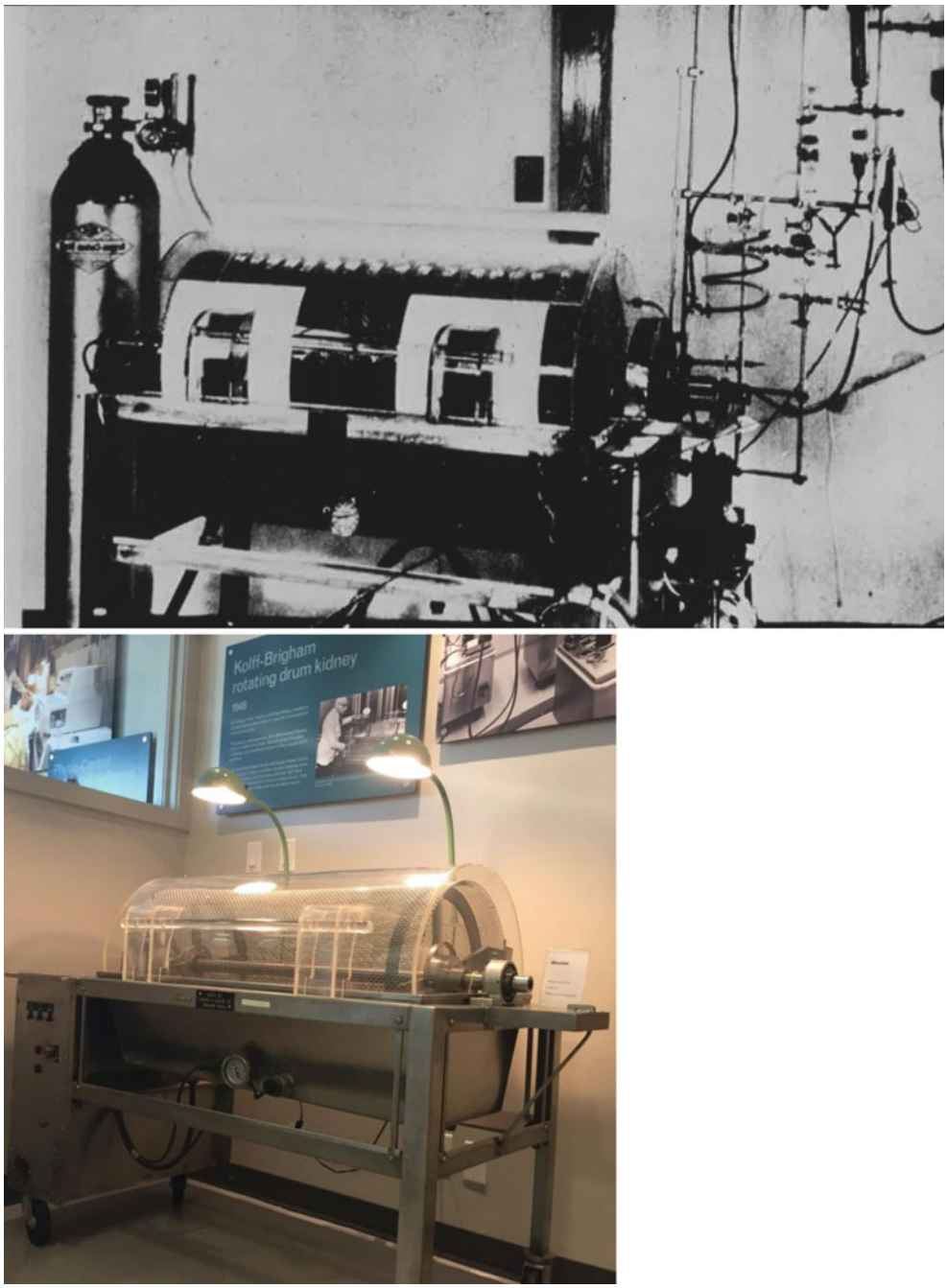

Fig. 1.1 The first hemodialysis machine used in the United States: the rotating drum artificial kidney. *Top panel*: the original Kolff rotating drum dialyzer (Image courtesy of Northwest Kidney Centers, Seattle, WA). *Bottom panel*: Kolff-Brigham rotating drum artificial kidney on display at Northwest Kidney Centers' Dialysis Museum (Seattle, WA)

The First Arteriovenous Shunt

The prospect of living with end-stage renal disease (ESRD) became a reality on March 9, 1960, when a Teflon arteriovenous shunt made dialysis possible for a Boeing machinist, Clyde Shields, at the University of Washington in Seattle. Mr. Shields survived for 11 years on chronic hemodialysis (Fig. 1.2) [5]. The original shunt was developed as a result of the efforts of three people: Belding Scribner, the nephrologist, who came up with the concept; Wayne Quinton, the hospital engineer, who developed the technology; and Dave Dillard, the pediatric cardiac surgeon, who implanted the shunt. The story of developing the shunt is recalled by Scribner and colleagues as follows [6]:

> On February 9, 1960, a 42-year-old patient, Neil Ward, was transferred from Spokane to the University of Washington in Seattle in a near terminal condition from uremia and congestive heart failure or you to acute renal failure. He responded dramatically to intense dialysis and ultrafiltration, and within a week he was up and around and nearly normal health. Unfortunately, anuria made the diagnosis of reversible renal failure suspect, and a biopsy showed total renal destruction from rapidly progressive glomerular nephritis. The dilemma we face is well expressed in an expert from a letter we wrote to his referring physician on February 25, 1960: "We have had a tremendous problem in deciding in our own minds what the reasonable thing to do here. His wife has been most cooperative and understanding the dilemma, and she fully realizes the prognosis. The question was raised as to whether he should be returned to Spokane, but his wife said that she thought it would be better to keep him here. We have tried to be objective and discussing his case among ourselves, and have asked the question of whether we have the right to prolong his life in the fashion we have. It was our feeling that until we had the biopsy we could not be sure the prognosis, and we were unable to get a biopsy until we could get him in good enough shape to do so, hence from the point of view of the ethics of the case, we have considered the dialysis procedure part of our diagnosis procedure and only incidentally therapeutic. Mr. Ward does seem to be enjoying his brief respite, and as far as we or his wife are able to determine, he does not understand his prognosis. By carefully observing his fluid balance, we hope to be able to keep him free of heart failure and allow him to slip into uremic coma, before he realizes what has happened. We have very carefully considered the possibility of keeping him alive and definitely by means of dialysis. And, whereas this might be possible in a few selected cases, we have never been in a position to attempt it, and we do not think that we would be ready at this time, nor do we think Mr. Ward would be a candidate for such a drastic undertaking". With great sadness we finally were able to convince Mrs. Ward to take her husband back to Spokane, where he died on March 6, 1960.

Fig. 1.2 Belding Scribner (*right*) with Clyde Shields (*left*) (Image courtesy of Northwest Kidney Centers, Seattle, WA)

This experience caused Dr. Scribner to awaken in the middle of a mid-February night with the idea of the arteriovenous shunt that he subsequently developed with Wayne Quinton and Dave Dillard. The shunt (Fig. 1.3) consisted of Teflon tubing inserted into the radial artery and forearm vein that can be connected to the hemodialysis machine [7]. When not in use, the shunt was connected by a bypass loop on a metal arm plate secured to the patient's forearm, thus eliminating the need for anticoagulation between treatments [7]. The use of Teflon tubing was important because the experience with Teflon tubing in cardiac surgery demonstrated that the material was nonreactive and the blood did not clot off easily in this type of tubing [2]. In 1960 there was no FDA or device regulation; thus the shunt was implanted and used. Scribner and Quinton presented the shunt during the annual meeting of the American Society for Artificial Internal Organs in Chicago [7, 8]. Several attendees took away the materials to place in patients but had problems with the shunt. This was attributed to lack of surgical expertise [2]. Dillard would spend between 1 and 3 hours carefully inserting the cannulas, and success of the shunt was attributed to his meticulous surgical technique [2].

The original Teflon shunt lasted for a few weeks or months, and the original patients including some with acute renal failure required several shunts in the upper and lower extremities. To increase cannula flexibility and longevity, Quinton added a silicone rubber segment, creating the so-called Silastic-Teflon bypass cannula where the tapered Teflon tips were inserted into the artery and vein and a Silastic tube made the exit through the skin (Fig. 1.4) [6]. Despite these advances, the shunts were useful only for a few months before failing. Complications included cellulitis, skin necrosis, sepsis, pulmonary emboli, shunt dislodgement or cannula extrusion, vessel stenosis, hemorrhage, and thrombosis. The mean half-life of the shunt was reported to be 6 months [9]. Despite these complications, the shunt was the decisive breakthrough that made maintenance hemodialysis possible [3].

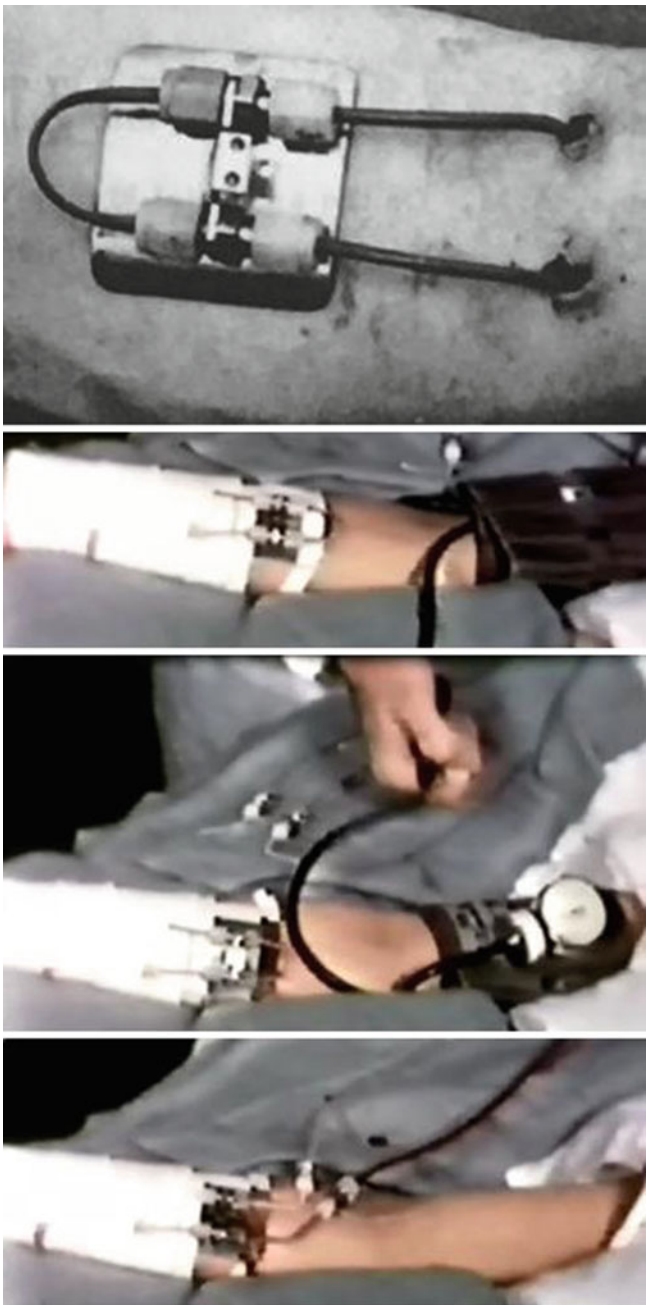

Fig. 1.3 The Quinton-Scribner arteriovenous shunt in 1960. *Top panel*: Teflon tubing cannulas inserted into the radial artery and a forearm vein with the bypass loop and the metal arm. *Bottom panel*: the bypass loop is removed when placing the patient on hemodialysis, and the free blood flow was controlled using a blood pressure cuff while connecting to the dialysis machine (Courtesy of Northwest Kidney Centers, Seattle, WA)

During these early times of hemodialysis access, candidates for maintenance hemodialysis were carefully selected, and given the limited resources, many were turned down creating national headlines [10]. The history of hemodialysis is closely intertwined with the birth of bioethics, and this period of evolution in medical practice is detailed by the firsthand account of Dr. Thomas R. McCormick, Professor of Bioethics and Humanities at the University of Washington School of Medicine, in Chap. 8.

In 1973, T.J. Buselmeier and colleagues (Minneapolis, USA) developed a modification of the Scribner AV shunt. The Buselmeier shunt is a compact U-shaped Silastic prosthetic AV shunt with either one or two Teflon plugged outlets which communicated to the outside of the body. The U-shaped portion could be totally or partially implanted subcutaneously (Fig. 1.5) [11]. This shunt was designed to address some limitations of the Scribner shunt, namely, the long tubing that was prone to dislodgment and had high resistance to blood flow, and to limit the vascular intimal trauma that is the result of transmitted vessel tip movement. The Buselmeier shunt gained some acceptance during the following years, especially for pediatric hemodialysis patients [3].

The Repeated Venipuncture Technique in Surgically Created Subcutaneous Arteriovenous Fistula

Vascular access remained the Achilles heel of chronic hemodialysis, James E. Cimino (New York, USA) observed. The external Teflon-Silastic AV shunt (also called the Quinton-Scribner shunt) was associated with infection and thrombosis, and the alternative of repeated direct puncture of arteries and veins damaged these conduits every time the patient was connected to the dialysis machine. A patient could receive only a few treatments before all available access sites were utilized [12].

In 1961, Cimino, a nephrologist, and Michael J. Brescia (New York, USA) described a "simple venipuncture for hemodialysis" based on the experience of Cimino when he worked part time as a student at the Bellevue Transfusion Center in New York [13]. After infiltration of the overlying skin with 1 % procaine, the most accessible forearm vein was punctured with a needle. Needles varied in size from 16 to 12 gauge. Patency of the vein and adequate blood supply were assured by the application of tourniquet pressure with a sphygmomanometer. A blood flow in the range of 150 and 410 ml/min was obtained using this technique if the patient was fluid overloaded, but this was not sustainable in hypovolemic patients.

Cimino also noted that arteriovenous fistulas (AVFs) caused by trauma in Korean War veterans did not have significant effects on their health. Additionally, experience with surgically created fistulas was not new. During the 1930s, surgically created fistulas were placed at the Mayo Clinic in children with polio whose legs were paralyzed and not growing in order to promote collateral circulation. Cimino began to wonder if they could take advantage of the rapid blood flow and accompanying venous distention that occurred in the presence of a surgically created AVF despite the risk of developing

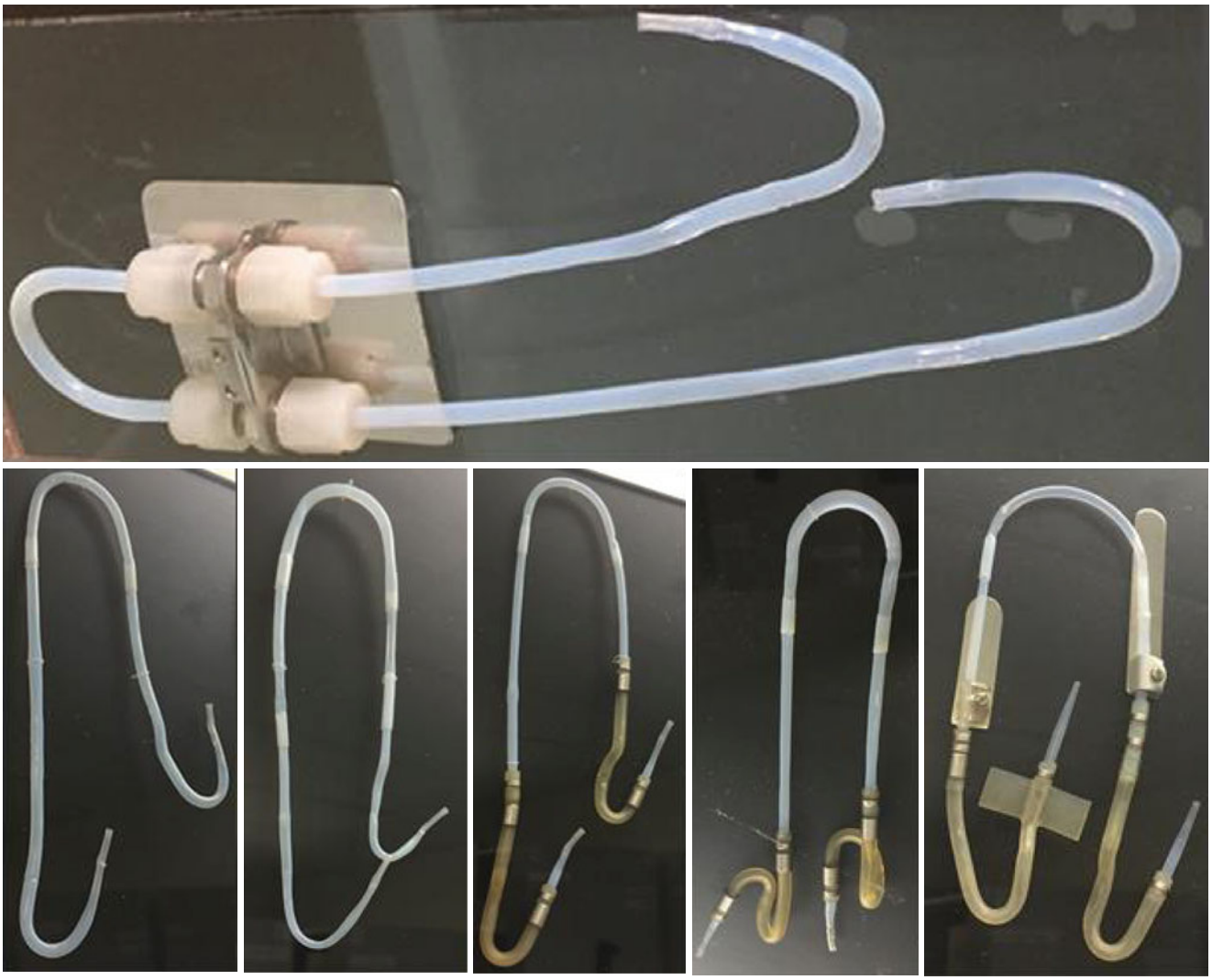

Fig. 1.4 The original Teflon Quinton-Scribner arteriovenous shunt as first designed in 1960 (*top panel*) and the developmental progression of the shunts from 1960–1967 (*bottom panel*, *left* to *right*) and the addition of the silicone rubber segment, creating the Silastic-Teflon bypass cannula with tapered Teflon tips that were inserted into the artery and vein and the Silastic tube to exit through the skin (shunts photographed at the Northwest Kidney Centers' Dialysis Museum, Seattle, WA)

heart failure as a long-term consequence. Dr. Cimino remarks that "We were bold in using a procedure that had always been considered physiologically abnormal, but without adequate vascular access our patients were doomed" [12].

On February 19, 1965, Drs. Brescia, Cimino, and Appel (surgeon) created the first autogenous arteriovenous fistula [14]. Dr. Appel performed a side-to-side anastomosis between the radial artery and the cephalic vein at the wrist using a 3–5 mm arteriotomy and venotomy in the corresponding lateral surfaces of the artery and the vein using arterial silk in continuous fashion for the anastomosis [14]. The fistula could then be accessed for dialysis by venipuncture. The first AV fistula dialysis attempt failed. Later, they realized it had failed for the same reason the original vein-to-vein technique had failed. "The patient had been prepared so diligently before the procedure that we removed too much fluid," Cimino says. "His blood pressure was inadequate for keeping blood flowing through the newly created fistula." After a period of trial and error, Cimino and his team were able to maintain adequate blood flow by using carefully placed tourniquets. They also found that despite their fears of inducing congestive heart failure from the fistula creation, patients' cardiac function remained stable or improved following the creation of a fistula. By 1966, an additional 14 operations followed. He presented the result of his work at the Congress of the American Society for Artificial Internal Organs. Twelve of the 14 AVFs functioned without complications, two never worked (in the first patient, the anastomosis "was made too small") [14]. To his surprise, the audience reacted with complete indifference [12] though over time

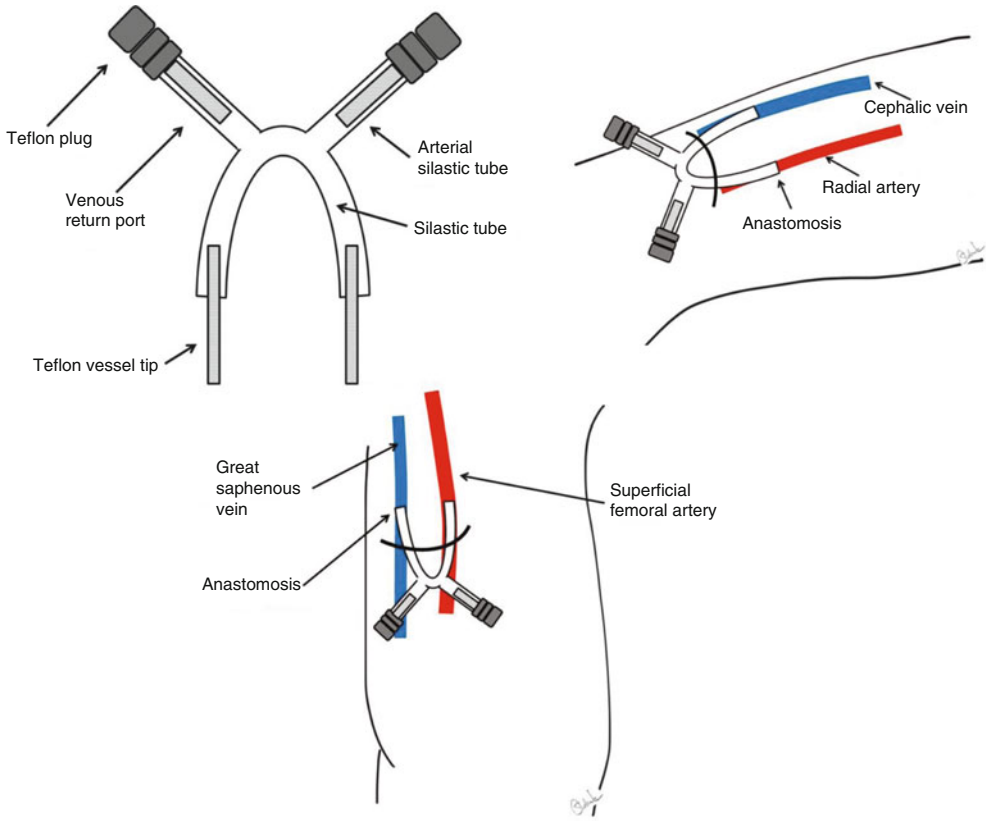

Fig. 1.5 A schematic of the U-shaped Silastic prosthetic Buselmeier arteriovenous shunt used in the 1970s with two Teflon plugged outlets that communicated to the outside of the body. The U-shaped portion could be totally or partially implanted subcutaneously

this changed; Dr. Scribner from Seattle was the first nephrologist to refer one of his patients to New York for the creation of an AVF [15].

The evolution of the hemodialysis access continued when M. Sperling (Würzburg, Germany) reported the successful creation of an end-to-end anastomosis between the radial artery and the cephalic antebrachial vein in the forearm of 15 patients using a stapler in 1967 [16]. The creation of the end-to-end anastomosis was technically challenging and the diameters of the artery and vein were different. Thus this type of AVF was abandoned.

In 1968, Lars Rohl (Heidelberg, Germany) published the results of 30 cases where he used an end-to-side cephalic vein to radial artery anastomosis [17].After completion of the anastomosis, the radial artery was ligated distal to the anastomosis, resulting in a functional end-to-end anastomosis. With this technique, an antebrachial cephalic vein located at a more lateral position in the forearm, thus not suitable for a side-to-side anastomosis, could be used successfully. Later on, the ligation of the radial artery distal to the anastomosis was used in patients with impending signs of peripheral ischemia [17].

Alternatives to the wrist AVF were being explored during the same time period. In 1969 W.D. Brittinger (Mannheim, Germany) published his case series of 17 patients who underwent successful "Shuntless hemodialysis by means of puncture of the subcutaneously fixed superficial femoral artery for chronic hemodialysis" [18]. Following a femoral arteriogram to exclude arterial anomalies or disease, the superficial femoral artery was exposed by mobilizing the sartorius muscle which was then transected, passed underneath the exposed artery, and joined again. The fascia lata was closed, ensuring that proximal and distal openings of the fascia were sufficiently large to prevent compression of the artery [3].

Another technique was that of mobilizing and fixing the radial artery underneath the skin throughout its length along the forearm by G. Capodicasa (Naples, Italy). However, there were no further publications to confirm the value of this procedure [3].

Dialysis Catheters

Dialysis catheters developed along the same timeline as the AV shunt and AVF were being developed. Initially due to necessity, as not all centers had the expertise to offer AV shunt placement, and later a debate ensued as to whether an AVF or an indwelling shunt is superior in providing vascular access [19]. AVF challenges included vein tortuosity making needle insertion difficult, patient anxiety related to venipuncture, and inability by trained personnel to repeatedly achieve successful venipuncture despite adequate AVF [19].

In the 1960s, while the external Teflon-Silastic AV shunt was gaining popularity, not all surgeons were willing to perform

the operation to place the shunt [20]. This led Stanley Shaldon (London, UK), a nephrologist, to introduce handmade catheters into the femoral artery and vein by the percutaneous Seldinger technique for immediate vascular access [20, 21]. Over time, vessels in different sites were used, including the subclavian vein. Shaldon concluded: "Eventually, veno-venous catheterization was preferred because the bleeding from the femoral vein was less than from the femoral artery when the catheter was removed" [20].

After the first use of the subclavian route for hemodialysis access by Shaldon in 1961, the technique was adapted by Josef Erben (former Czechoslovakia), using the infraclavicular route [22]. Dr. Erben reported that single-needle hemodialysis using subclavian or femoral vein cannulation gave the same results as the arteriovenous radiocephalic fistula; thus intermittent or combined use of both types of large vein cannulation is advantageous in long-term regular dialysis patients that are waiting for a new fistula [22]. The main risk of subclavian vein cannulation was bleeding due to arterial access and pneumothorax. The associated mortality rate was 0.12 % due to subclavian vein cannulation and 0.04 % due to femoral vein cannulation [22]. During the following 2 decades, the subclavian approach became the preferred route for temporary vascular access by central venous catheterization [3].

In 1972, James J. Cole, Robert O. Hickman, Belding H. Scribner, and colleagues (Seattle, WA, USA) presented a new concept "the fistula catheter." The design was extrapolated from the indwelling intravenous feeding catheter for hyperalimentation. They reasoned that placement of catheters of appropriate design in the high-flow environment in a vein proximal on an AVF might result in the creation of a thrombus-free, nonreactive semipermanent hemodialysis access. The catheters were designed as a single Silastic tube with an attached Dacron velour cuff for external fitting or a double-lumen implant consisting of a paired Silastic tubes bonded together and introduced into the fistula at a single entry point (Fig. 1.6).

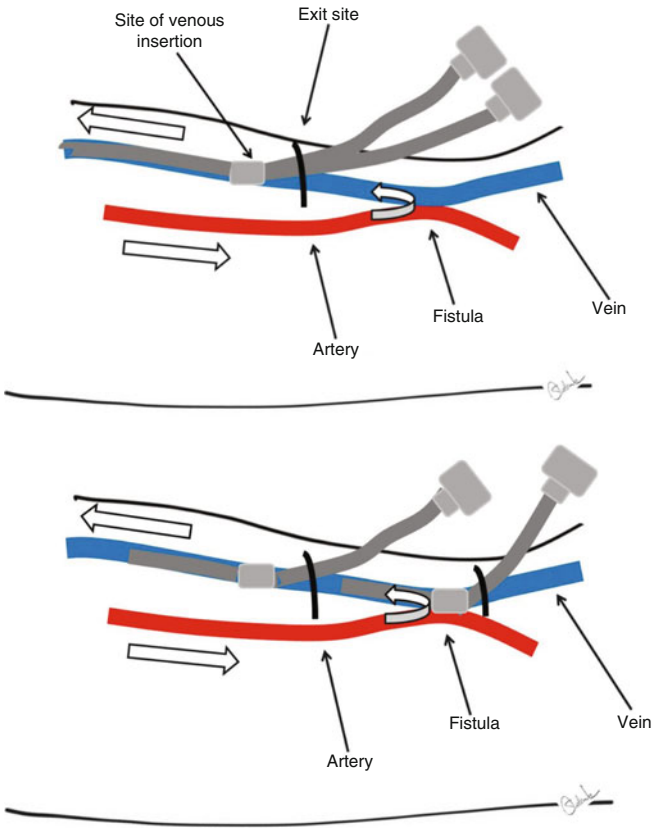

Fig. 1.6 A schematic of the fistula catheter used in the 1970s. *Top panel*: using two single catheters inserted at separate entry points. *Bottom panel*: using a double catheter

Hybrid External Arteriovenous Shunts

Limitations of the Teflon-Silastic AV shunt and dialysis catheters were becoming obvious over time. As multiple revisions are performed on the patients, cannulation sites become fewer and fewer. These repeat operations were noted to be difficult for the patient and surgeon as they became longer and longer in an attempt to explore and find satisfactory arteries and veins for cannula sites [23]. In hopes of providing the patient with a permanent AV shunting system and based on animal experiments, Dr. George I. Thomas (Seattle, USA) felt that certain principles of restorative vascular and prosthetic surgery could be applied to eliminate some of these problems. These principles included removing all foreign bodies from the vessel lumen to eliminate vessel stenosis, applying graft material at all vessel junctions to obtain good healing, and avoiding thromboembolism by maintaining continued blood flow in the host vessel. Dr. Thomas presented his cases series in ten patients using the "Dacron appliqué shunt" technique in 1970. In this technique he sutured oval Dacron patches to the common femoral artery and the saphenous/common femoral vein [23]. The Dacron patches were connected with Silastic tubes and brought to the surface of the anterior thigh approximately 10 cm distal to the femoral incision (Fig. 1.7). In reviewing a more recent history, a retrospective study published in 2001 of 27 femoro-femoral Thomas shunts implanted in ten patients (ages 27–75 years) who had 80 failed vascular accesses (average of 8.6 accesses per patient). The average shunt duration was 43.7 months (range 3–151 months). One and two year survival rates were 85 % and 57 %, respectively. Five patients spent more than 10 years on maintenance hemodialysis using the Thomas shunt. Complications included infection (one episode every 37.5 patient-months), thrombosis, and stenosis. Percutaneous angioplasty was successful in the majority of stenosis episodes. The authors concluded that his shunt offers high dialysis efficacy without recirculation and access duration comparable to AVF [24].

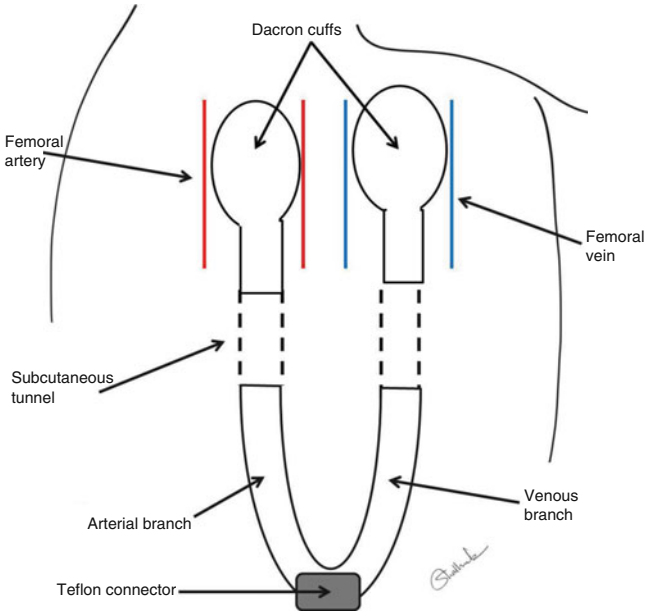

Fig. 1.7 A schematic of a right thigh femoro-femoral Thomas arteriovenous shunt that was used in the 1970s: oval Dacron patches were sutured to the common femoral artery and the common femoral vein and then connected to Silastic tubes tunneled subcutaneously to the surface of the anterior thigh approximately 10 cm distal to the femoral incision

Alternative Conduits in Dialysis Access

Limitations of the autogenous radiocephalic arteriovenous fistula included lack of maturation that led to a search for alternative conduits for the venipuncture hemodialysis technique. In 1972, the bovine carotid artery graft and the Dacron velour vascular graft were introduced. The modified bovine carotid artery biologic graft for vascular access (Artegraft, Johnson & Johnson), was the first xenograft used and was introduced by Joel L. Chinitz (Philadelphia, USA) in a case series of eight hemodialysis patients [25]. The graft received some acceptance during the 1970s. The technique described included upper (four cases) and lower extremity (four cases) arteriovenous grafts. The venous anastomosis is sutured with 6.0 Dacron sutures, while the arterial anastomosis is sutured with 5.0 Dacron suture and the graft proximal section tightened with a Dacron cuff to reduce the diameter in a tapered manner to 5 mm Dacron velour vascular graft. In the same year, Irving Dunn (Brooklyn, USA) chose Dacron velour vascular graft for the creation of AV bridge grafts, initially in animal experiments and then in a uremic female patient [26]. Subsequently, this material did not yield satisfactory results for vascular access.

The use of mandril grafts was described by R.K. Beemer (Portland, USA) in 1973 [27]. Mandril grafts are reinforced autogenous graft grown in situ. This technique was originally developed by Charles H. Sparks (Portland, USA) based on a series of animal experiments starting in 1965 to create an alternative to the great saphenous vein conduits for femoral popliteal bypass [28]. The technique consisted of preparing a smooth silicone rubber rod of desired diameter and length with a covering or coverings of specially prepared, large-mesh, knitted Dacron tubes and implanting the resulting assembly in the location of the contemplated arterial grafting procedure [29]. It was left in place for 6 weeks so that the Dacron mesh became organized after invasion of the surrounding tissue. The mandril was then removed and the endings of the matured subcutaneous tunnel were anastomosed to the native vessels. Beemer described patients with inadequate superficial veins in the forearm for AVF creation. He implanted the mandril graft in the forearm in a straight configuration between the radial artery at the wrist and the basilic vein in the arm (four cases) or in a forearm loop configuration between the brachial artery and basilic vein. The silicone rods were removed after 6 weeks and the anastomoses made [27]. Because of the unfavorable results and the availability of more successful prosthetic materials, this technique was abandoned a few years later.

In 1975 and 1976, two groups detailed experiences with the use of human umbilical cord vein. The enthusiasm for this conduit was due to the perceived advantages of an antithrombogenic intimal surface and the absence of valves and branches. B.P. Mindich (New York, USA) used chemically processed umbilical cord veins without external support [30], whereas H. Dardik (New York, USA) surrounded the graft with a polyester fiber mesh [31]. This conduit did not achieve a real breakthrough because of insufficient resistance against the trauma of repeated cannulation and of problematic surgical revision in the case of aneurysms and infection.

In 1976, L.D. Baker Jr. (Phoenix, USA) presented the first results with expanded PTFE grafts in 72 hemodialysis patients [32]. The majority of these grafts were 8 mm in diameter. Numerous publications during the subsequent years demonstrated the value and the limitations of this prosthetic material, which has remained the first choice of grafts for vascular hemodialysis access even today.

The No-Needle Dialysis

In 1981, A.L. Golding and colleagues (Los Angeles, USA) developed a "carbon transcutaneous hemodialysis access device" (CTAD), commonly known as "button," as a means for a "no-needle dialysis" approach [9]. This was in response to reports of many patients not tolerating repeated needle punctures well and requiring "desensitization therapy by a psychiatrist" [9]. The repeated needle puncture was a deterrent to home hemodialysis, and when unsuccessful, it leads patients to switch to peritoneal dialysis or transplantation [9]. The device consisted of two components: a vitreous

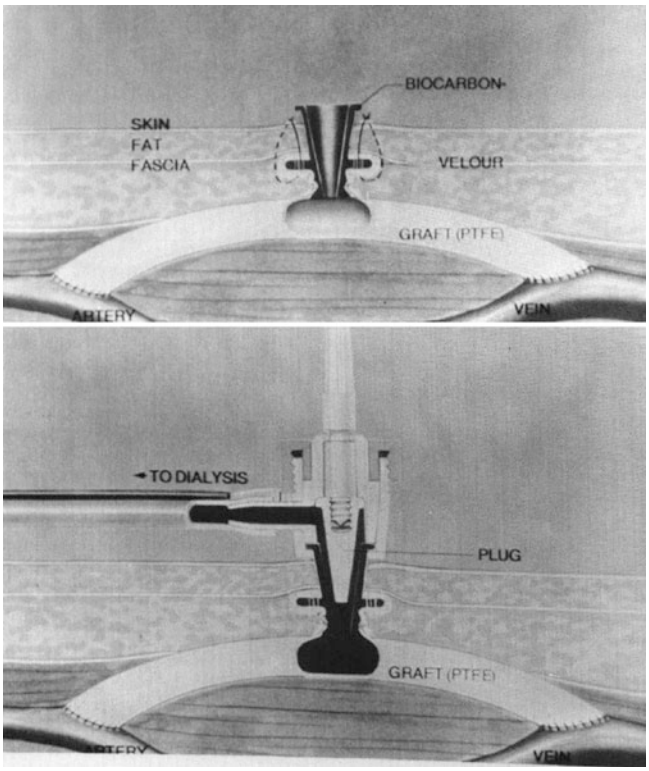

Fig. 1.8 The carbon transcutaneous hemodialysis access device commonly known as "button" for a "no-needle dialysis" approach. (**a**) The design of the device. (**b**) The device with the connector allowing hemodialysis (Reproduced with permission Nissenson et al. [9])

carbon access port sealed with a conical polyethylene plug and a PTFE graft attached to the port (Fig. 1.8). A disposable connector provides for the movement of blood from the device into and out of the dialyzer. The authors reported a case series of 21 of the devices implanted in 18 patients. Overall the 9-month patency rate is 64.3 %, comparing favorably with conventional PTFE grafts. These devices were expensive and never gained widespread acceptance [3].

In 1983, J.L. Wellington (Ottawa, Canada) reported a case series of implanted "buttons" developed by F.L. Shapiro [33] (Minneapolis, USA), a device similar to that developed by Golding. Wellington implanted these buttons along an arterialized, superficialized basilic vein, but the results were disappointing [3].

Final Remarks and Conclusions

Vascular access for hemodialysis is closely associated with the history of dialysis. This was a chapter written from the perspective of a vascular surgeon and thus did not delve greatly into the history of dialysis machine and technology development. This, too, has its own rich history. Throughout the book, the history of dialysis access continues to unfold as each of the authors adds elements of historical perspective as they deem relevant to their chapter topic thus adding to our knowledge about how our practice continued to evolve.

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The Natural History of Hemodialysis Access

2

Fionnuala C. Cormack

Background

One of the most critical aspects of planning for long-term hemodialysis (HD) is obtaining vascular access. The prospect of living with end-stage renal disease (ESRD) became a reality in 1960 when Belding Scribner, in collaboration with Wayne Quinton and David Dillard, developed a Teflon arteriovenous shunt which enabled Boeing machinist Clyde Shields to survive for 11 years on chronic hemodialysis. The shunt consisted of Teflon tubing inserted into the radial artery and forearm vein, connected by a bypass loop on a metal arm plate when the patient was not dialyzing [1]. To increase cannula flexibility and longevity, Quinton later added a silicone rubber segment, creating the so-called Silastic-Teflon bypass cannula where a tapered Teflon tip was inserted into the blood vessel and a Silastic tube made the exit through the skin [2]. Shortly thereafter, in 1965, Drs. Brescia, Cimino, and Appel created the first autogenous arteriovenous fistula by creating a side-to-side anastomosis between a radial artery and cephalic vein. These first fistulas were cannulated within a day of creation [3].

It is widely accepted that native arteriovenous fistulas (AVF) are the preferred hemodialysis vascular access [4]. AVF have lower complication and infection rates and longer survival and superior patency, provide consistently adequate dialysis, cost less, and are associated with decreased morbidity and mortality when compared to arteriovenous grafts (AVGs) and tunneled central venous catheters (CVCs) [5–14].

As the ESRD population expanded in the 30 years after the development of arteriovenous (AV) fistulas, so too did options for prosthetic AV accesses. In the 1990s, the predominant form of vascular access was the polytetrafluoroethylene (PTFE) graft [15]. For the 1990 incident cohort of hemodialysis patients, the rate of AV graft placement was 1.7 that of AVF construction [16]. High reliance on AVGs was associated with significantly increased cost, with grafts having three to sevenfold greater access complications compared with AV fistulas [17, 18].

In 2003, in response to rising costs, increased morbidity and mortality associated with AVG and catheter use, and a low prevalent AVF rate at 32 %, the Centers for Medicare and Medicaid Services (CMS), along with the End-Stage Renal Disease (ESRD) Networks, the Institute for Healthcare Improvement (IHI), and dialysis stakeholders, joined forces to establish the National Vascular Access Improvement Initiative (NVAII), a continuous quality improvement project aimed at increasing autogenous arteriovenous fistula use. In 2005 NVAII became known as the Fistula First Breakthrough Initiative (FFBI) [19]. The FFBI led to a national push by CMS and the dialysis community to increase the placement of functioning AVFs in patients undergoing hemodialysis in the USA. The original goal was for 60 % AV fistulas among incident and 40 % among prevalent hemodialysis patients, in line with the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) target [10]. In 2009, FFBI set a goal of 66 % AV fistula utilization in prevalent hemodialysis patients, a target similar to AVF prevalence in Europe and Asia, as reported in the Dialysis Outcomes and Practice Patterns Study (DOPPS), an international prospective observational study of an international prosective observational study of hemodialysis practices and patient outcomes [20]. The FFBI outlined strategies or "change concepts" to facilitate a multidisciplinary approach among nephrologists, dialysis personnel, vascular access surgeons, and patients to increase the production and use of autogenous AV accesses.

Epidemiology

In 2011, 430, 273 patients were on dialysis, of which 395,656 patients (92 %) were undergoing hemodialysis in the USA. 103,744 patients initiated hemodialysis in that year [21]. Hemodialysis is the most common dialysis modality

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worldwide. In over 76 % of reporting countries, at least 80 % of patients are on hemodialysis [22]. Despite improvements in survival in recent years, mortality in the dialysis population is ten times greater than among Medicare patients of similar age without kidney disease. Forty-six percent of ESRD patients die within three years of starting hemodialysis [23]. Most deaths occur in the first year of dialysis initiation. Among 2011 incident hemodialysis patients, all-cause mortality was 421 deaths per 1000 patient-years in month 2, decreasing to 193 per 1000 patient-years in month 12 [23]. The rates of infection-related deaths were 38 per 1000 patient-years at month 3 and fell to 17 by month 12. There is consistent evidence that infection-related deaths are related to catheter use and that mortality is reduced when dialysis patients switch to an AV fistula or AV graft within the first year of dialysis initiation [24, 25]. In 2010, the three-month mortality for patients initiating dialysis with a catheter was 9.7 % versus 3.1 % for patients dialyzing with an AVF [26]. Twenty-six percent of patients starting dialysis with a catheter died within 12 months, compared to 11 and 16 % in patients initiating with an AVF and AVG, respectively [26].

As a result of the efforts of the FFBI, the national prevalent rate for native arteriovenous fistulas in the USA among in-center and home hemodialysis patients almost doubled in the last decade, increasing from 32 to 61 % [27]. Using data from DOPPS, Pisoni et al. reported AVF use increased from 24 % in 1997 to 68 % in 2013. Internationally, among 20 countries studied in 2012–2013, the USA fell in the middle with respect to AVF and CVC use, but had the highest AVG use among all DOPPS countries at 18 %. AV access differs by race with 58 % AVF use in black patients, compared with 74 % in Hispanic and 70 % in white patients. Further, AVG use was twofold higher among black versus nonblack HD patients. There was no significant difference in CVC use among the three groups. Lower AVF use was also found in women with 50 % for black women versus 65 % for black men and 65 % for nonblack woman versus 75 % for nonblack men. CVC use was 1.4- to 1.5-fold higher among women versus men. Allon et al. noted 30 % less AVF creation in women versus men and blacks versus whites, suggesting that women and black patients are likely deemed poor candidates for AVF placement, perhaps due to smaller vessel size [28].

Despite an increase in fistula use among prevalent hemodialysis patients in recent years, catheter utilization remains unacceptably high in both incident and prevalent HD patients, and there has not been significant improvement in the number of patients initiating dialysis with a functional AV fistula. According to the United States Renal Data System (USRDS), in 2011, approximately 80 % of incident hemodialysis patients initiated treatment with a catheter as their vascular access (Fig. 2.1) [21]. This number has remained relatively unchanged since 2005. Of these, only 17 % had a maturing AVF and 1.6 % a maturing AVG. Even among hemodialysis patients followed by a nephrologist for over 12 months prior to starting ESRD therapy, 63 % started hemodialysis with a catheter. Reassuringly, a greater percentage had an arteriovenous fistula or AVG, at 31.9 and 20.8 %, respectively. Ninety-five percent of patients with no nephrology care started treatment with a catheter, with only 14 % having a maturing AVF or AVG. In the USA, significantly fewer patients initiate dialysis with a functional vascular access, compared to other countries where AVF use among incident patients is 50–60 % in most European countries and 84 % in Japan.

Complications of Catheter Use

In 2011, USRDS reported that 51 % of hemodialysis patients were dialyzing with a catheter at day 91 of treatment. According to US DOPPS, 19–38 % of patients were dialyzing with a CVC in 2013 [29]. FFBI has set a goal to decrease catheter use to <10 % for patients on HD longer than 90 days. In fact, in recent years, the FFBI has transitioned to the Fistula First Catheter Last (FFCL) Workgroup Coalition "to focus on the development of tools and resources to help dialysis facilities and clinicians reduce catheters and increase AV fistula rates in hemodialysis patients" [19]. Catheter use

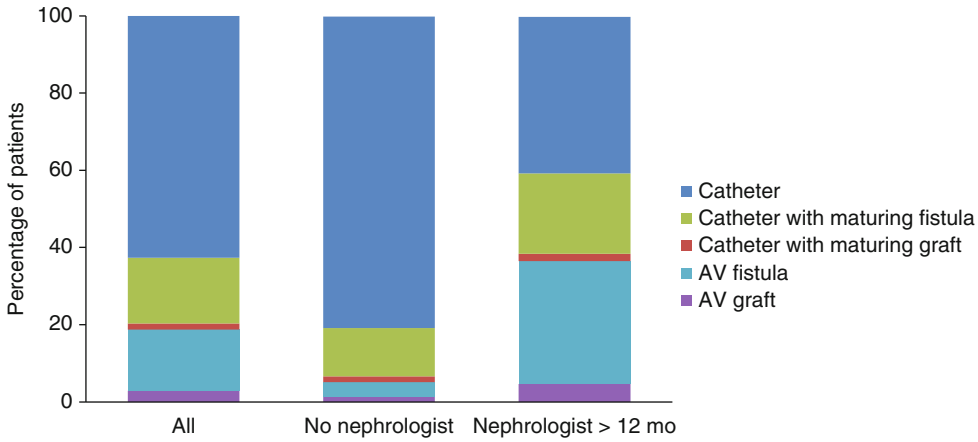

Fig. 2.1 Vascular access use at the initiation of dialysis. Eighty percent of patients initiate dialysis with a catheter

is associated with significant morbidity, mortality, and cost. A major complication of catheter use is catheter-related bacteremia and the attendant risks of hematogenous spread causing complications such as endocarditis, septic emboli, and osteomyelitis. The cumulative risk of an episode of catheter-related bacteremia is close to 50 % in the first 6 months of use, and each hospitalization for catheter-related bacteremia costs around $23,000 [30, 31]. One study reports a threefold increased mortality in patients dialyzing through catheters compared to AVFs [7]. In one large cohort of almost 80,000 patients, changing from a catheter to a fistula or graft significantly improved patient survival, with a 30 % decrease in risk of death in prevalent hemodialysis patients [24]. With respect to impact on future vascular access, Rayner et al. found prior catheter use was associated with a significantly increased risk of fistula failure [32].

Many factors contribute to the increased use of catheters in incident hemodialysis patients [33]. While many point to delayed nephrology referral, as shown above, even among patients followed by a nephrologist for a year, 60 % initiate hemodialysis with a catheter in place. Some posit that attempting fistula placement in the vast majority of patients has the potential to increase catheter use, compromise vasculature for future vascular accesses, and necessitate more interventions for salvaging the existing access and creating a new vascular access [26, 34–36].

While a functioning fistula is the gold standard of vascular access and is associated with the best outcomes, AVF may not be the optimal choice for all patients [37]. For instance, AV fistulas may not be the best choice for patients who are older and have multiple comorbidities, shorter life expectancy, or unsuitable vessels. In such cases, AV grafts may be a more appropriate HD access and may translate into less catheter use [38]. In the 2006 guidelines for vascular access, the KDOQI Work Group recognized that the "fistula first at all costs" approach may not be the optimal approach for all patients [10]. Many now agree that a universal policy of fistula first may not be appropriate for all incident patients and, instead, providers should take a patient-centered approach in determining the optimal vascular access. Factors affecting the reduced number of working fistulas at dialysis start and contributing to increased catheter time, as discussed below, include (1) inadequate timing of vascular access placement, (2) fistula nonmaturation, (3) inadequate fistula surveillance postoperatively, and (4) inadequate reimbursement for vascular access procedures.

Timing of Vascular Access Placement

Establishing a functional AV fistula takes time. There are a number of steps involved in vascular access placement: referral to surgery, surgical evaluation, scheduling the surgery, time for maturation, and the possibility of a need for a salvage procedure to achieve usability [39].

Even among those patients followed by a nephrologist, the above process is often not initiated with sufficient time to ensure patients initiate hemodialysis with a mature fistula. KDOQI encourages educating patients with a glomerular filtration rate (GFR) less than 30 ml/min/1.73 m^2 on all modalities of kidney replacement therapy, so that timely referral can be made and a permanent dialysis access placed, when indicated. Both KDOQI and the Society for Vascular Surgery (SVS) recommend that an AVF should be placed at least 6 months in advance of the anticipated need to start hemodialysis [10, 12]. This timing allows for adequate maturation, as well as potential revisions or placement of a new vascular access when an access fails to mature.

A complicating factor in timely vascular access creation is the difficulty in accurately predicting the rate of progression of kidney failure, especially in cases of acute-on-chronic kidney injury where patients need to initiate dialysis urgently [33]. Further, many patients resist permanent access placement, hoping their kidney function will stabilize with improved blood pressure and glycemic management [33].

Regarding surgical planning, KDOQI recommends duplex ultrasound of the upper extremity arteries and veins. Routine preoperative vessel mapping has not consistently translated into improved fistula maturation rates. Preoperative mapping is associated with an increase in fistula placement in several observational studies, but is not necessarily associated with improved maturation [40]. Patel et al. reported increased fistula creation from 61 to 73 % but decreased maturation rate from 73 to 57 % after implementing preoperative vascular ultrasounds [41]. In another study, radiocephalic fistulas constructed with veins less than 2.0 mm had a primary patency of 16 % at 3 months compared with 76 % with veins greater than 2.0 mm [42]. Wong et al. reported that when the radial artery or cephalic vein diameter was <1.6 mm, fistulas did not mature [43]. Peterson et al. found that older age, female gender, and forearm location were associated with a significantly higher risk of primary fistula failure despite adequate preoperative vessel size [44]. Most studies support a minimum vein diameter of 2.5 mm and artery diameter of 2 mm for successful fistula creation.

There are no randomized controlled trials comparing anatomic order with respect to access construction. Both SVS and KDOQI recommend that the first access should be placed as far distally as possible to preserve proximal sites for future accesses. Per KDOQI, "good surgical practice makes it obvious that when planning permanent access placement, one should always consider the most distal site possible" [10]. In patients with small vessels, some advocate for the placement of a forearm AV graft to mature upper arm veins, which both enables a future successful upper arm AVF and provides a functioning access without the need for catheter use.

AVF Nonmaturation

In 1966, Cimino and Brescia reported that 13 of their 16 patients were dialyzed successfully using their radiocephalic fistulas. These accesses were cannulated with 14-gauge needles on postoperative day 1 and used for as long as 15.5 months in some patients. In contrast to hemodialysis patients today, these were young nondiabetic patients with an average age of 43 years, and all but one had chronic glomerulonephritis [3]. In contrast to fistulas placed decades ago where primary failure ranged from 10 to 24 % [40, 45–49], fistulas placed today have reported primary failure rates ranging from 30 to 60 % [41, 44, 50–52], and primary patency rates are lower at 40–70 % [53]. These high failure rates and low primary patency rates have largely been attributed to changing patient demographics and comorbidities [36, 41, 44, 51].

Factors associated with failure to mature include diabetes mellitus, peripheral vascular disease, congestive heart failure, advanced age, and female gender [54, 55]. The highest failure rates are reported in older and female patients, Hispanics and African-Americans, and patients with cardiovascular disease and forearm fistulas [56–59].

The NIH-funded Dialysis Access Consortium (DAC) clopidogrel study is the largest randomized controlled trial evaluating fistula outcomes. It examined the effects of clopidogrel on AVF thrombosis and suitability for dialysis use in newly created fistulas. Dialysis suitability was defined as the ability of the AVF to support a dialysis treatment with two needles at a blood flow rate of ≥300 ml/min or greater than eight hemodialysis sessions during a 30-day period [60]. While clopidogrel significantly improved primary patency with reduction in early fistula thrombosis by 37 % (mainly in forearm fistulas), it did not improve fistula maturation. High nonmaturation rates were observed in both groups, despite 75 % of patients undergoing preoperative vascular mapping: 61.8 % in the clopidogrel group and 59.5 % in the placebo group. The authors comment that "our finding of a beneficial effect of clopidogrel on fistula patency but not on suitability is important to the evolving understanding of the pathophysiology of fistula maturation…and suggests that early patency is necessary but not sufficient for fistula maturation" [60].

In a study of the natural history of AVFs, only 11 % of AVFs matured without the need for intervention, while 36 % of fistulas required at least one intervention [61]. Similarly, other studies report that approximately one-third of all AVFs require an intervention to facilitate maturation [62–64]. In the DAC clopidogrel study, only a small percentage of fistulas underwent angioplasty or surgical revision to aid in maturation. Authors query whether more procedures to promote maturation would have translated to a beneficial effect of clopidogrel on fistula suitability.

The mechanisms underlying AVF maturation are complicated and remain poorly understood. Three main biologic reasons for nonmaturation are failure of arterial dilation, failure of venous dilation, and accelerated neointimal hyperplasia [65]. Given our limited understanding of the complex vascular remodeling involved in fistula creation, the National Institute of Diabetes and Digestive and Kidney (NIDDK) Diseases is sponsoring a multicenter prospective cohort study evaluating patients undergoing fistula surgery. This Hemodialysis Fistula Maturation (HFM) study is ongoing and will study patients pre-, intra-, and postoperatively to assess vascular anatomy and biology, clinical attributes, and processes of care with the goal of identifying modifiable predictors of fistula maturation [66].

Postoperative AVF Surveillance

A mature, functional fistula is defined as one that has adequate blood flow to support dialysis and is large enough for successful repetitive cannulation [10, 65]. Studies show that an increase in blood flow and vein diameter occurs soon after fistula creation. In one study, blood flow increased from 20.9 ± 1.1 ml/min in the radial artery to 174 ± 13.2 ml/min in the AVF 10 min after the anastomosis was created [67]. Other investigators documented blood flows of 539 ± 276 ml/min on postoperative day 1 and 848 ± 565 ml/min 1 week following fistula creation [68]. Robbin et al. found increases of venous diameter to >4 mm and blood flow >500 ml/min at 4 weeks that did not significantly change in subsequent months. Vein diameter ≥4 mm and access blood flow ≥500 ml/min were associated with a 95 % likelihood that the access will be usable for dialysis [69]. On balance, adequate blood flow and access diameter are achieved within 4–8 weeks of creation [68–70], and fistulas not achieving these benchmarks are unlikely to mature to support dialysis [43, 69].

The KDOQI Work Group suggests the so-called rule of 6 s to describe characteristics of a mature or functional fistula: the access has a blood flow greater than 600 ml/min, a diameter greater than 0.6 cm, and a depth of approximately 0.6 cm from the skin surface [10]. Both physical examination and ultrasonography are useful tools for assessing fistula maturation and early AVF failure. In one study where experienced nurses examined fistulas for maturation, their overall accuracy of prediction was 80 % [69]. The two most common causes of fistula nonmaturation – juxta-anastomotic stenosis and the presence of accessory veins – can be identified on physical examination [71]. Both the SVS and KDOQI Work Group guidelines recommend further investigation to identify "potentially remediable anatomic lesions" if a fistula is not maturing adequately at 6 weeks [10, 12]. Some estimate that at least 80 % of nonmaturing AV fistulas can be salvaged after intervention on an underlying lesion [71, 72].

Regarding timing of cannulation, Rayner et al. showed that the median time to first AVF cannulation differed among countries, ranging from <28 days in Japan and Italy to as long

as 98 days in the USA. Fistulas used within the first 2 weeks after fistula creation were two times more likely to fail than those cannulated after 14 days [32]. There was no increased risk of failure in fistulas accessed after 14 days, and failure was not significantly different among any of the cannulation interval groups greater than 14 days. This prolonged time to fistula use in the USA increases the likelihood of catheter dependence, as patients often need to initiate dialysis before fistulas are ready for cannulation.

Inadequate Reimbursement for Fistula Placement

A major barrier to increasing fistula use among incident hemodialysis patients is inadequate coverage for predialysis vascular access placement. In 2010, a clinical technical expert panel, convened by CMS to make recommendations about ways to decrease vascular access-related infections, posited that improving reimbursement for vascular access would ultimately reduce the prevalence of catheters and catheter-related costs [73, 74]. It identified a number of financial and regulatory barriers to timely AVF placement and recommended changes to Medicare reimbursement for vascular access placement, including (1) earlier disbursement of Medicare benefits for vascular access procedures for the uninsured, (2) full payment when fistulas and catheters are placed on the same day in hospitalized patients, and (3) payment for access surgery when patients are hospitalized to initiate hemodialysis. The panel argued that changing reimbursement for vascular access will, not only, motivate providers to place more timely vascular access, but will improve patient outcomes and reduce the high costs associated with dialyzing with a central venous catheter. Potential annual cost savings are estimated at close to a $1 billion [73].

Role for AV Grafts Among Hemodialysis Patients

Lok et al. reported that AV grafts were more likely to be placed in high-risk patients, yet cumulative survival was similar to those lower-risk patients who received AVFs [36]. Patients with grafts were more likely to be female, diabetic, and black. Comparing cumulative patency between fistulas and grafts, they found the primary failure rate for AVFs was 40 %, two times greater than for grafts. Fistulas demonstrated better cumulative patency than grafts, but when primary failures were included in the access survival analysis, cumulative survival was similar between both forms of vascular access. Lee et al. reported similar patency findings between AV grafts and AV fistulas when primary AVF failures were excluded and actually observed superior graft compared to fistula survival within the first 18 months of access creation [75]. Based on these findings, judicious use of AV grafts may afford similar cumulative patency compared with AVFs while reducing exposure to the risks associated with catheter use.

An advantage of graft placement is grafts can often be cannulated within 2 weeks of creation. In fact, KDOQI recommends not placing an AVG earlier than 3–6 weeks before initiation of hemodialysis because of the high risk of venous outflow stenosis which can occur anytime after placement [10]. The downside to grafts is, once in use, they require twice as many interventions to maintain patency [36]. Maintaining long-term graft patency requires 2.4- to 7.1-fold higher frequency of salvage procedures, including angioplasty, thrombectomy, and surgical revision [40].

While fistulas have superior cumulative patency to grafts and require fewer interventions to maintain patency, they are associated with higher primary failure rate, more interventions to achieve maturation, and longer catheter dependence [75]. As such, many argue they may not be the optimal vascular access for all hemodialysis patients, especially elderly patients. Patients with lower likelihood of fistula maturation may benefit from having an AVG placed upfront [58].

Of the 382,029 prevalent hemodialysis patients in 2012, approximately 80 % were over age 50 and about a third were ≥70 years. Over the last decade, the prevalence of patients on hemodialysis has increased 31 % among patients between the ages of 65 and 74 years and 48 % in those ≥75 years [21]. In one study looking at outcomes in octogenarians, 89 % initiated hemodialysis with a tunneled catheter, and 56 % of patients died within 180 days of dialysis start. Among the patients who died, 70 % had a fistula placed that was never used [76]. De Silva et al. found similar survival outcomes in octogenarians and nonagenarians whether an AVF or AVG was placed predialysis. Further, among the octogenarians, patients were 77 % more likely to initiate dialysis with a catheter if an AVF was in place [77]. Lok et al. found that patients >65 years have a two times greater fistula nonmaturation rate compared with younger patients [58]. Given such findings, Tamura et al. proposed a conceptual framework to guide decision-making regarding the choice of vascular access in older patients with ESRD that takes into account life expectancy, the benefits and harms of competing strategies, and patients' preferences [78].

Conclusion

Vascular access is the lifeline for patients requiring hemodialysis. Delayed vascular access placement is associated with significant patient morbidity and mortality and an increased number of inpatient hospitalizations [26]. It takes time and coordination to achieve a permanent vascular access. Encouraging timely placement of an arteriovenous fistula remains the goal for suitable patients and necessitates coordination of care among many providers: primary care providers, nephrologists,

vascular surgeons, and dialysis staff. Many posit that a dedicated vascular access program with an appointed vascular access coordinator is critical for ensuring an integrated, multidisciplinary approach to vascular access care [79]. Successful vascular access creation and maintenance depends on timely referral to vascular surgery, close monitoring and surveillance postoperatively (especially in the first 6 weeks), early intervention for non-maturation (when indicated), and expert cannulation to ensure access preservation.

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The Current State of Hemodialysis Access and Dialysis Access Initiatives in the United States

3

Matthew B. Rivara and Rajnish Mehrotra

Introduction

Over 450,000 individuals with end-stage renal disease (ESRD) are currently undergoing maintenance dialysis in the United States, the vast majority of whom are treated with maintenance hemodialysis (HD) [24]. Additionally, of the nearly 115,000 individuals who initiate renal replacement therapy each year in the United States, over 90 % are treated with HD. Although recent trends have shown substantial growth in the adoption and use of peritoneal dialysis, it is likely that HD will remain the predominant dialysis modality in the United States for the foreseeable future. Although the past five decades have also witnessed dramatic transformations in the dialysis technology, healthcare infrastructure, and demographic characteristics of patients undergoing dialysis in the United States, the fundamental dependence of each patient undergoing maintenance HD on long-term reliable vascular access has remained unchanged.

In 1960, Dr. Belding Scribner and Wayne Quinton working together at the University of Washington in Seattle pioneered the development of the arteriovenous (AV) shunt, originally made of polytetrafluoroethylene, or PTFE, and then later modified through the addition of flexible silicon rubber tubing to extend its lifespan. This innovative work for the first time permitted long-term maintenance dialysis for patients with ESRD. However, it was the development of the arteriovenous (AV) fistula by Drs. Cimino, Appel, and Brescia in 1962 that has provided the gold standard and to this day remains the preferred HD vascular access [5]. The subsequent decades saw the introduction of the synthetic PTFE arteriovenous graft in 1970s [3] and then the silicon cuffed, tunneled central venous catheter (CVC) in 1987 [23]. Together, the AV fistula, AV graft, and tunneled CVC represent the three options for long-term vascular access for maintenance HD.

Although vascular access provides the critical lifeline for patients undergoing maintenance HD, vascular access-related issues are also among the top five causes of hospitalization for HD patients, and infection-related complications (in many cases related to vascular access) are the second most common cause of death in patients with ESRD [24]. Dialysis access failure is also costly, representing 14 % of all ESRD expenses in the United States [15]. Accumulated data over the past two decades have consistently demonstrated that the use of AV fistulas is associated with lower risk for all-cause and cause-specific mortality compared to the use of either AV grafts or CVCs and that central venous catheters are associated with worse outcomes than either fistulas or grafts [2, 19, 20]. The past decade has thus witnessed the rise of a number of vascular access initiatives led by a variety of different stakeholders, largely focused on increasing the prevalence of fistulas and limiting the use of CVCs in HD patients. The objective of this chapter is to summarize recent trends in the differential use of vascular access types among individuals undergoing maintenance HD in the United States and to review the last decade and current state of vascular access initiatives.

The Fistula First Initiative

1990s–2003: KDOQI and the CMS Clinical Performance Measures

Following the advent and widespread adoption of the synthetic PTFE AV graft and the silicone tunneled dialysis CVC in the 1970s and 1980s, overall rates of the use of AV fistulas fell, and the use of these alternative vascular accesses grew. By the mid-1990s, accumulating evidence suggesting that overreliance on tunneled cuffed CVCs was contributing to an

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excess of infection and cardiovascular-related mortality led to calls to develop strategies to promote AV fistula creation and use and to limit the use of CVCs [10]. In 1997, the National Kidney Foundation (NKF) published its first clinical practice guidelines for vascular access as part of the NKF-Dialysis Outcomes Quality Initiative (DOQI), subsequently known as the Kidney Disease Outcomes Quality Initiative (KDOQI). The objective of this guideline was to promote optimal management of vascular access in patients undergoing HD by emphasizing the primacy of the AV fistula and discouraging long-term CVC use.

In the same year of the publication of the original NKF-KDOQI vascular access guidelines, Congress passed the Balanced Budget Act of 1997, which among many other ramifications, required the Centers for Medicare and Medicaid Services (CMS) to develop and implement a method to measure and report the quality of dialysis services provide under the Medicare ESRD program. Thus, in the following year, CMS partnered with Qualis Health, a nonprofit health-care quality improvement organization, to develop a set of clinical performance measures for dialysis facilities based on KDOQI guidelines. Ultimately, in addition to measures focused on HD and PD adequacy and anemia management, three performance measures focused on vascular access were adopted: (1) A primary AV fistula should be the vascular access for at least 50% of all new patients initiating maintenance HD; (2) less than 10% of maintenance HD patients should be maintained on CVCs for longer than 90 days; and (3) a patient's AV graft should be routinely monitored for stenosis. Although only very few dialysis facilities in the United States are able to meet these stringent thresholds, these performance measures have continued to be tracked and expanded upon over the subsequent decade and a half.

Development and Implementation of the FFI

In 2003, in order to engage ESRD stakeholders to work toward the clinical performance measure goals for vascular access, CMS partnered with the ESRD Networks to implement what was initially known as the National Vascular Access Improvement Initiative, which was renamed in 2005 as the Fistula First Breakthrough Initiative or more simply the Fistula First Initiative (FFI) [9]. The core activities of the FFI were education forums and dissemination and information and best practices to engage all stakeholders in the dialysis community, including nephrologists, surgeons, dialysis facilities, nurses, patients, and others. An initial target of 40% prevalent AV fistulas among maintenance HD patient across the country was set. At the time the FFI was first implemented, although the previous years had seen a small increase in the percentage of prevalent HD patients using AV fistulas, the prevalent AV fistula percentage was only 32% (Fig. 3.1). Furthermore, the years immediately prior to 2003 had seen a continual increase in the percentage of all HD patients using CVCs [11].

Importantly, the FFI from its inception was based on the concept of continuous quality improvement (CQI). At its essence, the CQI involves an iterative process of development of guidelines, implementation in clinical practice, assessment of both process and clinical outcomes, and then revision and improvement of the initial guidelines and measures. Thus, monitoring and review of timeliness of placement of dialysis access, patency rates, and long-term CVC prevalence rates is a critical part of the FFI. The original 11 core change concepts of the FFI with the specific implementation steps which represent its roadmap to achieve the KDQOI vascular access recommendations are shown in Table 3.1. Since the initial change concepts were elaborated, an additional two have been added to advocate: (1) modifying hospital systems to detect chronic

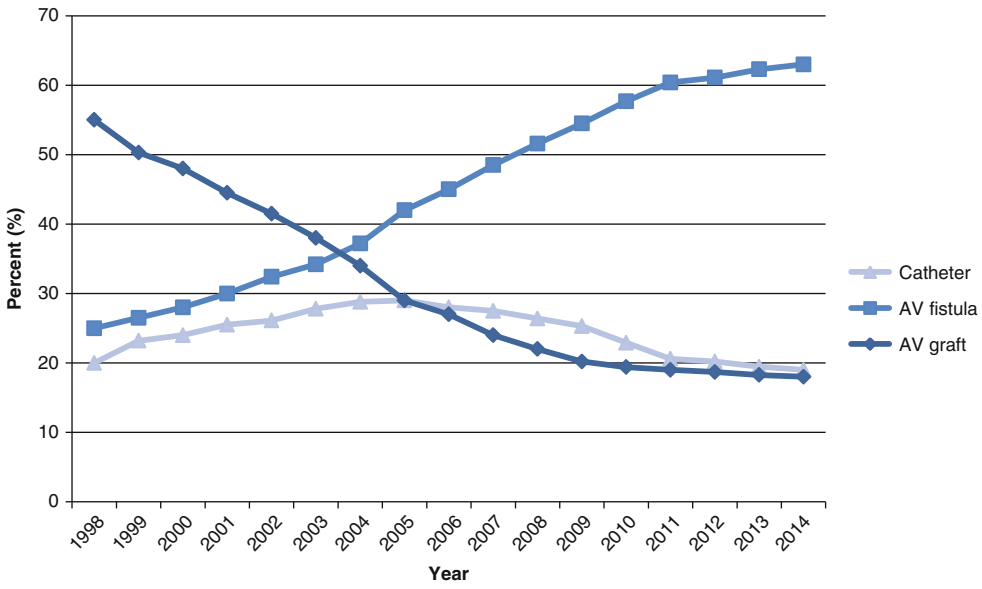

Fig. 3.1 Trends in proportional vascular access type use among prevalent hemodialysis patients in the United States, 1998–2015. *Abbreviations*: *AV* arteriovenous (Data sources: ESRD National Coordinating Center [9]; and Finelli et al. [11]. No data on AV graft prevalence were available from 2010 to 2011; these data points are interpolated values)

Table 3.1 The Fistula First Initiative (FFI) 11 change concepts

	Change concept	Implementation steps
1	Routine CQI review of vascular access	Designate staff member in facility responsible for vascular access CQI Assemble multidisciplinary access CQI team Investigate and track all non-fistula access placements, and fistula failures
2	Timely referral to nephrologist	Primary care physicians utilize referral criteria to ensure timely referral Nephrologist documents fistula plan for all patients expected to require dialysis Designate nephrology staff person to educate patient and family to protect vessels
3	Early referral to surgeon for "Fistula only" evaluation and timely placement	Nephrologist/skilled nurse performs evaluation and exam prior to referral Nephrologist refers for vessel mapping prior to surgery referral Nephrologist refers patients for "fistula only" evaluation, no later than stage 4 chronic kidney disease If timely placement of fistula does not occur, nephrologist ensures that patient receives evaluation and placement at time of dialysis initiation with CVC
4	Surgeon selection based on best outcomes, willingness, and ability to provide access	Nephrologists communicate expectations to surgeons performing access surgery Surgeons are continuously evaluated on frequency, quality, and patency of access placements
5	Full range of surgical approaches to AV fistula evaluation and placement	Surgeons utilize current techniques for fistula placement, including vein transposition Surgeons ensure mapping is performed for any patient not clearly suitable based on exam
6	Secondary AV fistula placement in patients with AV grafts	Nephrologists evaluate AV graft patients for possible secondary fistula conversion Staff and nephrologists examine outflow vein of all graft patients during dialysis. Identify patients who may be suitable for elective secondary fistula conversion
7	AV fistula placement in patients with catheters	Regardless of prior access, all patients with CVCs are evaluated as soon as possible for fistula, including mapping Facility implements protocol to track all CVC patients for early removal
8	AV fistula cannulation training	Facility uses best cannulators and tools to teach cannulation Facility offers option of self-cannulation to patients who are interested
9	Monitoring and maintenance to ensure adequate access function	Nephrologist/surgeon conducts post-op evaluation in 4 weeks to detect early failure Nephrologists/surgeons/facilities adopt standard procedures for monitoring
10	Education for caregivers and patients	Routine facilities staff in-servicing and education in vascular access Facilities educate patients to improve quality of care and outcomes
11	Outcomes feedback to guide practice	Review data monthly or quarterly in staff meetings. Present and evaluate data trended over time for incident and prevalent rates of access use

Adapted from the ESRD National Coordinating Center Fistula First Catheter Last Initiative, available at: http://esrdncc.org/ffcl/change-concepts
Abbreviations: *AV* arteriovenous, *CVC* central venous catheter, *CQI* continuous quality improvement

kidney disease and promote AV fistula planning and placement and (2) supporting patient efforts to enhance quality of life through self-management. Change concept #3, which advocates early referral of patients with advanced chronic kidney disease to a vascular surgeon for "fistula only" evaluation and timely placement, has been the subject of extensive debate and criticism, particularly among the nephrology community [15, 26]. Specifically, many voiced concerns at the time that the focus on "fistula only" evaluations would lead to placement of "inappropriate" fistulas at high risk of primary maturation failure in high-risk individuals instead of placement of a graft which may have a greater likelihood for successful use at dialysis initiation. Underlying these concerns was fear that such an advocacy message would not result in an overall reduction in CVC usage and in fact might lead to an increase in CVC prevalence [15].

Trends in Vascular Access After the FFI

The years immediately following the rollout of the FFI saw a substantial increase in the proportion of prevalent HD patients using AV fistulas (Fig. 3.1), such that by August of 2005, the original target of 40 % set at the start of the FFI had been achieved, nearly a year prior to the projected schedule. It should be noted that the increase in use of AV fistulas, accompanied by a concomitant fall in AV graft prevalence, was ongoing even prior to implementation of the FFI. However, a well-recognized inflection point in the increased adoption of fistulas by prevalent HD patients is generally felt to be secondary to the effects of FFI [25]. In response to these observations, the FFI AVF target of 40 % was revised upward to 66 % where it stands today as a CMS national goal. The NKF-KDOQI vascular access guideline was also subsequently revised and updated in 2006, with a newly formulated structured approach to the type and location of long-term HD access, with the overall goal to optimize access survival and minimize complications [17]. The new access guidelines specifically promoted fistula placement first, followed by synthetic grafts if fistula placement was not possible. The guidelines also specifically noted that CVCs should be avoided for HD and used only when other options are not available. The new guidelines also specified that radiocephalic fistulas should be the first option considered followed

by brachiocephalic, then transposed brachial basilica fistulas. The NKF-KDOQI guidelines have not been subsequently revised since 2006 and remain as the most recently updated HD vascular access clinical practice guidelines for practicing clinicians in the United States.

The most striking trend in vascular access distribution among prevalent ESRD patients over the past decade since implementation of the FFI is a continuation of the marked transition from graft dominance to fistula dominance among individuals in the United States undergoing maintenance HD. As shown in Fig. 3.1, in the last years of the twentieth century, over 50 % of prevalent HD patients were dialyzing using synthetic AV grafts, and less than 30 % of patients were using AV fistulas. By the time of the promulgation of the FFI change concepts and stakeholder engagement in 2003, the gap between these two numbers had closed substantially to 40 % and 34 %, respectively. Following 2003, the trend of increasing fistula prevalence and decreasing graft prevalence continued in a nearly linear fashion until 2011 when data from the FFI has demonstrated a relative plateau of these prevalence rates at 60–63 % for fistulas and 18–19 % for grafts.

In contrast to these dramatic changes in prevalent usage rates for fistulas and grafts, the use of CVCs for long-term HD access has shown far less fluctuation. As shown in Fig. 3.1, prior to implementation of the FFI, a slow upward trend in CVC prevalence was evident that continued through 2005 and approached a nationwide prevalence of 30 %. In spite of early concerns among some observers that the FFI strategy might paradoxically increase CVC use among prevalent HD patients, by 2008 these rates had started to show a slow decline, which continued over the subsequent 4–5 years. Like fistulas and grafts, however, the proportion of maintenance HD patients utilizing CVCs has plateaued in recent years, with the most recent data from the FFI indicating a point prevalent proportion of 19–20 %. Similarly, data from the ESRD Networks has shown that the percent of patients with a CVC in use for greater than or equal to 90 days (a clinical performance measure tracked by CMS and the metric for which the NKF-KDOQI threshold of 10 % pertains) has declined only very slightly over the past 10 years and continues to hover just above 10 %.

In contrast to the distribution of vascular access types used by prevalent ESRD patients, the distribution of access use by incident patients starting maintenance HD in the United States is markedly different and of note has shown remarkably little change over the past decade even in the face of the FFI (Fig. 3.2). Data from the most recent US Renal Data System Annual Data Report, which includes data through 2012, shows that 81 % of all incident HD patients in the United States commence dialysis using a CVC, compared to 17 % using a fistula, and only 3 % using an AV graft. These numbers are not dissimilar from the 83, 13, and 4 % a decade ago, even at the height of FFI outreach to dialysis stakeholders. There is substantial geographic variation in the distribution of HD vascular access at dialysis initiation in the United States; Fig. 3.3 shows state-level estimates for the percentage of incident HD patients starting dialysis with an AV fistula. The highest rates of AV fistula use at dialysis initiation are in the Northwestern and Northeastern states, while the lowest rates are in the Southwestern, Southern, and Southeastern states.

The Transition to "Catheter Last"

Over the past 3–4 years, recognition of the plateauing proportion of prevalent HD patients using fistulas as well as the persistently and unacceptably high proportion of incident HD patients starting dialysis with CVCs has led to calls to

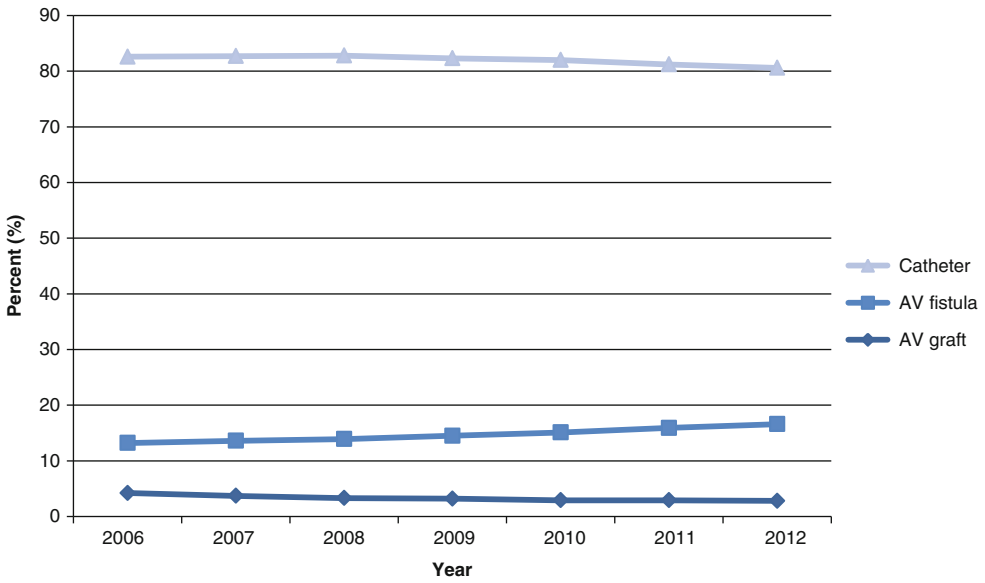

Fig. 3.2 Trends in proportional vascular access type use at hemodialysis initiation, 2006–2012. *Abbreviations*: *AV* arteriovenous (Data source: USRDS 2014 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD)

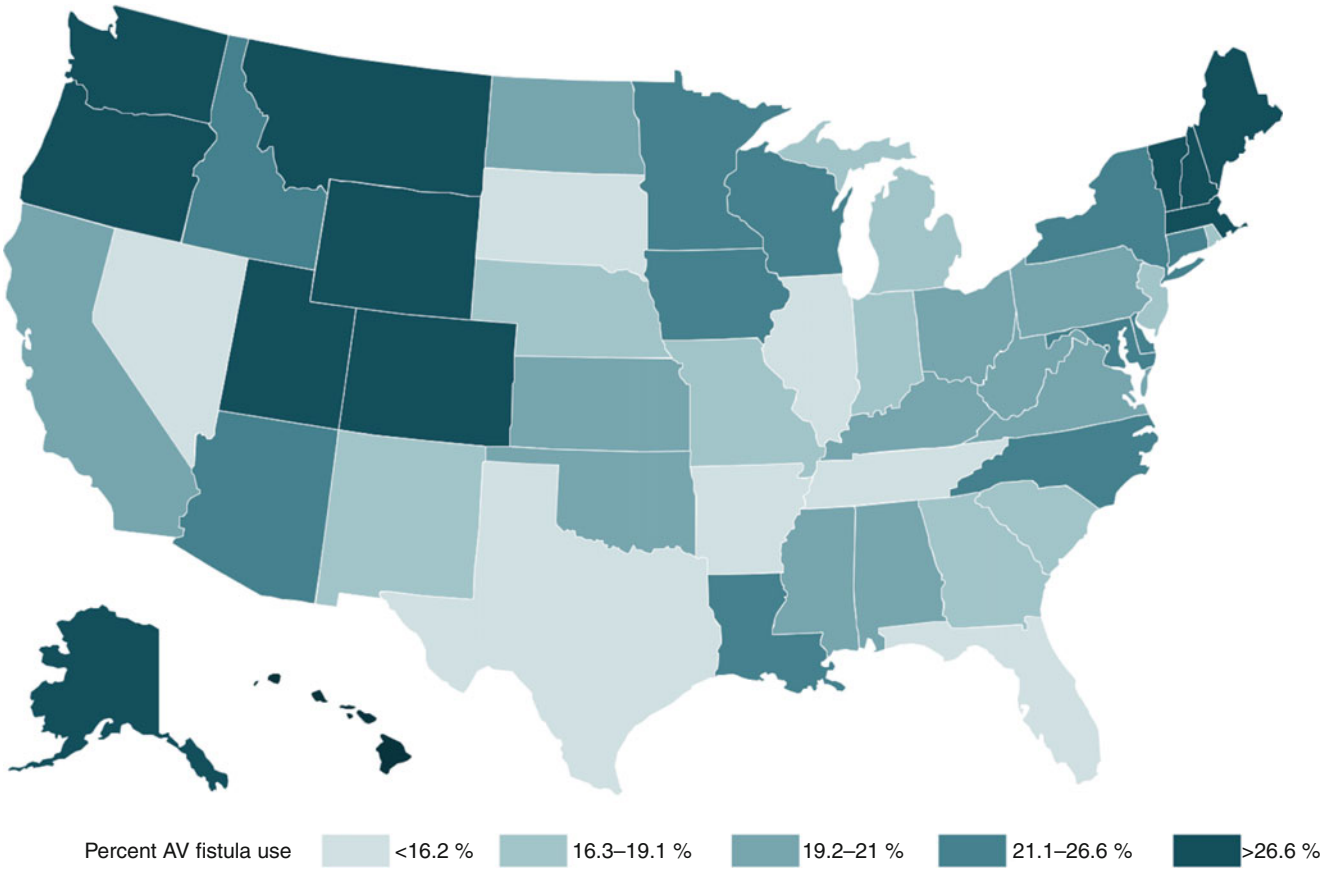

Fig. 3.3 Geographic variation in the percentage of arteriovenous fistula use at HD initiation, March 2015. *Abbreviations*: *ESRD* end-stage renal disease, *HD* hemodialysis (Data source: ESRD National Coordinating Center [9])

reorient the FFI to include not only a primary focus on promoting AV fistulas but also a renewed emphasis on discouraging and seeking alternatives to long-term CVC use [6, 25]. Such calls have been accompanied by evidence from accumulating research suggesting that in some cases, outcomes for patients utilizing fistulas and grafts may be approximately comparable. Research focused on vascular access in elderly patients suggested that clinical outcomes for older individuals using AV grafts may equal those achieved by individuals using fistulas, at least in part due to a high rate of primary fistula maturation failure [8, 12, 14]. For patients dialyzing with CVC, multiple groups have recently demonstrated that changing to an AV access is associated with significantly lower risk for death and that risk estimates associated with an AV fistula versus an AV graft are similar if not equal [4, 13]. Currently, the national prevalence of CVC use for greater than 90 days without a maturing AV access in place of 10.5 % still stubbornly exceeds the NKF-KDOQI clinical outcome goal of less than 10 % established over a decade ago. As a symbol of shifting national policy priorities regarding vascular access in HD patients, and in response to the above observations and to expert opinion, CMS and ESRD Networks renamed the FFI as the Fistula First Catheter Last (FFCL) Coalition to emphasize the dual importance of both goals.

The reasons for persistently high rates of CVC use among prevalent and incident HD patients in the United States even in the face of an aggressive campaign to reduce their use are likely complex and multifactorial. One possible explanation is a high and increased number of patients initiating dialysis with preexisting comorbid disease, such as diabetes, congestive heart failure, and atherosclerotic cardiovascular disease that limit fistula placement and maturation. This explanation is only partly supported by the available data, as in fact AV fistula maturation rates have increased in parallel with fistula prevalence over the past decade. Another possible explanation may include persistently low rates of early referral and consultation with a nephrologist for patients with advanced chronic kidney disease who subsequently developed ESRD, which limit the ability to accomplish timely vascular surgery referral and fistula or graft placement. Data from the US Renal Data System show that the percentage of ESRD patients initiating maintenance HD who had received care from a nephrologist at least 12 months prior to initiation was only 33 % in 2012, although this was an increase of 29 % from 2005 [24]. Even among HD patients who have been

followed by a nephrologist for greater than 12 months prior to initiating dialysis, however, less than 50 % start dialysis with a permanent arteriovenous access. The FFI has had a profound impact on the distribution and trends in vascular access type over the past decade in the United States. The next phase of the FFI, now the FFCL Coalition, will focus on trying to improve these measures in an effort to work toward reducing CVC usage to as low a level as possible and thereby improving outcomes for patients living with ESRD.

Timing of Hemodialysis Access Placement

One area of interest that may serve as a potential target for interventions to achieve lower CVC usage rates is the appropriate timing of permanent AV access placement. The NKF-KDOQI vascular access clinical practice guideline updated in 2006 states that fistula placement should occur at least 6 months prior to the anticipated dialysis start. The FFCL Coalition has recommended even earlier, up to 12 months before anticipated HD start. The goal of identifying these specific thresholds is to ultimately optimize the transition from medical management of advanced chronic kidney disease to maintenance dialysis. This transition period is characterized by exceptionally high risk for adverse patient outcomes; the mortality rate in the first 3 months after dialysis initiation approaches 50 per 100 patient-years [24]. One key contributor to such adverse patient outcomes may be urgent initiation of dialysis in patients unprepared for this important transition, including the need for placement and use of CVC instead of an AV access. Ideally, AV access should be placed far enough in advance of dialysis initiation to allow for maturation and for potential corrective intervention in fistulas that fail to fully mature after initial placement. Advanced AV access placement must be planned, however, incorporating recent evidence showing that for some key patient subgroups, in particularly older patients, early AV access placement may result in a large number of unnecessary surgeries in patients who never initiate renal replacement therapy [18]. For elderly patients, there is a substantial risk of primary failure or nonuse. Estimates of primary failure rates for fistulas in the United States are widely variable, but one recent study found that while overall primary failure occurred in 23 % of fistulas placed, this rate increased to 37 % in patients over the age of 65 [1]. Another found that of patients over the age of 66 who had an AV fistula placed, only 50 % actually used that fistula at initiation of dialysis [8]. Given that the elderly represent a rapidly growing segment of the ESRD population in the United States, age-specific policies for timing of vascular access creation may need to be considered in the future.

One important issue of central importance in vascular access planning for patients in the United States approaching ESRD is the observation that over the past two decades, there has been an inexorable rise in the level of kidney function at which patients are undergoing dialysis initiation [22]. For example, the percent of patients initiating dialysis with an estimated glomerular filtration rate (eGFR) of ≥ 10 ml/min/1.73 m^2 body surface area rose from 13 % in 1996 to 41 % in 2012 [24]. This increase in average eGFR at the start of renal replacement therapy suggests that for patients who did have nephrology care prior to dialysis initiation, there may be less time available for appropriate planning for vascular access, surgical referral, AV access placement, and fistula maturation. The eGFR at dialysis initiation appears to have plateaued and may have even started to decline over the past few years, and the impact of this trend over the upcoming years on vascular access at the time of dialysis initiation will need to be examined going forward.

Medicare ESRD Vascular Access Initiatives

The ESRD Quality Incentive Program

In 2008, the US Congress passed the Medicare Improvements for Patients and Providers Act (MIPPA), which among other requirements, stipulated that ESRD providers must meet certain quality metrics, to be defined annually. This requirement was implemented in 2012 in the form of the Medicare Quality Incentive Program (QIP), which became the first pay-for-performance program in the history of Medicare. The original purpose of the QIP was to incentivize dialysis facilities to provide high-quality care as increasing cost pressures surfaced in an era of changing reimbursement. There were originally three measures implemented, one focused on dialysis adequacy and two on anemia management. Based on scores on these measures, dialysis facilities were potentially at risk for up to 2 % reductions in total annual Medicare reimbursements. In 2014, the number of measures expanded to six, and for the first time, a vascular access clinical performance measure was included. The vascular access measure was a combination of two measures into a single performance score: (1) use of an AV fistula during the last HD treatment of the month and (2) catheter use ≥ 90 days as the only vascular access. No measure specifically assessing AV graft use was implemented. This vascular access measure has continued to be included in the QIP clinical measures even as others have been added over the subsequent years.

In January 2015, CMS launched “Star Ratings” on its Dialysis Facility Compare website, with the goal to provide easy-to-use information to patients, their family, and caregivers regarding quality of care in dialysis facilities. The Star Ratings system assigns a single rating of between one and five stars to dialysis facilities based on reports on nine clinical

performance measures. Of these nine measures, two pertain to vascular access for patients undergoing maintenance HD and are identical to the ESRD QIP vascular access measures. Because of measure weighting, these two measures actually comprise one third of the entire star rating for each facility. Given the relatively recent implementation of the vascular access measures in the ESRD QIP and of the launch of the Star Ratings system, the extent to which these initiatives will impact the distribution of vascular access type among incident and prevalent HD patients in the United States remains to be seen.

The 2011 Expanded ESRD Prospective Payment System

In 2009, the CMS released a proposed rule for an expanded prospective payment system (PPS) for the Medicare ESRD program, a rule ultimately adopted and implemented on January 1, 2011. Overall, the core of the new expanded ESRD prospective payment system replaced a mixed payment system that featured payments for dialysis-treatment-related services as well as separately billed fee-for-service payments for injectable medications and additional laboratory services. The expanded PPS now includes these previously separately billable items (including erythropoiesis-stimulating agents, iron compounds, vitamin D receptor activators, and tissue plasminogen activator or tPA) in a single bundled composite rate payment. Some observers have suggested that the inclusion of tPA, which is commonly used as a thrombolytic to resolve CVC-related dysfunction in individuals undergoing HD, in the composite rate payment may motivate dialysis providers to further reduce CVC use and proactively identify appropriate patients for AV access placement [16]. The true total costs of CVC-related dysfunction in the United States are unknown. However, if the trend of further bundling of separate services into a composite payment continues in the future, the known higher rate of access-related complications in patients using CVCs relative to AV access may further motivate dialysis providers to work with patients and nephrologists to limit long-term CVC use.

Other Vascular Access Initiatives

The Healthy People 2020 Campaign

Over the past 5 years, a number of vascular access initiatives in the United States beyond the FFI/FFCL Coalition and those implemented by CMS have been launched. Perhaps the most broadly reaching has been the Healthy People 2020 initiative, developed by a Federal Interagency Working Group that included representatives from the US Department of Health and Human Services as well as eight other federal departments and agencies launched in 2010. Built upon three previously 10-year Healthy People campaigns, the overarching objectives of Healthy People 2020 are to (1) attain high-quality, longer lives free of preventable disease, disability, injury, and premature death; (2) achieve health equity, eliminate disparities, and improve the health of all groups; (3) create social and physical environments that promote good health for all; and (4) promote quality of life, health development, and healthy behaviors across all life stages. Healthy People 2020 focuses on 42 topics covering a large number of challenges in health care, public health, and health disparities, including chronic kidney disease. The goal for chronic kidney disease elaborated by the Healthy People 2020 initiative is to reduce new cases of chronic kidney disease and its complications, disability, death, and economic costs. To achieve this goal, 14 objectives and 16 sub-objectives have been defined, of which 15 focus on patients with ESRD. One objective and three sub-objectives are specifically devoted to improving vascular access for HD patients, including increasing the proportion of adult HD patients who use AV fistulas and reducing the proportion who use CVCs (Table 3.2). Data bearing on these objectives is taken from the CMS clinical performance measures project.

Data reporting on Healthy People initiatives is provided in the Annual Data Report of the US Renal Data System since 2001, in the inaugural year of the Healthy People 2010 campaign. For example, in response to the Healthy People 2020 objective CKD-11.3, in 2012 37 % of adult HD patients used an AV fistula or had a maturing fistula in place at the start of renal replacement therapy, an increase from 31 % in

Table 3.2 Healthy People 2020 vascular access objectives for patients with end-stage renal disease

Objective	Sub-objective
CKD-11. Improve vascular access for hemodialysis patients	CKD-11.1. Increase the proportion of adult hemodialysis patients who use arteriovenous fistulas as the primary mode of vascular access
	CKD-11.2. Reduce the proportion of adult hemodialysis patients who use CVCs as the only mode of vascular access
	CKD-11.3. Increase the proportion of adult hemodialysis patients who use arteriovenous fistulas or have a maturing fistula as the primary mode of vascular access at the start of renal replacement therapy

Data source: Healthy People 2020, available at: www.healthpeople.gov/2020

Abbreviations: *CVC* central venous catheter

2005. The next iteration of the Healthy People initiative will be launched in 2020 and will provide a further opportunity for setting national priorities regarding vascular access for patients with ESRD.

The Renal Physicians Association Vascular Access Initiative

In 2010, the Renal Physicians Association (RPA), a national advocacy and professional association representing practicing nephrologists, launched its own vascular access initiative, specifically targeted at improving the unacceptably high rate of CVC use in patients undergoing HD. Its goals are to:

1. Reduce the percentage of patients initiated on dialysis with a CVC by 10 % per year, with the ultimate goal to meet the NKF-KDOQI threshold of less than 10 % CVC use in prevalent HD patients
2. Reduce the percentage of patients followed by a nephrologist for greater than 6 months who were initiated on dialysis with a CVC by 20 % per year
3. Ensure that all patients initiated on HD with a CVC have plans for an AV access within 90 days
4. Achieve a 66 % AV fistula rate in all patients receiving care from a nephrologist for more than 6 months [21]

To achieve these goals, the RPA has actively engaged with its constituents to encourage nephrologist to assume responsibility and leadership for reduction in CVC use, provided specific guidance as to the role of the nephrologist in promoting CVC reduction, and has also produced guidance documents for surgeons regarding decision-making approaches to access placement in patients with stage 4 and 5 chronic kidney disease. It has specifically targeted regional Quality Improvement Organizations and hospital CEOs as collaborative partners.

The Future of Dialysis Access and Dialysis Access Initiatives in the United States

As reviewed in this chapter, the past two decades have seen dramatic shifts in the relative distribution and proportional use of different vascular access types among patients undergoing maintenance HD in the United States. Even as multiple stakeholders have launched and implemented vascular access initiatives to increase the use of AV fistulas and reduce the use of CVCs, the distribution of vascular access use at the time of initiation of dialysis for individuals who have newly develop ESRD has remained static. Perhaps the greatest challenge in vascular access for the next decade is to make an appreciable impact in reducing CVC use at dialysis initiation. Currently established initiatives will continue to engage physicians, dialysis facilities, hospitals, and payers to achieve this goal. Additionally, new trends in health-care infrastructure and changes in clinical practice such as the rise of dedicated multidisciplinary vascular access centers and the growing field of interventional nephrologists may affect health-care quality and cost in the coming decade. Close observation will be needed to analyze the impact of these transformations on the prevalence of types of vascular access and complications and on the inevitable appearance of new challenges.

One particularly novel recent transformation is the appearance of ESRD seamless care organizations, or ESCOs, which are the first disease-specific Accountable Care Organizations designed and approved by CMS. ESCOs are partnerships between dialysis facilities, nephrologists, and other Medicare providers (which may include hospitals, vascular surgeons, extended care facilities, and others) with the goal to reduce overall costs of ESRD while maintaining or improving quality with resulting cost savings shared by members of the group. Given that participating ESCOs will be clinically and financially responsible for all care for a group of ESRD patients, including for complications and hospitalizations related to vascular access issues, ESCOs have the potential to incentivize AV access placement and reduction in use of CVCs. As the first ESCOs roll out in the 2015, the degree to which vascular surgeons will participate in these stakeholder groups, and the extent to which the ESCOs will change vascular access practices, remains to be seen.

Beyond new ESRD payment mechanisms and vascular access initiatives, new and ongoing research studies have the potential to shed new light on persistent challenges in ESRD vascular access. The Hemodialysis Fistula Maturation (HFM) Study is a large multicenter prospective cohort study funded by National Institutes of Health that has enrolled 602 patients undergoing creation of a new AV fistula at seven centers in the United States [7]. The goals of the HFM study are to improve prediction of AV fistula maturation by exploring the contribution of basic biologic, anatomic, and care system mechanisms to fistula failure. Patients underwent preoperative ultrasound and venous mapping, flow-mediated and nitroglycerin-mediated brachial artery dilation, arterial pulse wave velocity, and intraoperative specific collection for analyses of histology, morphometry, immunohistochemistry, and gene expression. As of May 2014, all participant follow-up had been completed, and data analyses are ongoing. The results of the HFM study will provide a wealth of information about fistula creation and maturation and will undoubtedly reveal targets for future interventions to increase maturation rates, as well as identify risk factors which identify patients who may benefit from AV graft placement instead.

Substantial progress has been made over the past two decades in vascular access management among patients

starting and undergoing maintenance HD in the United States. Many challenges remain, however, with the two most prominent being the overwhelming dominance of the CVC as the vascular access for patients initiating renal replacement therapy, and persistent challenges with primary fistula maturation failure, particularly among older adults. Critical to reducing CVC use at dialysis initiation are efforts to optimize and improve care during the high-risk transition from medical management of advanced chronic kidney disease through the start of renal replacement therapy, including earlier identification of patients with kidney disease, as well as reorganizing systems and practices to favor expedient access placement and revision. Existing evidence suggests that we may have reached a plateau or "ceiling" for the proportion of prevalent HD patients undergoing maintenance dialysis using an AV fistula. However, given that significantly greater than 10% of prevalent HD patients still use CVCs for long-term vascular access, many of whom are not acceptable candidates for attempting fistula placement, further clinical benefit may be achieved by a focus on conversion of access in these patients to AV grafts. Finally, critical to any effort to improve vascular access management and proportional use in the United States is optimizing interdisciplinary collaboration among nephrologists, vascular surgeons, primary care physicians, vascular access coordinators, dialysis facilities, and hospitals.

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Hemodialysis Access Outcomes and Quality Improvement Initiatives in the United States

4

Devin S. Zarkowsky and Philip P. Goodney

Introduction

Outcomes research evolved in the 1970s as a method to evaluate and improve patient care delivery. Recent efforts by CMS to identify trends in vascular access for end-stage renal disease (ESRD) lead to the Fistula First Catheter Last (FFCL) initiative aimed at increasing incident and prevalent arteriovenous fistula usage. There is a significant protective effect from autogenous conduit employed as the access modality for renal replacement therapy. Surgeons demonstrate varying results establishing and maintaining fistulas. Current efforts to create large registry reports and level 1 evidence aimed at guiding this field are ongoing. This chapter describes the science associated with reporting health and procedural outcomes, particularly vascular access for end-stage renal disease patients. The chapter is divided into sections: xx, patient-level AVF outcomes.

Outcomes Science History

Patients across the United States do not experience health care in a uniform fashion. Like regional accents flavor spoken language, so do local trends affect medical systems. Wennberg and Gittelsohn reported variation in utilization, facilities, manpower, and expenditure rates across Vermont hospitals during 1969 in a landmark *Science* report that introduced outcomes research as an essential quality improvement tool for health systems [1]. "Variations in utilization indicate," they write in the article's conclusions, "that there is considerable uncertainty about the effectiveness of different levels of aggregate, as well as specific kinds of, health services." Identifying variation in modern health-care delivery from physician-to-physician, hospital-to-hospital, and state-to-state opened an entirely new area in medical science focused on improving processes and decision-making.

Similar to the medical conditions reported by Wennberg and Gittelsohn, ESRD care varies across the United States [2]. The ability to maintain life in the absence of native kidney function with extracorporeal dialysis evolved from the work by Georg Haas and Heinrich Necheles in 1924 was simplified by Cimino, Brescia, and Appel in the 1960s, codified into law by Richard Nixon in the 1970s, and extended with the introduction of percutaneous catheters in the 1980s. Large trials at the end of the 1990s and beginning of the 2000s identified a mortality risk associated with these catheters, which had supplanted fistulas as the dominant access modality in the preceding two decades [3–5]. The Fistula First Catheter Last (FFCL) initiative written in the mid-2000s created policy intended to reverse this problematic trend. By the 2010s, significant increases in fistula prevalence occurred, but more than 80 % of patients still began dialysis with catheters and suffered the attendant mortality risk, thus presenting an opportunity for quality improvement. Identifying these trends would not have been possible without health professionals contributing information to a large database administered by the United States Renal Data System (USRDS).

ESRD Disease Burden in the United States

Annual reports published by the USRDS detail information on all patients diagnosed with end-stage renal disease as well as those started on dialysis; electronic versions are available at usrds.org and data lag two years behind the publication year. According to the 2014 report, 114,318 patients were diagnosed in 2012, marking the second consecutive year-over-year decline in new ESRD cases (Fig. 4.1) [6].

The total number of people actively treated with ESRD in the United States on December 31, 2012, was 636,905, of which 450,602 received dialysis and 186,303 had a

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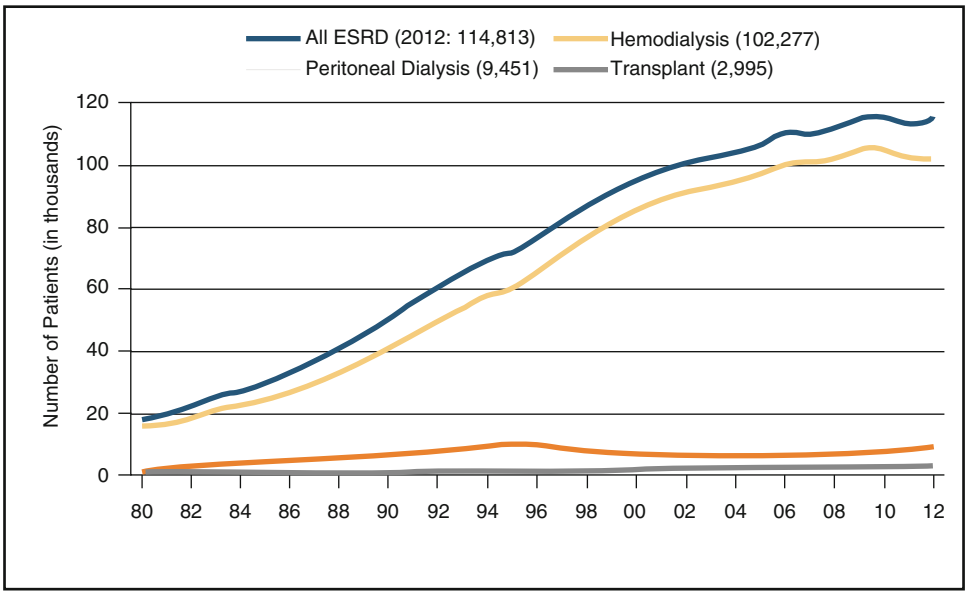


Fig. 4.1 Incident ESRD treatment trends [6]

functional kidney transplant; 88,638 patients with ESRD died between January 1 and December 31, 2012. Medicare spent $28.6 billion or 5.6 % of its total budget, providing ESRD care during this time period. Figure 4.2 places ESRD in context with other surgical diseases, including cancer and cardiovascular disease [6–8].

Each year, about 610,000 people suffer their first stroke, while 10,000 develop testicular cancer in comparison to the 110,000 who develop ESRD. About 40 % of those patients treated with ESRD with hemodialysis (HD) will survive for 5 years in comparison to 98 % of those diagnosed with prostate cancer, and 75 % treated for an abdominal aortic aneurysm. Almost 90,000 people with ESRD die every year, whereas 160,000 die annually from lung cancer, and 40,000 die from breast cancer.

Variation in ESRD Diagnosis

Affected patients are not distributed evenly across the United States (Fig. 4.3) [6].

Southern states experience approximately twice the yearly incidence of ESRD in comparison to New England and the Pacific Northwest. Eggers, Rosansky, and colleagues reported this trend in 1990 [9]. Despite differing population characteristics, particularly density of African-American residents who demonstrated significantly higher ESRD frequencies, patient demographics could not completely account for variation in treatment. This finding was recapitulated in contemporary studies derived from recent USRDS and Medicare data [10, 11].

Variation in AVF Construction

Hemodialysis, rather than peritoneal dialysis, is the dominant renal replacement therapy in the United States. Surgeons occupy a key position in the initiation algorithm, namely, establishing reliable intravascular access. Arteriovenous fistulas (AVFs) are the preferred method. The prominent FFCL public policy campaign initiated in 2005 focused on increasing fistula-based access.

Incident and Prevalent Vascular Access

According to the FFCL Dashboard, approximately 63 % of all patients in the United States on hemodialysis use an AVF, a significant improvement over the early 2000s, when only 33 % of patients did so [12]. Malas et al. suggest approximately 99 % of ESRD patients are amenable to fistula creation based on demographic analysis [13]. Were incident fistula-based access to be pursued at this aggressive level, Malas et al. estimate saving $2 billion annually in 2010 dollars [13]. Most patients, however, still initiate dialysis with transcutaneous catheters – either temporary or permanent. Incident surgical access – either AVF or arteriovenous grafts (AVGs) – has not changed significantly since the Centers for Medicare and Medicaid Services (CMS) instituted the FFCL initiative in 2005 (Fig. 4.4) [14].

Furthermore, AVF construction for incident dialysis varies by nearly 100 % across the United States (Fig. 4.5) [15].

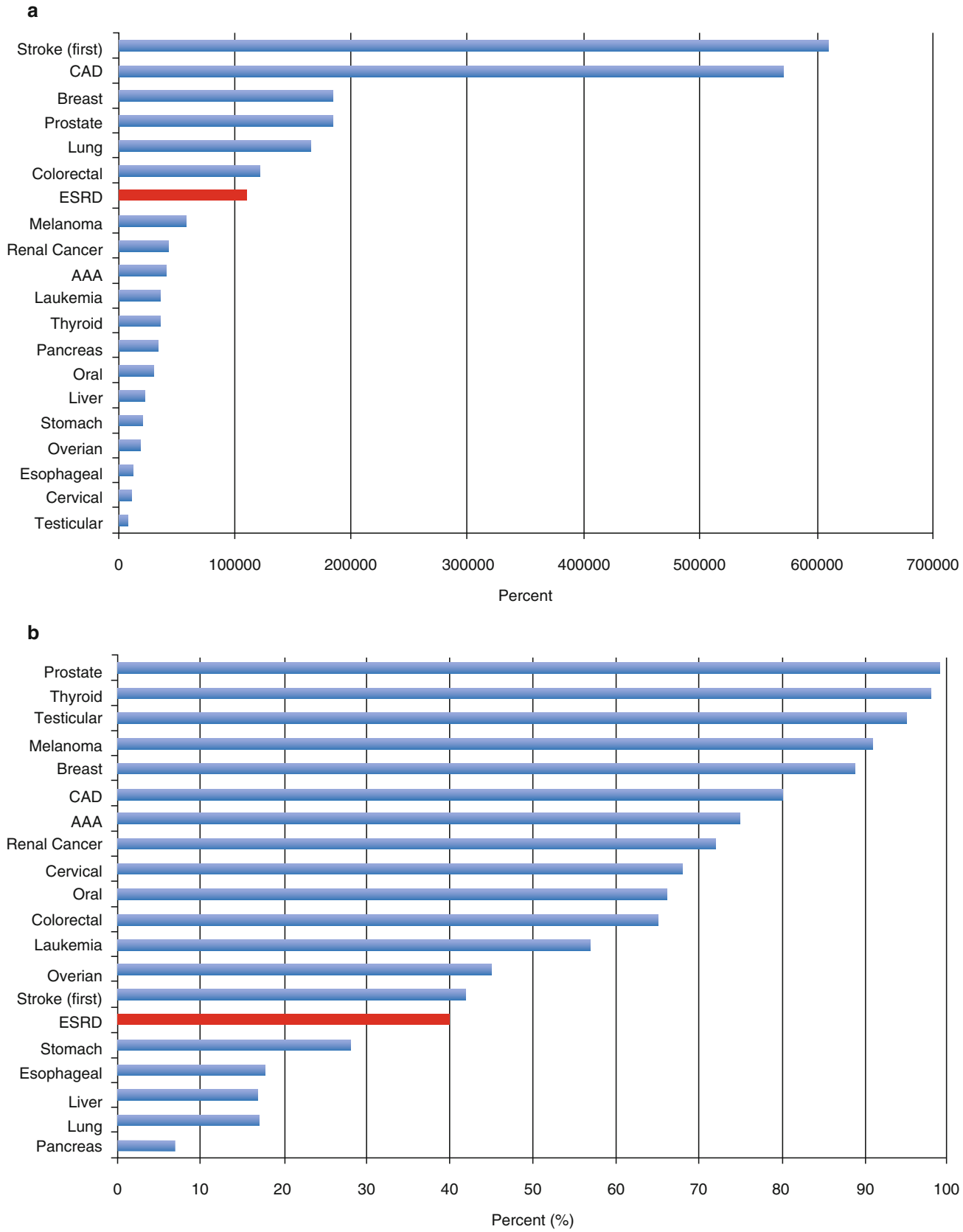


Fig. 4.2 ESRD epidemiology in relationship to other surgical diseases [6–8]. (**a**) Annual incidence, all ESRD patients, (**b**) 5-year survival, ESRD treated with HD, (**c**) Annual mortality, all ESRD patients

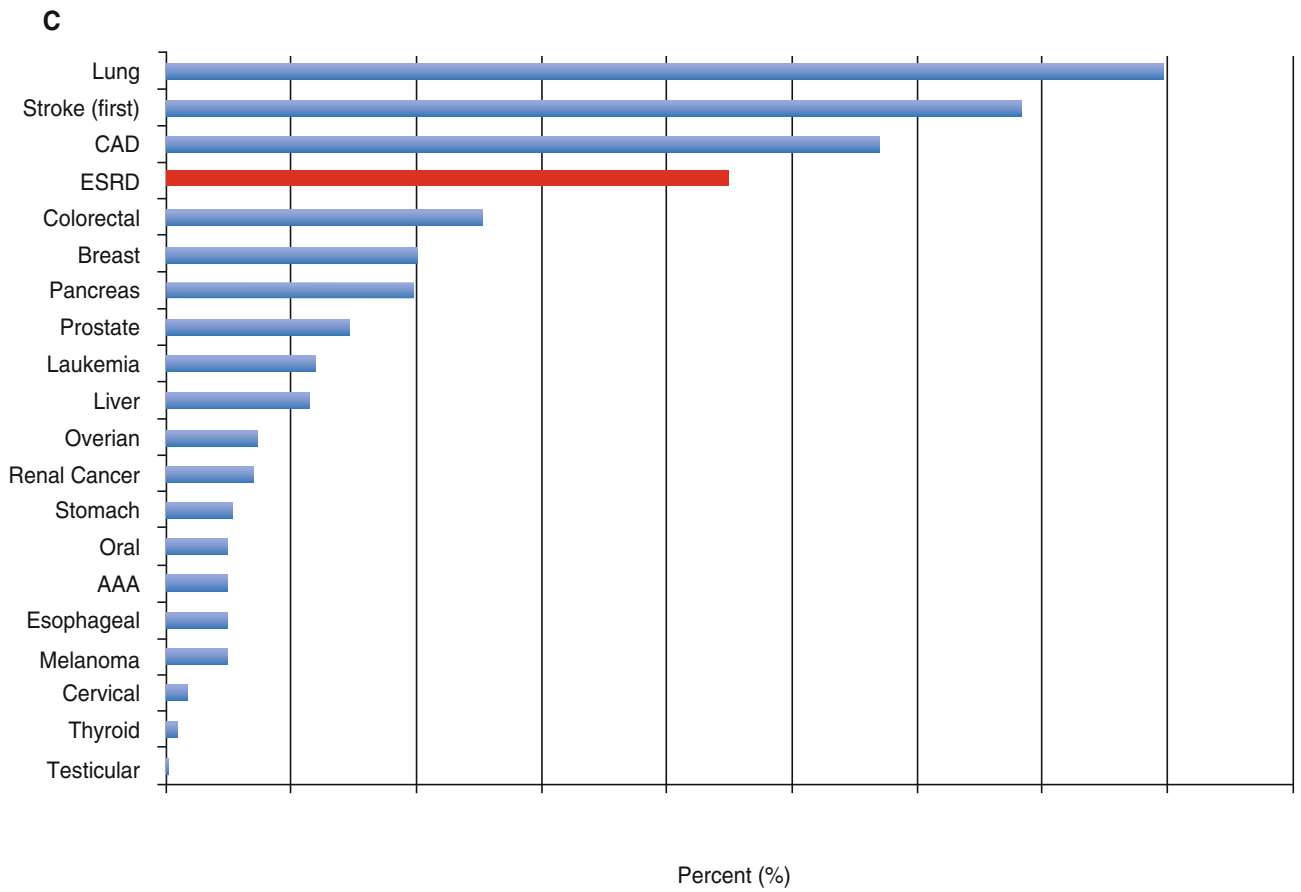


Fig. 4.2 (continued)

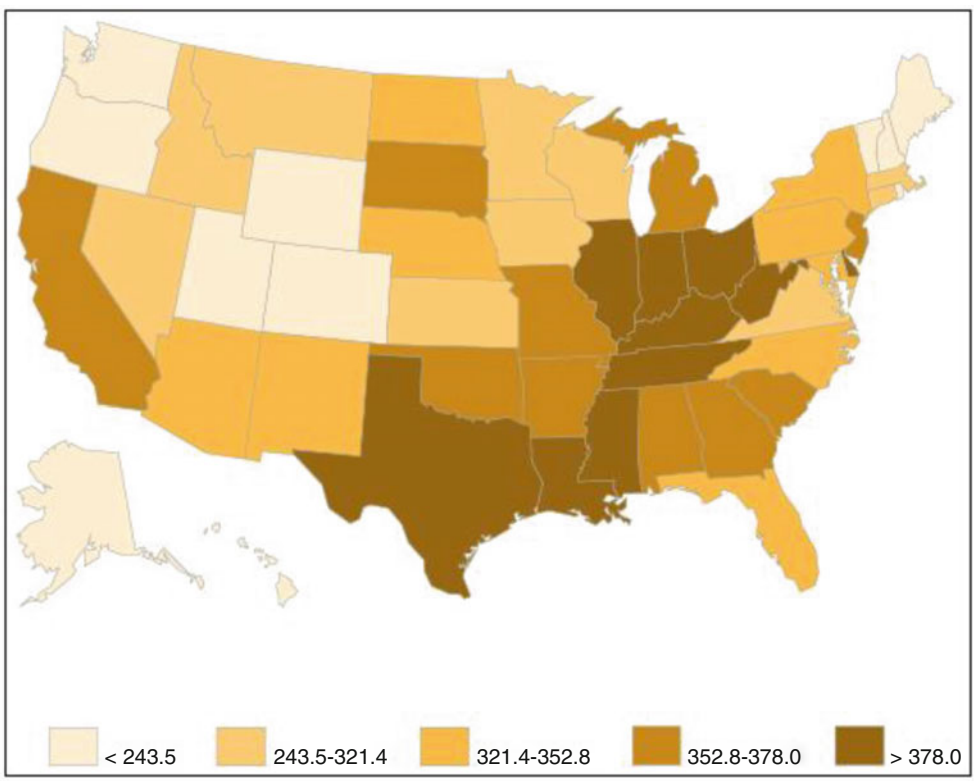


Fig. 4.3 ESRD incidence rate, million population per year by state [6]

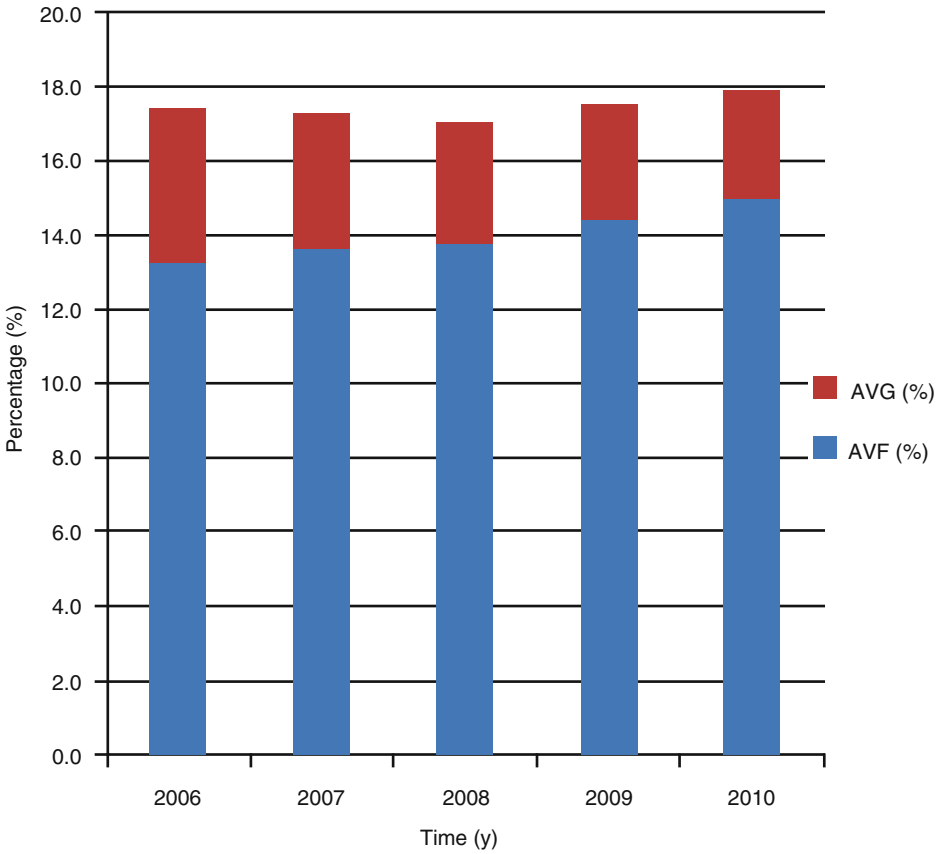


Fig. 4.4 Incident intravascular access modalities, 2005–2010 [14]

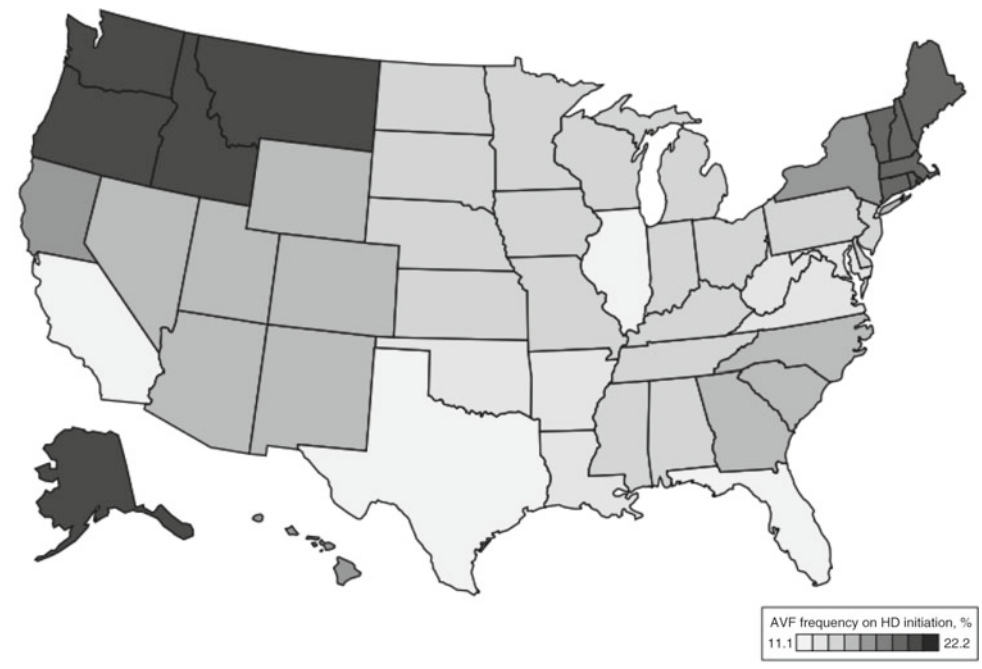


Fig. 4.5 Regional variation in AVF construction [15]

Nephrology care increases the likelihood of a patient beginning hemodialysis with a functional fistula by a factor of 11 [16]. This finding reemphasizes the necessity interdisciplinary coordination plays in optimal ESRD patient care.

Variation in Mortality Associated with Incident Vascular Access Type

Estimated 5-year survival varies by 35 % based on initial HD access type (Fig. 4.6) [13].

Catheters and prosthetic graft material are hypothesized to subject patients to increased infection and cardiovascular event risks, accounting for this difference in mortality [17]. Furthermore, adjusted mortality hazard for patients varies by location within the United States (Fig. 4.7) [15].

Appraised together, these findings suggest that locoregional variation in surgical decision-making significantly impacts ESRD patient care at a systemic level.

Patient-Level Surgical Outcomes

The following section discusses patient-level AVF outcomes:

Fistula Maturation

Effective hemodialysis presupposes technical success in the operating room, defined as a patent fistula, graft, or catheter on concluding a procedure. Whereas catheters are immediately usable, AVG and AVF require – at a minimum – 2 and 4 weeks, respectively, to develop into viable intravascular access sites. Guidelines from the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) section 3.2.2 deem AVF mature when they display: (1) a 6 mm vein diameter, (2) a 600 mL per minute blood flow rate, and (3) a vein depth below the skin of 6 mm [18]. This process, usually appraised as maturation failure, varies between patients. Published frequencies in large series encompassing AVF at all upper extremity position range from 9 to 81 % [19–23]. The most compelling preoperative patient characteristics predicting failure to mature (FTM) include age, CAD, PAD, and race [19]. A scoring system developed by Lok et al. based on these preoperative patient characteristics categorized FTM risk into low, medium, high, and very high with frequencies of 24, 34, 50, and 69 %. Voormolen and coauthors identified postoperative hemodynamic risk factor assessment as 58 % sensitive and 88 % specific for maturation failure in a systematic literature review [21]. Fistula flow and fistula venous diameter as well as a composite value for both variables in addition to radial artery resistive index were employed together or individually as hemodynamic assessment variables in the examined studies. These parameters predicted maturation failure with better sensitivity and specificity than presurgical patient characteristics or preoperative hemodynamic assessment. Combined, these studies guide patient selection but also have implications into postoperative surveillance and intervention.

Cannulation

Preparing patients to receive renal replacement therapy is best practiced in a proactive fashion, as suggested by Fistula First Catheter Last guidelines. While selecting patients who will successfully mature fistulas is complex, predicting which patients ultimately progress to end-stage renal disease is a challenge in and of itself. Chronic kidney disease (CKD) progresses in a discontinuous fashion. An exact accounting of CKD patients within the United States does not exist. However, the National Health and Nutrition Examination Survey (NHANES) is a yearly cross-sectional study capturing, in addition to other variables, kidney disease prevalence and severity [24]. Between 2007 and 2012, about 0.5 % of the 50,000 NHANES participants demonstrated CKD stage 4 or 5 levels at which surgical referral is recommended by FFCL Change Concept 3 [6]. Extrapolating this finding to the US population as a whole, about 1.6 million of the estimated 320 million United States citizens in 2015 likely suffer from surgically actionable kidney disease. Figure 4.1 shows about 115,000 people progress to ESRD every year or about 7.2 % per year of those patients with CKD stage 4 or 5. Progression among patients receiving AVF prior to initiating HD – either due to selection bias, more aggressive disease, or non-initiator patients dying – appears to be significantly higher in reported cohorts. Solid et al. identified 550 non-ESRD patients who had received an AVF in the 2005 Medicare 5 % random sample; 71 % progressed to hemodialysis through their AVF within 2 years [25]. A large randomized trial corroborated this result with 81 % of patients not requiring renal replacement therapy prior to AVF creation, achieving successful cannulation within the study period [26]. Lastly, a recent retrospective cohort reported 65 % of patients proactively treated with an AVF eventually employed it on HD [27].

Patency

Once cannulated, fistulas must be durable. Hemodialysis is, philosophically, a bridge to kidney transplantation – the most efficacious ESRD treatment [6]. Practically, AVF must last for years and are often definitive therapy. Several meta-analyses published within the last 5 years improve on single-center results; Table 4.1 summarizes their findings.

Al-Jaishi et al. found pooled forearm and brachium fistula, 1- and 2-year primary patencies to be 60 % and 51 %, respectively [31]. Subgroup analysis demonstrates statistically fewer primarily patent lower arm fistulas at 1 year,

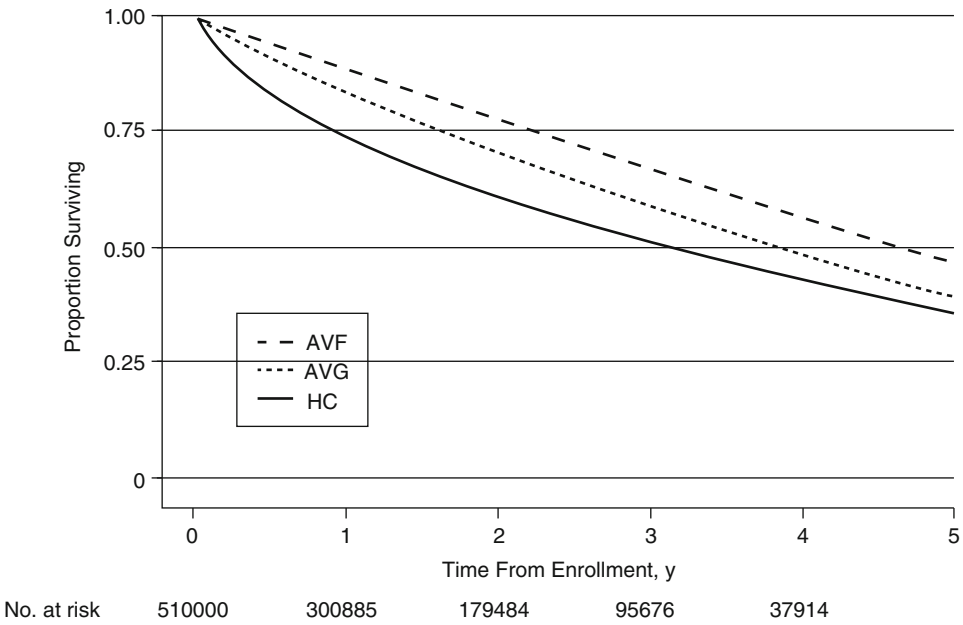
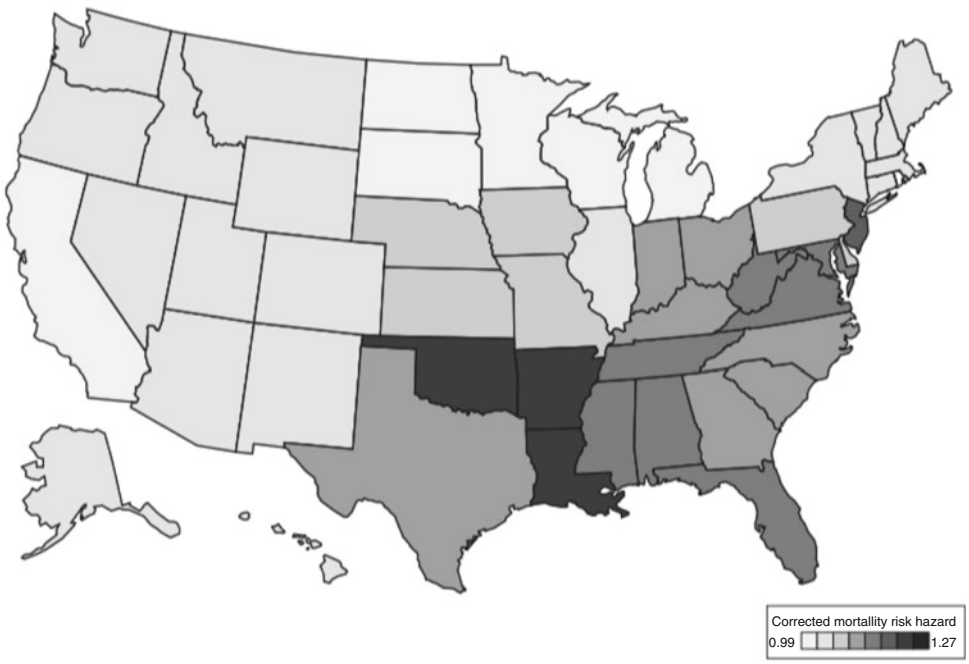


Fig. 4.6 Kaplan-Meier 5-year survival estimate stratified by incident hemodialysis access type [13]



Corrected mortallity hazard by-stage renal disease Google's GeoMaps tool was used to create the heat maps.

Fig. 4.7 Variation in adjusted Cox mortality hazard by ESRD Network [15]

Table 4.1 Meta-analysis data on primary and secondary upper extremity fistula patencies [28–30]

Patency	Primary		Secondary	
Time	1 year	2 years	1 year	2 years
Radial-based	74 %	71 %	80 %	74 %
Brachiocephalic	82 %			
One-stage	57 %		82 %	
Two-stage	59 %		77 %	

55 %, in comparison to upper arm fistulas, 65 %. At 2 years, both positions primary and secondary patencies were statistically similar, 46 % and 49 %, respectively. Focusing on radial artery-based fistulas, Wu and coauthors report 74 % and 71 %, 1- and 2-year primary patencies [30]. Brachiobasilic fistulas created in either a one-stage or two-stage fashion demonstrated no difference in primary patency, 57 % versus 59 %, respectively [28]. Finally, 82 % of brachiocephalic fistulas in elderly patients were patent at 1 year without reintervention [29]. Each meta-analysis reports significant heterogeneity associated with endpoint reporting and surveillance strategies employed by the primary studies; all call for randomized trial data to supplement their findings.

Maintenance

Medical Therapy

Preventing AVF thrombosis with an antiplatelet agent is a common strategy. Oral agents, including clopidogrel, aspirin, ticlopidine, and dipyridamole, reduce graft loss by half during the 6-month period after construction [32]. Major and minor bleeding events are not statistically different, and maturation appears unaffected. The meta-analysis authors state clearly that AVGs are not protected by antiplatelet agents.

Warfarin does not appear to have a beneficial effect on patency, possibly owing to the platelet-based thrombosis mechanism in arteries and arterialized veins. The 2008 Cochrane collaboration analysis on medical treatment to increase AVF patency reports a single randomized trial with low-dose warfarin resulting in a significant increase in bleeding for the treatment group with a concomitant increase in graft loss [33]. This result confirmed similar retrospective data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) [34].

Surgical and Interventional Therapy

Clinical examination is integral in managing ESRD patients' ongoing vascular access needs. Unlike other bypass surgeries, AVF and AVG are followed extremely closely often three times per week or more in local dialysis units. Monitoring cannulation and flow parameters during renal replacement therapy ensures failing intravascular access is identified and addressed. Routine multidisciplinary AVF assessments that discuss findings from the dialysis clinic improve primary and secondary patencies while decreasing morbidity experienced by patients [35]. A small series from Bountouris and coauthors in Malmö, Sweden, examined repeated angioplasty on AVF. Of the 50 % of fistulas in their cohort requiring more than one angioplasty, 85 % remained patent at 1 year [36]. Interventions on recently constructed fistulas and those with longer lesions demonstrate increased patency loss after balloon angioplasty, suggesting hemodynamic shear stress and fistula anatomy determine stenosis progression [37]. Likely, new fistulas that require an intervention are intrinsically disadvantaged, either due to a poor conduit, coagulation cascade abnormality, or technical error necessitating revision.

If a patient's thrombosed AVF or AVG requires recanalization, Kuhan and coauthors found no difference between open surgery and interventional techniques, including aspiration, balloon angioplasty or thrombectomy, and mechanical or chemical thrombolysis, aimed at reestablishing flow in a meta-analysis of randomized trials from the mid-to-late 1990s and early 2000s [38]. Technical success was 75 % in the endovascular group and 80 % in the open surgery group, while primary patencies were 14 % and 24 % at 1 year, respectively, a statistically nonsignificant difference. Though the meta-analysis authors emphasize that these findings stem from randomized trials evaluating somewhat antiquated techniques, these results nonetheless reemphasize the necessity of close patient surveillance aimed at identifying failing – rather than failed – vascular access.

Complications

Unsuccessful reintervention incurs significant consequences. Conversion from permanent access – either AVF or AVG – to a catheter during a patient's first year on dialysis entails a confounding-adjusted 1.81-fold increase in mortality hazard [39]. Roughly, 20 % of patients will experience this problem. Catheters confer a 1.38-fold relative risk for major cardiovascular events and a 2.12-fold relative risk for fatal infections in comparison to fistulas [17]. Similarly, AV grafts subject patients to a 1.07-fold relative risk for major cardiovascular events and a 1.36-fold relative risk for infection by comparison to patients with fistulas, but AVG significantly outperform catheters in each category.

Hemodialysis Fistula Maturation Consortium Study

Lastly, level 1 evidence will be provided by the Hemodialysis Fistula Maturation Consortium study, which completed patient follow-up in May, 2014, and was actively analyzing outcomes as of December, 2014 [40]. A total of 602 participants receiving single-stage fistulas at seven centers around the United States were followed for up to 4 years [41]. Data collected on vascular anatomy and biology as well as patient demographics and care processes will better inform nephrologists, access surgeons, and health systems interested in providing high-quality ESRD care. Supplementing this work are registries acting as active feedback mechanisms to inform and guide surgeons based on real-world clinical outcomes.

Current Quality Improvement Initiatives

American College of Surgeons National Surgical Quality Improvement Program

Whereas as the USRDS database is adequately designed to examine trends in ESRD care at systemic and regional levels, the granularity to inform individual surgeons is not present. Reporting surgical outcomes hinges on the variables tracked

by databases, and those created over the last 30 years have become increasingly specialized. The best known is the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).

Motivated by high operative mortality at Veterans Health Administration hospitals, Public Law 99–166 passed on December 3, 1985, compelling each center to report, "…significant deviations in mortality and morbidity rates for surgical procedures performed by the Department of Medicine and Surgery from prevailing national mortality and morbidity standards for similar procedures [42]." No such mortality and morbidity benchmarks existed, however [43]. Between October 1, 1991, and December 31, 1993, 44 VA medical centers participated in the National VA Surgical Risk Study (NVASRS) in efforts to create a risk model applicable to nine surgical specialties [44–46]. Between NVASRS' completion and a follow-up study in 1998, 30-day mortality and morbidity fell by 9 % and 30 %, respectively, at VA medical centers, confirming the positive impact outcomes science exerts on patient care [47]. A successful pilot study in 1999 enrolled three non-VA, private sector hospitals, and in 2004, ACS-NSQIP evolved to its current form, encompassing both VA and private sector hospitals.

Feedback to providers and administrators is the essential quality improvement tool afforded by the ACS-NSQIP effort [43]. Each site receives an annual report. High- and low-performing institutions receive special periodic appraisal. Self-assessment instruments allow individual programs to analyze their own outcomes. Voluntary site visits generate detailed findings when providers and administrators express concerns about outcomes to ACS-NSQIP. Finally, best practices are identified and disseminated.

Despite this framework, few authors have examined ACS-NSQIP data available for ESRD-specific procedures. At this writing, only two papers have been published with ACS-NSQIP data on this topic [48, 49]. Beyond 30-day morbidity and mortality, as discussed in the Siracuse et al. paper, failure to mature frequencies, patency, and other relevant long-term follow-up parameters are not recorded.

The Vascular Quality Initiative

Launched in 2011, the Vascular Quality Initiative (VQI) captures information on 12 vascular surgeries, including hemodialysis access from 350 centers around the United States. Participation occurs on an institutional level; is endorsed by the Society for Vascular Surgery, American Venous Forum, as well as the Society for Vascular Medicine; and satisfies the CMS requirement that hospitals enroll in a Patient Safety Organization (PSO). Figure 4.8 maps centers currently participating in VQI.

Fig. 4.8 Active VQI centers

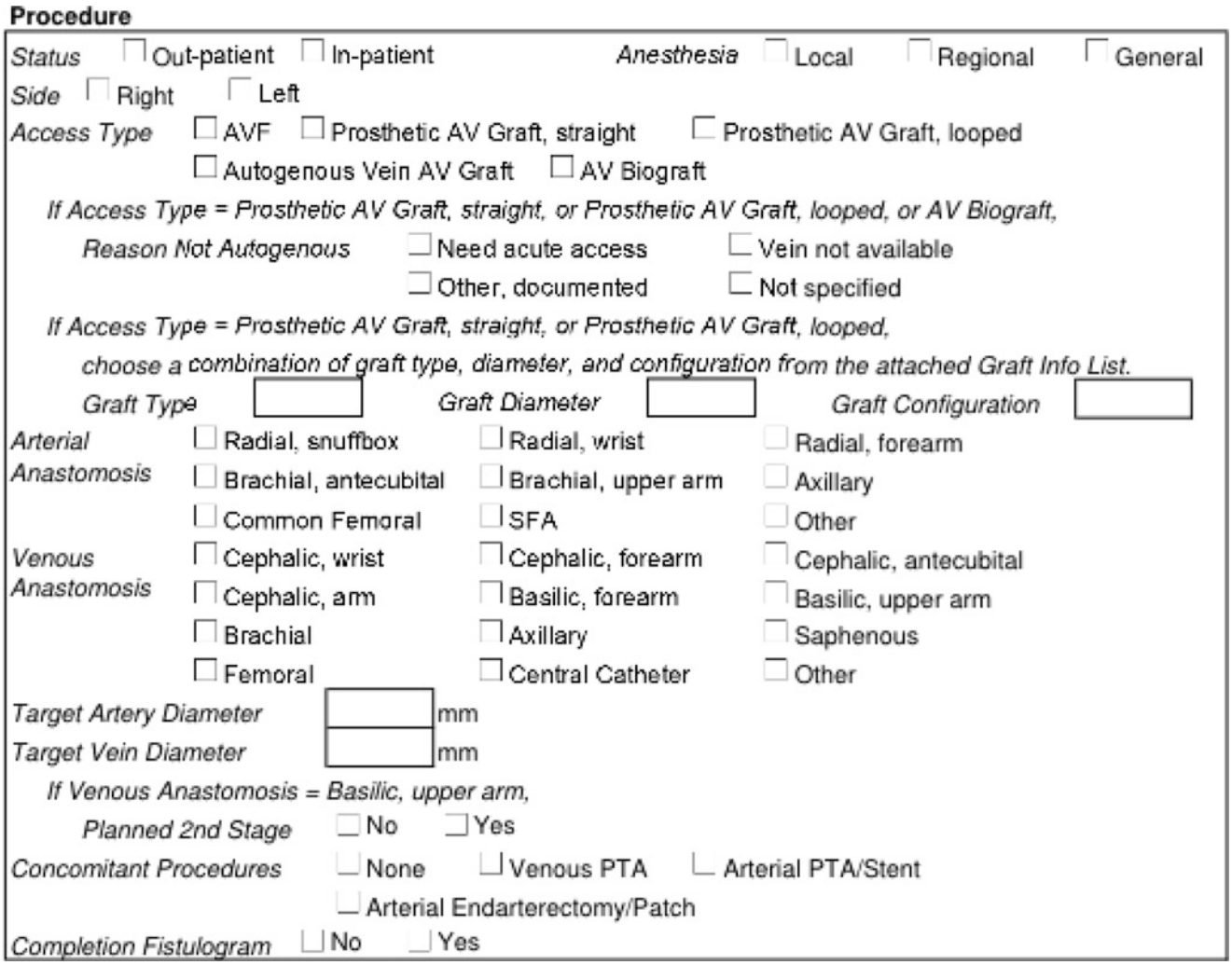


Fig. 4.9 VQI vascular access form web interface

Similar to ACS-NSQIP, the VQI aims to improve safety and care quality through data sharing. General information and patient demographics are collected, as well as medical history, procedural and postoperative details, and follow-up information for at least 1 year. The collected vascular access data is similar to CMS Form 2728 which is filled out by practitioners enrolling ESRD patients in Medicare but also includes details on fistula location, construction, and conduit selection, in addition to specific follow-up imaging modalities not present on the government form. Surgeons or their representatives log data electronically. The interface is web based and administered by a private company with cloud network data storage (Fig. 4.9). Of the 216,000 total cases accrued in VQI by June, 2015, more than 10,000 vascular access cases have been collected.

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Coding and Billing for Hemodialysis Access Procedures in the United States

5

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Introduction

Continuous assessment of the process by which care is rendered in order to optimize billing, coding, and ultimately reimbursement is essential. Charge entry staff in each medical practice generate an insurance claim for a given medical provider by linking a diagnosis code with a procedure code and adding modifiers as needed. Claims are typically submitted to the insurance carrier electronically [1]. The appropriateness of this coding translates into timely reimbursement to the provider. Each time a submission is rejected for any reason, the chance of that service ever being paid to the physician decreases significantly. Therefore, the ultimate goal is to generate a claim that is without error and medically appropriate and correctly describes the intervention. This chapter provides an overview of coding and billing for hemodialysis access procedures in the United States and should be used only as a guideline for the physician and coder since each insurance payer has their own rules and regulations.

History of Coding and Reimbursement

The Centers for Medicare and Medicaid Services (CMS) began utilization of the resource-based relative value scale (RBRVS) in 1992. The basis for this methodology relies on a basic element termed the relative value unit or RVU. All procedure codes within the current procedural terminology (CPT) manual have a set amount of RVUs. Each code is assigned a specific amount of physician work [2], practice expense, and malpractice risk. These RVU sets are totaled and then multiplied by a variable [3] termed the "conversion factor" which is determined every year by statute. Reimbursement is also tied to the cost of living in each region. Therefore, the United States is broken down into districts that each has a geographic practice cost index (GPCI) which can alter payment based on the economy in the location that a medical practice serves.

Since 2004, congress has overridden a sustainable growth rate (SGR) decrease in the conversion factor over a dozen times. In April 2015, the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA, Public Law No. 114-10) legislation was passed without a "pay for" in congress, abolishing the SGR-mandated changes to the conversion factor for a 10-year period. The first 5 years will receive a 0.5 % payment increase and the latter five, a 0 % update. This must also be compared to the estimated 3 % cost of living inflation rate which will have a negative effect in each medical practice for the next 10 years as well.

Surgical Access Procedures

There are six primary surgical (open) arteriovenous (AV) access procedures. Five deal with the use of autogenous tissue and one with prosthetic or "non-autogenous" conduit. The most straightforward is the direct fistula where a vein is sewn to an adjacent artery through a single incision. This operation is delineated by CPT code 36821. Examples include the snuff box fistula or the wrist fistula using radial artery and cephalic vein or an elbow fistula where the cephalic or median cubital vein is sewn to the brachial artery in an end-to-side fashion. The most rarely performed is CPT code 36825 which depicts construction of an AV graft using autogenous conduit such as saphenous vein harvested from a remote site and then tunneled in the superficial subcutaneous plane. There are instances in which vein must be "transposed" from one incision in a subcutaneous tunnel to a separate incision for anastomosis. The remaining three CPT codes describe these autogenous-based procedures. If a transposition occurs in the forearm regardless of vein, CPT code 36820 is appropriate. In the upper arm, basilic vein transposition is reported using CPT code 36819, whereas

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cephalic vein transposition requires CPT code 36818. Basilic vein transpositions have been performed in either one or two stages. CPT code 36819 describes a single-staged procedure with mobilization of the entire vein, tunneling as needed to bring the access just under the skin and the arteriovenous anastomosis. Alternatively, the first of the two-stage approach is simply a direct arteriovenous anastomosis at the elbow. CPT code 36821 would be most appropriate for this construction. When the patient is returned to the operating room for superficialization of the access, a separate "revision without thrombectomy" CPT code 36832 would be submitted. CPT code 36830 describes use of non-autogenous conduit to create an arteriovenous graft regardless of location. Examples include a forearm loop, an upper arm bridge, or a thigh loop graft. All six of these primary open access procedures have a 90-day global period associated with them for preoperative and postoperative care.

The RVU content of the six primary access procedures is described in Table 5.1 and has undergone a complete revaluation in 2015. Because of several concerns by CMS over where the actual procedures were performed (i.e., the site of service being either hospital inpatient versus hospital outpatient), the entire family of primary and secondary AV access surgeries underwent a reassessment relative to each other and the whole fee schedule. This resulted in minor changes in all six procedures in 2015 compared to prior years.

There are three standard secondary open AV access procedures. CPT code 36831 describes operative thrombectomy of an AV access with no revision to the circuit. CPT code 36832 describes revision of an AV access without thrombectomy. This typically involves venous outflow patch angioplasty or jump grafting. Ligation of fistula side branches at a separate setting, mid-access aneurysm/pseudoaneurysm repair, the second stage of a basilic vein transposition, or proximalization of arterial inflow qualifies as well. Lastly, CPT code 36833 describes thrombectomy of an occluded AV access and subsequent revision using open techniques in the same setting. Completion angiography after open arterial or venous surgery is bundled into the procedure. However, preoperative contrast imaging on the same day as the open dialysis may be reported with a -59 modifier appended to the radiologic coding. These surgery descriptions have a 90-day global period associated with them as well and realized a significant increase in RVU content in 2015 due to the reassessment of all open AV access surgeries.

Two additional open procedure codes should be mentioned. CPT code 37607 depicts either AV access banding to limit flow through the hemodialysis circuit or ligation of the AV access in its entirety to completely obliterate flow. CPT code 36838 describes a secondary procedure code that is sometimes employed in those patients who have developed steal syndrome. To maintain patency of an autogenous access while helping with limb salvage, the distal revascularization and interval ligation (DRIL) procedure may be employed, which includes ligation of the brachial artery distal to the AV access arterial anastomosis, vein harvest, and remote brachial to brachial artery bypass. CPT code 36838 describes such an intervention in the upper extremity and cannot be reported for treatment of steal syndrome in the lower extremity. The RVU content for these five secondary procedures is listed in Table 5.2.

Table 5.1 Open primary arteriovenous access creation CPT codes and their total RVU content from 2009 through 2015 Medicare Physician Fee Schedule

Description	CPT code	2009	2010	2011	2012	2013	2014	2015
Cephalic transposition	36818	18.75	19.07	20.8	20.57	20.45	19.64	20.36
Basilic transposition	36819	21.98	22.71	24.77	22.74	22.46	21.57	21.56
Forearm transposition	36820	22.05	22.82	24.95	24.69	24.58	23.58	21.41
Direct AV anastomosis	36821	18.19	19.35	21.25	21.19	21.15	20.3	19.53
Autogenous AV graft	36825	15.91	21.94	25.22	24.02	24.25	23.32	23.55
Non-autogenous AV graft	36830	18.22	18.76	20.42	20.19	19.98	19.25	19.63

CPT current procedural terminology, *RVU* relative value unit, *AV* arteriovenous

Table 5.2 Open secondary arteriovenous access revision CPT codes and their total RVU content from 2009 through 2015 Medicare Physician Fee Schedule

Description	CPT code	2009	2010	2011	2012	2013	2014	2015
Thrombectomy	36831	12.57	12.97	14.18	14.04	13.88	13.3	18.16
Revision	36832	16.06	16.56	18.02	17.81	17.63	16.97	22.28
Thrombectomy and revision	36833	18.1	18.7	20.37	20.13	19.93	19.24	23.82
Ligation or banding	37607	10.26	10.62	11.63	11.57	11.55	11.03	11.01
Distal revascularization/interval ligation	36838	32.45	33.42	36.15	35.53	35.06	33.83	33.67

CPT current procedural terminology, *RVU* relative value unit

Endovascular Procedures

Diagnostic hemodialysis access evaluation using angiography is usually performed with a catheter inserted directly into the AV access circuit itself, followed by contrast injection for imaging from the arterial anastomosis through the central system. Using component coding in 2009, the catheterization was reported with CPT code 36145 for catheter placement and CPT code 75790 for the imaging. The American Medical Association/Specialty Society Resource Based Relative Value Scale Update Committee (RUC) is a group of medical professionals who continuously assess the Medicare fee schedule claims data and RVU values. These screening efforts attempt to identify when any two CPT codes such as these listed above are reported together in Medicare beneficiaries over 75% of the time. The identified CPT code descriptions are then assessed by specialty society representatives for mandated bundling into a new CPT code followed by reevaluation of the associated reimbursement. In 2010, CPT code 36147 became valid through the efforts of the American Society of Diagnostic and Interventional Nephrology (ASDIN), the American College of Radiology (ACR), the Society for Interventional Radiology (SIR), and the Society for Vascular Surgery (SVS). This bundled code describes both the work of establishing single catheter access and the diagnostic contrast imaging of the dialysis circuit. The CPT manual defines an AV access angiogram as imaging from the arterial anastomosis to the superior vena cava in an arm AV access and from the arterial anastomosis to the inferior vena cava in a leg AV access. Therefore, inferior cava venography (CPT code 75825) and superior cava venography (CPT code 75827) are never appropriate to report with 36147 regardless of catheter manipulation unless a completely separate puncture outside the access circuit is obtained. Additionally, advancing the catheter centrally into the superior or inferior vena cava does not alter the coding for the procedure as of 2010.

In the new coding scheme, situations exist where direct catheter placement into the hemodialysis shunt is not performed. The radiology code 75791 describes the performance of a radiological evaluation through an already existing access into the shunt or from a catheter that is not a direct puncture of the shunt. For example, after arch and upper extremity angiography for steal from a CFA puncture, the catheter is advanced to the arterial anastomosis of the AV access, and this imaged to the SVC. The access imaging is described without direct puncture of the access and therefore is reported with CPT code 75791.

When a second catheter access is required, specifically for therapeutic purposes, the add-on CPT code 36148 describes the additional work associated with the subsequent catheterization. If two or more catheters are required to perform a diagnostic fistulagram and no endovascular intervention is completed, CPT code 36148 may not be reported. CPT codes 36145 and 75790 were deleted in 2010 concurrent with the addition of these three new codes.

As stated, CPT code 36147 includes all the necessary catheter placement and manipulation to perform a graft/fistula diagnostic radiological study, but the work of CPT code 36215 (selective catheter placement, arterial system; each first-order thoracic or brachiocephalic branch, within a vascular family) is not inherent to the work of 36147. When a catheter is maneuvered from a puncture of the dialysis graft/fistula into the proximal inflow vessel for formal inflow diagnostic arteriography, CPT code 36215 is reported. If the catheter tip is simply positioned at or near the arterial anastomosis of the AV access, CPT code 36215 is not appropriate. If one catheter is used for cannulation of the graft and that catheter traverses the arterial anastomosis retrograde for upper extremity angiography, 36215 and 36147 would be reported along with 75710 for the extremity arterial angiogram.

Lastly, the situation may arise where selective catheterization of one or multiple outflow (draining) veins off the AV access circuit is necessary (i.e., use of 36011). The new bundled coding includes the catheterization within the circuit and the diagnostic angiogram. However, selective catheterization within branch draining veins off the circuit is not bundled and is separately reportable. Single catheter placement into the access, angiography from arterial anastomosis to the SVC, and subsequent draining vein by first-order venous catheterization would be reported using 36011 and 36147. Should embolization of outflow vein branches to promote maturation of the circuit be required, CPT code 37241 (vascular embolization or occlusion inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage) would be reported as well. This last code description implies placement of thrombogenic material through a selective catheter in an attempt to occlude a vessel. Glue and coils are typical agents employed in the process. It is reportable once for each operative field treated. Keep in mind that multiple branch vessel occlusions of a single AV access can be submitted only once to the carrier.

For endovascular intervention billing, the introductory wording in the CPT manual defines the AV access circuit in the upper extremity from arterial anastomosis to axillary vein as a "vein" and defines it as a single "vessel." Additionally, the subclavian vein, innominate vein, and superior vena cava are also bundled as a separate and distinct but single "vessel." In the lower extremity, the AV access circuit extends from arterial anastomosis to common femoral vein as a single "vessel" with a separate and distinct additional "vessel" that includes the external iliac vein, common iliac vein, and inferior vena cava.

That said, the segment of artery immediately adjacent to the arterial anastomosis, the anastomosis itself, and the vessel or graft immediately distal to the anastomosis are called

"the perianastomotic region." An endovascular treatment such as angioplasty or stent placement in this perianastomotic region is reported as an arterial intervention. Since the entire segment from the arterial anastomosis up to and including the axillary vein is considered a single "vessel" for coding purposes, the arterial angioplasty also includes the work of opening all other "venous" stenoses that are treated within this segment.

Venous percutaneous transluminal angioplasty (PTA) is billed using CPT codes 35476 and 75978, while arterial PTA of the upper extremity requires 35475 and 75962. Stenting of the venous outflow requires use of CPT code 37238 for the first vessel and 37239 for each subsequent vessel. All angioplasty in the territory that undergoes endovascular stenting is bundled. When a covered stent graft is required, no difference in coding or reimbursement exists compared to deployment of a bare metal endoprosthesis.

A thrombosed AV access may sometimes require percutaneous mechanical thrombectomy for salvage as an alternative to operative intervention. Introduction of any thrombolytic agent by injection into the access is always bundled. CPT code 36870 specifically describes this technique in hemodialysis fistula as well as an AV autogenous or non-autogenous graft. Separate codes are available for reporting arterial and venous mechanical thrombectomy outside the AV access circuit. Unlike all other endovascular imaging and interventions in the AV access circuit which have been assigned a 0-day global period, CPT code 36870 has been given a 90-day global period. Subsequent mechanical thrombectomy in the post-procedure period will therefore require the use of appropriate modifiers (usually modifier -78, related procedure within the global period).

Catheter Access

When immediate vascular access is required for initiation of hemodialysis, central catheters may be necessary. CPT code 36556 describes placement of a non-tunneled centrally inserted catheter in patients over the age of 5. When a tunneled central venous access is required in a similar situation, CPT code 36558 illustrates a standard catheter, whereas CPT code 36565 describes a catheter that necessitates two puncture sites (i.e., Tesio-type catheter). These prosthetic devices may fracture from excess bending or stretch. If a catheter requires repair, CPT code 36575 is reported. Lastly, CPT code 36589 describes removal of a tunneled catheter. Insertion of the tunneled catheters and removal of the tunneled catheters have an associated 10-day global period. The RVU content for this is listed in Table 5.3.

Vascular Laboratory

Vascular laboratory testing is an integral part of any center that helps to ensure adequate hemodialysis access for its patients. Vein mapping has become standard in the preoperative evaluation of patients about to undergo surgical construction of an access. When vein mapping is done for the first time in a patient who has never had an access constructed before, CMS requires the use of the governmental code G0365. This code, implemented in 2005, describes both arterial and venous evaluations of a unilateral extremity but cannot be reported using the -50 modifier (bilateral procedure). Therefore, any study of the contralateral limb requires either an additional G0365 code with the -59 modifier or simply one submission with "units of 2." If a patient has failed arteriovenous access at least once, G0365 is no longer a valid code for submission. The standard venous duplex evaluation codes 93970 or 93971 are suitable. Since the 93970 code requires a complete and bilateral procedure, this is never appropriate when only superficial mapping is assessed. However, no written standard is available to define this "complete" terminology. Adequacy of the arterial inflow may be objectively determined with physiologic noninvasive arterial evaluation. CPT code 93922 describes bilateral testing at one or two levels, while CPT code 93923 is appropriate when a bilateral study is performed at three or more levels. Lastly, CPT code 93990 describes duplex evaluation of a hemodialysis access. This is governed in Medicare beneficiaries by a national coverage determination with specific published indications. Routine screening of the dialysis circuit for volume flow and/or the presence of a hemodynamically significant stenosis is strictly forbidden. It is important for all medical practices to understand when such testing is deemed medically appropriate.

Table 5.3 Catheter CPT codes and their total RVU content from 2009 through 2012 Medicare Physician Fee Schedule

Description	CPT code	2009	2010	2011	2012	2013	2014	2015
Non-tunneled catheter	36556	3.31	3.38	3.61	3.6	3.57	3.51	3.49
Tunneled catheter	36558	7.89	7.89	8.5	8.35	8.32	8.08	8.03
Tunneled catheter (Tesio-type)	36565	9.26	9.75	10.64	10.58	10.55	10.14	10.1
Repair of tunneled catheter	36575	1.12	0.99	1.07	1.06	1.05	1.03	1.01
Removal of tunneled catheter	36589	3.82	3.89	4.22	4.18	4.19	4.01	3.99

CPT current procedural terminology, *RVU* relative value unit

Upcoming Changes

The joint CPT/RUC workgroup reviews codes that are reported together on the Centers for Medicare and Medicaid Services' (CMS) 75 % or more screen. They identified CPT codes 35475, 35476, 36147, 36148, 37236, 37238, 75791, 75962, and 75968 as being frequently reported together in various combinations. Some of these codes have been addressed in previous coding change proposals. ACR, SIR, ASDIN, and SVS are working on the creation of new bundled CPT codes to report all endovascular hemodialysis imaging and intervention at present time which potentially will become effective in 2017.

Conclusion

Vascular surgery billing has numerous CPT code sets given the multitude of therapies required to care for the hemodialysis patient. Understanding the coding rules maximizes reimbursement which a practice can realize, minimizes inappropriate diagnosis and procedure reporting to insurance carriers, and may lower practice rejection rates. The hemodialysis endovascular evaluation and treatment coding set will undergo a complete overhaul in the near future and should be reviewed by each practice to ensure compliance and lower the potential for audit.

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Vascular Access: Experiences in the Aged Japanese Society

6

Sachiko Hirotani, Shinya Kaname, and Shinobu Gamou

Dialysis Treatment in Japan

Hemodialysis access was first performed in Japan in 1966 and was introduced to the national healthcare system in 1967 [1]. The continuous ambulatory peritoneal dialysis (CAPD) clinical trial began in 1980, and CAPD was approved for the national health insurance (NHI) system by the Ministry of Health and Welfare in 1983. Currently, over 300,000 patients with chronic renal failure receive maintenance dialysis (Fig. 6.1) [2].

Japanese dialysis treatment is characterized by several unique aspects: (1) the number of dialysis patients continues to increase; (2) 96 % of patients are treated by hemodialysis, while only 3 % are treated by peritoneal dialysis; (3) the rate of kidney transplantation is low at approximately 1,500 cases per year; (4) the majority of patients who receive hemodialysis do so for a relatively long period of time; (5) there is an increase in the number of elderly patients and the number of patients with diabetic nephropathy and nephrosclerosis as their primary illness; and (6) approximately 90 % of patients receiving hemodialysis are treated through an autogenous arteriovenous fistula (AVF).

The History of Dialysis Treatment in Japan [1]

There were several pioneering dialysis studies performed in Japan. In 1954, Dr. Kishio Shibusawa (a lecturer in the department of surgery in the University of Tokyo) developed an original renal replacement machine, using Skeggs and Leonards-type dialysis equipment. He moved to the University of Gunma and reported the first clinical dialysis cases, which included patients with acute and chronic kidney failure, at the annual meeting of the Japanese Circulation Society. Following this, several improvements were made to the dialysis machine, and a number of clinical trials were performed. In 1966, maintenance hemodialysis treatment using an external AV shunt was introduced at the department of surgery in Chiba University. In 1967, dialysis treatment received national health insurance (NHI) coverage; insurance subscribers were fully covered for dialysis treatments, and there was partial coverage for family members who needed dialysis. Since 1972, all patients who are in need of dialysis have been fully supported by the NHI system. A national clinical trial of peritoneal dialysis (CAPD) began in 1980, leading to CAPD approval as a NHI benefit in 1983.

The Current Status of Dialysis [2, 3]

The Japanese Society for Dialysis Therapy (JSDT), which was founded as an artificial dialysis research group in 1968, conducts a nationwide statistical survey of chronic dialysis patients at the end of each year. The data are available through its official journal of JSDT "Therapeutic Apheresis and Dialysis" and through the society's Web site [2].

The 2013 survey (the most recent survey, as of the 31st of December 2013) was sent to 4,325 facilities throughout Japan; 4,264 facilities (98.6 %) responded [3]. Most of the responding facilities (4,163 facilities, 96.3 %) sent back two types of survey questionnaires: the facility survey which includes location, history, capacity, etc. and patient survey which includes gender, age, primary disease, etc. The data

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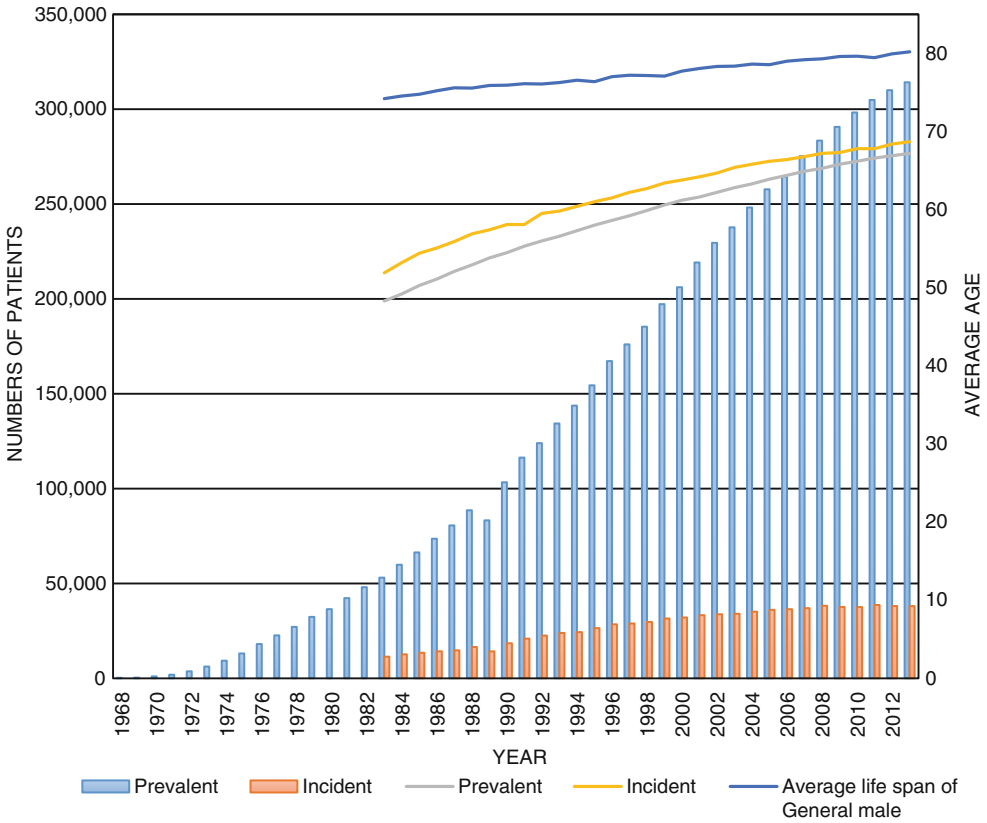

Fig. 6.1 Numbers of dialysis patients and their aging (Modified from Ref. [3]. The data reported here have been provided by the Japanese Society for Dialysis Therapy (JSDT). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the JSDT)

from the 2008 survey includes the institutional aspects of 3,968 facilities and the vascular access information of 208,096 patients [4]. Although the research group for peritoneal dialysis founded the Japanese Society for Peritoneal Dialysis in 2012, there has only been a minor increase in the number of patients who receive CAPD treatment. CAPD is chosen less frequently in Japan than in other countries.

Although there were only 215 chronic dialysis patients when dialysis treatment was first introduced in 1968 [1], the 2013 survey data [3] revealed that a total of 314,180 patients were receiving dialysis treatment, indicating there are 2,468 dialysis patients per million population, which amounts to 1 out of 405 Japanese citizens. Although the total number of chronic dialysis patients continues to increase, the rate of increase in recent years has been relatively minor. The aging of dialysis patients is also remarkable: the average patient's age is 67.20 years (male, 66.42 years; female, 68.57 years). This is in line with the aging of the general Japanese population (the average life span of general male 80.21 years and general female 86.61 years in 2013) including chronic kidney disease (CKD) patients and also reflects the improved prognosis.

According to the 2013 survey data, 38,024 patients (male, $n=24{,}379$; female, $n=11{,}751$) started dialysis in 2013, and there was no increase in the annual number of incident patients since 2008. In contrast, 30,708 patients died during 2013, and there has been no apparent change in mortality since 2011. The average age of incident patients was 68.68 years (male, 67.86 years; female 70.37 years.), and there was an apparent peak in both males and females at around 75–80 years. More than 3,000 patients who were over 90 years of age began to receive dialysis treatment in 2013.

In 1983, the most common primary illness for incident patients who started dialysis was chronic glomerulonephritis (60.5 %) (Fig. 6.2a, b). Diabetic nephropathy became the most frequent primary illness in 1998. In 2013, the rates of diabetic nephropathy, chronic glomerulonephritis, and nephrosclerosis in incident patients were 43.8 %, 18.8 % and 13.0 %, respectively. The fourth primary illness was "unknown" (11.5 %), and the number of patients in this category gradually increased. The frequency of polycystic kidney disease patients was 2.6 % and has remained relatively constant.

As a result, the primary illness of the prevalent dialysis patients for each year has unique characteristics, and the ratio of chronic glomerulonephritis patients has decreased linearly, while that of diabetic nephropathy patients has increased linearly. In 2011, diabetic nephropathy was the most common primary illness in whole dialysis population, and the difference in the rates of diabetic nephropathy (37.6 %) and chronic glomerulonephritis (32.4 %) was larger in 2013 than ever before. In the same year, the third most frequent primary illness was "unknown" (8.8 %), and the fourth was nephrosclerosis (8.6 %), while the frequency of polycystic kidney disease patients was 2.6 %.

The aging of incident patients in each primary illness was well correlated with the aging of the whole CKD patient

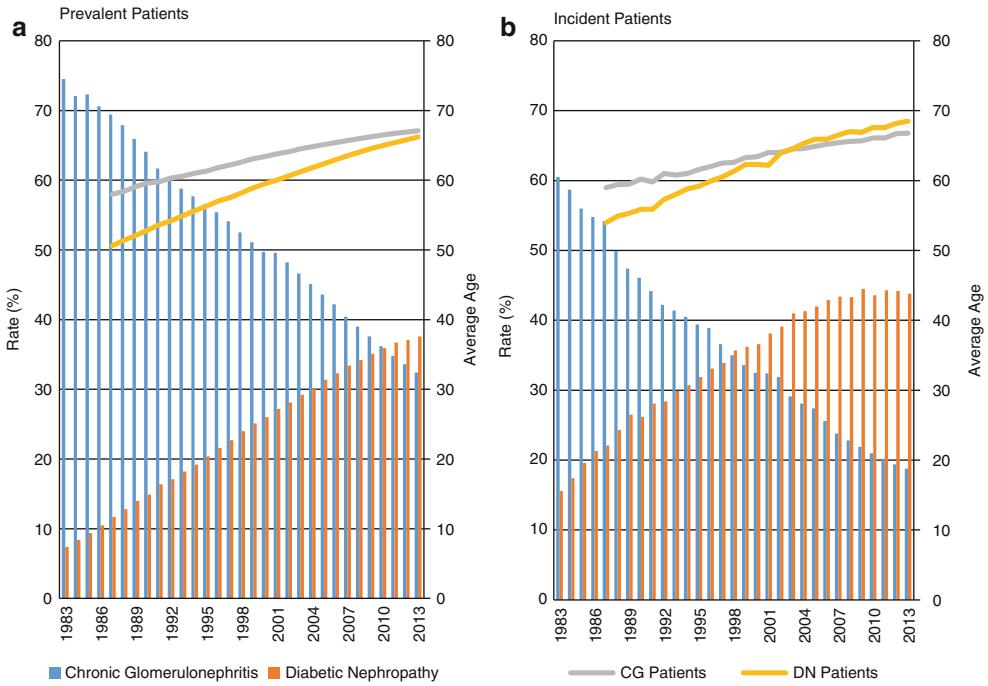

Fig. 6.2 Primary illness and patient aging (Modified from Ref. [3]. The data reported here have been provided by the Japanese Society for Dialysis Therapy (JSDT). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the JSDT)

population. Thus, there was an increase in the average age of patients with each illness. The most obvious case was nephrosclerosis. The average age of nephrosclerosis patients was 74.6 years in 2013. Although the average age of diabetic nephropathy patients had been higher than that of chronic glomerulonephritis patients, the average age of chronic glomerulonephritis patients became higher than that of diabetic nephropathy patients in 2004. The average age for incident patients with systemic lupus erythematosus (SLE) had been 39.7 years in 1987; however, dialysis therapy becomes introduced much later in patients with SLE and also in those with rapidly progressive glomerulonephritis (mostly ANCA-associated glomerulonephritis).

The duration of dialysis therapy increased, and there was an apparent increase in the number of long-term patients. The frequency of patients with a 20-year history of dialysis treatment increased to >1 % in the whole dialysis patient population in 1996 and has continually increased. Currently, the frequencies of patients with an over 20-year history and a 10-year history are 7.9 % and 27.6 %, respectively. The maximum duration of dialysis treatment is 45 years and 7 months [3].

The major causes of death in dialysis patients were heart failure (26.8 %) and infectious disease (20.8 %), followed by malignant tumor (9.4 %) in 2013.

The History of Vascular Access in Japan

The first meeting specific to "vascular access" was held in 1989, hosted by the Japanese Association of Dialysis Physicians. Then, the Japanese Society for Dialysis Access (JSDA) was established as an independent academic society in 1996 and currently has approximately 2,300 members [5]. The study group for vascular access intervention therapy (VAIVT) was also first established in 1996 and renamed in 2005 [6].

It is well known that Dr. Belding Scribner of the University of Washington, Seattle, developed the Teflon arteriovenous shunt in collaboration with Wayne Quinton and successfully applied the device in a clinical setting in the treatment of patients with kidney failure in 1960. In Japan, Dr. Kazuo Ota of the University of Tokyo received the Teflon shunt from the USA in 1964 and applied the device in his clinical practice. At the same time, there were several trials to develop new products in Japan. The technique to surgically create an arteriovenous fistula (AVF) was introduced soon after it was developed by James Cimino and M. J. Brescia in 1967. Dr. Ota reported the first use of the great saphenous vein to create dialysis access in 1971, followed by the first use of artificial blood vessels in the same year. Although there have been some discussions as to which procedure is superior, the autogenous AVF technique was rapidly accepted throughout Japan. Currently, the autogenous AVF technique is chosen for more than 90 % of dialysis patients in Japan. The arteriovenous graft (AVG) technique is chosen for most of the remaining patients. Surgical superficialization of the brachial artery (SSBA) is recommended as an effective alternative technique for gaining vascular access in patients with reduced cardiac function or those who lack superficial vessels that are suitable for AVF and AVG [4]. In cases in which AVF, AVG, and SSBA are not possible, access via a long-term tunneled central venous catheter is used as an alternative. Thus, it is unique that autogenous AVF is applied at a much higher frequency in Japan than in other countries.

The Current Status of Vascular Access in Japan

The Types of Vascular Access Used in Japan[1]

Aside from an annual overview survey, the JSDT conducts a detailed survey to investigate the characteristics of vascular access in dialysis patients every 10 years. The latest such survey was carried out in 2008, and the report, which included 47 tables, was published in "Therapeutic Apheresis and Dialysis [4]." In the report, the authors divided the types of vascular access into two categories: double-needle dialysis and single-needle dialysis (0.2 % of total); each of the categories was further divided into subcategories, such as autogenous arteriovenous fistula (AVF), arteriovenous graft (AVG), superficial brachial artery (SSBA), etc. The information was summarized in several tables: The types of vascular access in function with periods of dialysis (*Table 39*), blood flow rate (*Table 40*), and Kt/Vsp values (*Table 41*). In the present chapter, some details of the tables are compared with the 1998 survey [7] and summarized in Table 6.1. The authors stated the following:

> The types of vascular access for patients treated by facility hemodialysis. The percentage of patients who used a native vessel arteriovenous fistula was 89.7 %, and the percentage of patients who used an artificial vessel access was 7.1 %. In the survey conducted at the end of 1998, the former was 91.4 % and the latter was 4.8 %. Thus, the percentage of patients who used an artificial vessel access has increased over the past 10 years. The percentage of patients who used a temporary venous catheter was high for those on dialysis for less than 2 years. Temporary venous catheters are used for patients during the phase of introduction to dialysis. The percentages of patients who used an arteriovenous fistula via an artificial blood vessel and a superficial artery tended to increase with years on dialysis. Among the other types of vascular access, the percentages of patients who used a long-term implantable catheter were relatively high for patients on dialysis for less than 2 years and 25 years or more, although the values are small.

It is apparent that long-term implantable catheters (LTIC) are used in an increasing number of patients due to the long treatment history of the patients and the aging of the Japanese population.

Comparison to Other Countries

Next, we compare the current prognosis in Japanese patients with that in other countries based on the 5th DOPPS survey, which was conducted in 14 countries including Japan, to summarize the information on vascular access [8].

[1]The data reported here have been provided by the Japanese Society for Dialysis Therapy (JSDT). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the JSDT.

Although the 4th DOPPS survey showed that Japan had the highest rate of AVF patients, the 5th DOPPS survey showed that the AVF rates in many countries had reached a similarly high level to that in Japan. AVF seems to have been accepted throughout the world as the "gold standard" for vascular access.

As shown by Pisoni et al. [6], the AVF rate in Japan is the highest in the world: an AVF is used within 60 days of new initiation of dialysis in 84 % of patients. In addition, the typical time to the first cannulation of an AVF is shortest in Japan compared to other DOPPS countries; 94 % of new AVF are cannulated within 1 month. This is remarkable and far more rapid than in other countries and likely contributes to the high success rate of AVF treatment in Japan.

Pisoni et al. [9] also reported correlations between vascular access types and patient prognosis and compared the mortality rate associated with each of the vascular access types in three groups of countries based on the 2nd DOPPS survey. It is apparent that a high rate of AVF together with low rates of AVG and catheter treatment contributes to a good prognosis; a typical example of this is Japan.

Although it is apparent that AVF dialysis contributes to a good prognosis, it is important to maintain the AVF in a stable and patent condition for as long as possible. Asano et al. [10] demonstrated the good AVF survival in Japan and noted the following: patients with prior catheter use displayed higher rates of primary and final AVF failure. Final AVF failure rates were higher in facilities with higher median blood flow rates (BFR). They were also greater in North America and EUR/ANZ than in Japan, but this difference was substantially attenuated after accounting for regional differences in facility median BFR.

On the other hand, Robinson et al. [11] pointed out the twofold higher rate of mortality in incident patients and discussed the underlying causes as follows: the characteristics of patients starting dialysis may differ between countries because of differences in the epidemiology of chronic kidney disease (CKD), the access to care and quality of medical care for CKD patients, and the acceptance for and timing of initiation of dialysis. Processes surrounding "acceptance" for dialysis are complex, as these reflect a combination of patient preferences, provider preferences, and contextual effects reflecting cultural and societal differences. In Japan, our understanding is that the markedly elevated HR for early versus later mortality is driven by the standard that dialysis facilities initiate dialysis treatment on all patients with terminal kidney failure, regardless of health condition. Thus, patients with poor short-term prognosis typically start dialysis and may die shortly thereafter. The last part of his discussion is important for the oldest patients in Japan, as it examines whether and when we should start, continue, or quit dialysis for the oldest old. Dr. Seiji Ohira, the chairman of the JSDT, has currently opened the discussion on this topic [12].

Table 6.1 Comparison of vascular access type of dialysis

Vascular access type	1998 survey[a]	2008 survey[b]		
		Total		
		9 years[c]	10-19 years	20 years-
Arteriovenous fistula (AVF) via an autogenous blood vessel	120,620 (91.4 %)	154,904 (89.8 %)		
		118,213	28,064	8,627
		76.3 %	18.1 %	5.6 %
Arteriovenous graft (AVG) via an artificial blood vessel	6,367 (4.8 %)	12,318 (7.1 %)		
		8,466	2,703	1,149
		68.7 %	21.9 %	9.3 %
Surgical superficialization of the brachial artery (SSBA)	3,242 (2.5 %)	3,180 (1.8 %)		
		2,185	640	355
		68.7 %	20.1 %	11.2 %
Long-term implantable catheters (LTIC)	0 (0 %)	927 (0.5 %)		
		717	137	73
		77.3 %	14.8 %	7.9 %
Temporary venous catheter (TVC)	860 (0.7 %)	798 (0.5 %)		
		742	38	18
		93.0 %	4.8 %	2.3 %
Scribner shunt	359 (0.3 %)	0 (0 %)		
Others	461 (0.3 %)	426 (0.2 %)		
		297	85	44
		69.7 %	20.0 %	10.3 %
Total	131,909 (100 %)	172,553 (100 %)		
		130,620	31,667	10,266
		75.7 %	18.4 %	5.9 %

The data reported here have been provided by the Japanese Society for Dialysis Therapy (JSDT). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the JSDT

[a]From Refs. [5, 7]

[b]From Ref. [4]

[c]Periods of dialysis

Recent Topics in Vascular Access Management and Complications

The Guidelines for Vascular Access Construction and Repair for Chronic Hemodialysis

In order to establish standards for vascular access construction, maintenance, management, and repair, the guideline for vascular access construction was first published in 2005 by JSDT [13] and revised in 2011 [14]. The guideline basically followed the NKF-KDOQI guideline [15] and consists of the following seven chapters:

Chapter 1. Vascular Access-Related Informed Consent
Chapter 2. The Basics and Timing of Vascular Access Construction
Chapter 3. Vascular Access Construction and Pre-/Postsurgical Management
Chapter 4. Daily Management of Vascular Access
Chapter 5. Management of Vascular Access Trouble
Chapter 6. Vascular Access Types, Morbidity, and Mortality Rates
Chapter 7. Addendum: Patency of Vascular Access

From the revised version of the guideline, the evidence levels were designated as "A" for high, "B" for moderate, "C" for low, and "D" for very low quality of evidence; cases in which no evidence was shown were designated as "O" (expert opinion). In addition, two recommendation levels were included: Level 1 for strong recommendations and level 2 for weak recommendations. Thus, the guideline includes a total of nine categories: eight combinations of 1A, 2A, 1B, etc. and "O."

Although the guideline shows the standards for diagnosis and therapy, there are no legal or health economic obligations for the physicians. As an academic society, the JSDT is responsible for establishing the standard diagnostic protocol and the corresponding therapies, assessing as many results from variable clinical practices as possible, and conducting reviews to establish the most suitable and beneficial standards for individual patient needs.

Vascular Access-Related Topics in the Academic Societies

Besides the JSDT, there are two other active vascular access-specialized societies: the Japanese Society for Dialysis Access (JSDA) and the Vascular Access Intervention Treatment (VAIVT) society. Membership of the JSDA is open to all professionals. The members present a rather wide range of topics in relation to vascular access at their annual meeting. A total of 736 presentations were included in the official journal of the JSDA from 2000 to 2014. In contrast, at the annual meeting of the VAIVT, the presentations of the physicians are mainly focused on topics related to interventional radiology (IVR).

Table 6.2 summarizes the categories of presented topics in the JSDA every 3 years. In the first 3-year period of 2000 to 2002, the most frequent topic was standard vascular access surgical techniques (16 titles, 25 %). During 2003–2005, the most frequent topic was IVR (24 titles, 27 %), this was because the cutting balloon from Boston Scientific Corp. became available in Japan from 2002. During 2006–2008, the most frequent topic was vascular access assessment and monitoring (27 titles, 18 %), followed by vascular access management (24 titles, 16 %); this was because technicians and nurses had become more actively involved in dialysis treatment. During 2009–2011, the most frequent topic was catheters (42 titles, 17.4 %), followed by IVR (40 titles, 16.5 %). The increase in the number of elderly and/or long-term dialysis patients may be correlated with the increase in catheter treatment, and many of the titles on IVR treatment sought to summarize the authors' clinical assessment of the Conquest high-pressure balloon catheter (Medicon-BARD).

A total of 1,027 titles from the abstract booklet of the VAIVT annual meetings were classified into two categories: standard topics ($n=676$) and current topics ($n=343$). Interestingly, the presentations on cutting balloon catheter use rapidly increased and then diminished from 2003 to 2008. Although the catheter had been highly regarded at the beginning of the period, missing blades were reported in two patients at the 2005 VAIVT meeting, and the products were recalled in December 2006. Although the 4-mm cutting balloon catheter was available for use after January 2010, many physicians assessed it to be clinically ineffective. In October 2012, the 5-mm and 6-mm cutting balloon catheters were reapproved for clinical use with many restrictions and notices to prevent missing blades, which made the catheters more complicated for the physician to handle.

There were many reports on the Conquest high-pressure balloon catheter in the 2009 meeting (16 titles, 21.3 %). The Conquest high-pressure balloon catheter, which has a rated burst pressure of 30 ATM, became available from June 2008. This high-pressure balloon catheter appeared to be an alternative to the cutting balloon catheter, for post-restenosis dilatation treatment. However, Horita et al. [16] reported at the 2010 JSDA meeting that optical coherence tomography imaging revealed that vessels that were treated by the high-pressure balloon appeared to be heavily damaged, despite achieving good vasodilatation, on vascular imaging. Following his finding, which was published in the JSDA journal in 2011, there have been many reports in the VAIVT meetings (11 titles) which demonstrated that high-pressure vasodilatation did not greatly prolong the period to restenosis, and fewer reports described the efficacy of the use of the high-pressure balloon catheter in achieving vasodilatation. Instead, it is noteworthy that Ikeda et al. [17] reported that repeated dilatation under low pressure was effective for prolonging the period to restenosis based on clear optical coherence tomography imaging and 979 clinical cases.

There were eight titles on scoring balloon catheter in the VAIVT 2014 meeting, since the scoring balloon catheter is expected to be used as an alternative for cutting high-pressure balloon catheters. This new technique will be assessed over the next few years.

There were 20 titles on "vascular access management and imaging" in the VAIVT 2007 meeting and nine titles on "ultrasound-guided percutaneous transluminal angioplasty (PTA)" in the 2010 meeting. That these topics kept increasing suggests that Japanese physicians accept that ultrasound

Table 6.2 VA-related topics in JSDA annual meetings

Topics	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014
Standard VA surgical techniques	16 (25.0 %)	18 (20.5 %)	13 (8.7 %)	25 (10.3 %)	17 (8.9 %)
Specialized VA surgical technique	3 (4.7 %)	3 (3.4 %)	11 (7.3 %)	14 (5.8 %)	8 (4.2 %)
VA management	6 (9.4 %)	6 (6.8 %)	24 (16.0 %)	19 (7.9 %)	34 (17.7 %)
VA assessment and monitoring	3 (4.7 %)	11 (12.5 %)	27 (18.0 %)	32 (13.2 %)	17 (8.9 %)
Ultrasound guidance	0 (0 %)	8 (9.1 %)	7 (4.7 %)	31 (12.8 %)	23 (12.0 %)
Cannulation technique	0 (0 %)	2 (2.3 %)	9 (6.0 %)	12 (5.0 %)	19 (9.9 %)
IVR	14 (21.9 %)	24 (27.4 %)	21 (14.0 %)	40 (16.5 %)	33 (17.2 %)
VA complications	14 (21.9 %)	9 (10.2 %)	26 (17.3 %)	27 (11.2 %)	16 (8.3 %)
Catheter	8 (12.5 %)	7 (8.0 %)	12 (8.0 %)	42 (17.4 %)	25 (13.0 %)
Total	64 (100 %)	88 (100 %)	150 (100 %)	242 (100 %)	192 (100 %)

guidance is effective in vascular access treatment. In addition, Wakabayashi et al. [18] reported the safety and efficacy of ultrasound-guided endovascular treatment in 4,869 cases in 1,011 patients. Dr. Haruguchi of the Haruguchi Vascular Access Clinic organized the first meeting of vascular access – Ultrasound Research in 2008 – and has continued to hold the meetings once or twice a year to expand the knowledge and techniques of vascular access: ultrasound diagnosis to physicians, nurses, and technicians. He also published a textbook entitled, *Vascular Access – Ultrasound Textbook* [19].

Hemodynamic abnormalities including excess blood flow, venous hypertension, and steal syndrome are frequently observed as direct or indirect outcomes of excess blood flow after vascular access construction. Kanno et al. [20] reported many clinical cases of hemodynamic abnormalities underwent surgical and invasive treatments. It is necessary to develop a minimally invasive but effective treatment for hemodynamic abnormalities, such as IVR for restenosis.

There is a serious discussion on the medical cost, especially with regard to the "three-month rule," which is the insurance rule for PTA treatment. In general, the Ministry of Health, Labour and Welfare (MHLW) designates a certain amount of points for each type of medical treatment (1 point = 10 JPY). All Japanese citizens, permanent residents, and long-term visitors are required to be enrolled in the national health insurance (NHI) system and to pay designated insurance premiums according to their income. When the insured person uses a medical facility, he/she will only need to pay part of the designated cost (usually 10–30 % depending on age and income). The medical facility will then send invoices for the remaining amount to the Health Insurance Claims Review & Reimbursement Service (HICRRS), a part of NHI system, which reviews whether a treatment is appropriate or not and pays the medical facility according to the designated treatment score. In the case of specific illness with a need to continue large amount of treatment such as CKD, patients can apply the welfare support through their local government and receive the monthly self-pay ceiling benefit.

In the case of usual chronic hemodialysis (less than 4 h), the procedure is currently allocated 2,030 points/per procedure (20,300JPY). The total cost is more than 400,000 JPY/patient/month, which includes chronic dialysis on every other day, PTA if necessary, and other associated procedures. The dialysis patient is asked to pay to his or her medical facility up to 10,000 JPY per month regardless of how many times he or she undergoes dialysis in Tokyo. The medical facility will send the invoice to the HICRRS to pay the rest of the cost. HICRRS then asks for reimbursement from each responsible insurer and the local government and other government organizations which subsidize the patients' cost.

It is clear that physicians should provide appropriate and essential treatment for consenting patients. It is also necessary to avoid treatments that are futile in cases where the physician believes that treatment will be burdensome for the patient. To avoid medical futility and the unlimited increase of medical costs, the MHLW set a "three-month rule/ceiling rule" in 2012, under which the dialysis facility can request payment for PTA "once every three months," regardless of how many times the patients were treated by PTA. The score of PTA, which used to be 15,800 points, was reduced to 3,130 in 2002; it was then re-revised to 18,080 in accordance with the "three-month rule/ceiling rule" in 2012. It is unfortunate that physicians treat patients who are not amenable to open surgical VA reconstruction with IVR treatment to maintain VA patency for the next three months.

It is also noteworthy that many academic societies other than the JSDA and VAIVT actively discuss the dialysis management of the elderly Japanese population. As mentioned before, both incident and maintenance patients under dialysis will grow older. Thus, there are many serious issues to discuss including the clinical criteria for initiating dialysis treatment, the vascular access selection, the management of patients with dementia, the problems of medical costs, and the ethical issues. The president of JSDA has taken the initiative to discuss these serious issues.

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Hemodialysis Access: Fundamentals and Advanced Management, the Experience in Taiwan

7

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Epidemiology of Hemodialysis Access in Taiwan

The increasing chronic kidney disease (CKD) population is an important public health and social issue. In Taiwan, dialysis costs for end-stage renal disease (ESRD) patients have been fully reimbursed by the National Health Insurance (NHI) since 1995. Over the last two decades, the cases of ESRD requiring dialysis increased progressively, becoming an important issue in medical care [1]. The updated data from United States Renal Data System (USRDS) international report in 2012 indicated that Taiwan ranked first regarding to prevalence of dialysis [2]. Although a nationwide project for CKD prevention in Taiwan has been initiated since 2003, the prevalence and incidence of ESRD still increased steadily in 2005–2012. From subgroup analysis of latest Taiwan Renal Registry Data System (TWRDS), the prevalence of those older than 75 years and diabetes were increasing. Similar to other countries, diabetes mellitus (DM) remains the most common primary disease causing ESRD in Taiwan (47.9 %) [1].

Because of the high availability and easy accessibility of medical service, hemodialysis (HD) continues to be the most commonly utilized renal replacement therapy in Taiwan. Among the 67,665 prevalent ESRD patients, more than 60,000 of patients (89.7 %) undergo in-center HD twice to three times per week [3]. Although currently there is still lacking a national population study to estimate the proportion of vascular access devices in Taiwan, native arteriovenous fistula (AVF) is the most common form of vascular access for HD, owning to its lower risk of infection and thrombosis. According to a multicenter study reported by Chen et al. which enrolled 5161 patients receiving maintenance HD from 25 dialysis facilities in Taiwan since 2008–2012, the AVFs took up approximately 75 % of vascular access for HD, whereas arteriovenous graft (AVG) and tunneled dialysis catheter (TDC) contributed to 20 % and 5 %, respectively. Although there is a slight increase of the proportion of patients using AVG and TDC during the 5-year follow-up, 73.9 % of patients still use native AVF for HD and those with TDC composed only 5.8 % of the total participants in 2012. This increasing trend may be attributed to the increasing poor vascular conditions in aging and DM patients [4]. However, TDCs have significant infectious, thrombotic, and anatomic complication rates comparing to arteriovenous (AV) access for HD. By using claims data from the National Health Insurance Research Database (NHIRD) in Taiwan, Ng et al. reported that in incident patients starting HD with TDCs, the 1- and 3-year mortality and infection rates were lower in conversion to AVF and AVG than in no-conversion group [5]. Since vascular access type is significantly associated with patient survival, it is important for physicians to identify factors for predicting the successful maturation of HD vascular access, as well as therapies for maintaining long-term patency.

Risk Factors of Vascular Access Failure in Taiwan

Careful evaluation and periodic surveillance of the function of vascular access play fundamental roles in the integrated care for HD patients. Given that patient's age, gender, race, comorbidity, surgical technique, and vascular conditions could affect the patency and prognosis of AV access, it will be helpful to identify the precipitating factors individually, to

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avoid multiple interventions in treating AV access malfunctions. On the other hand, with the advantages of genetic analysis, more and more genetic polymorphisms were discovered in association with the patency rate of HD devices. In this paragraph, we will focus on the recent advances in Taiwan investigating the precipitating and prognostic factors in association with AV access patency for HD.

Demographic Characteristics

In Taiwanese incident HD patients, by using NHIRD claim data, Ng et al. included 5890 incident HD patients with AVF (84 %) or AVG (16 %) during a 3-year period, to investigate the effect of demographic characteristics on AV devices patency. Similar to the results of previous literatures, AVG, female and elderly were associated with a shortened HD access survival [6]. History of diabetes mellitus also showed a deleterious impact on AVF patency, but not for AVG in this study [7]. On the other hand, as regarded with the impact of the timing of AV access maturation before or after HD on AV access patency, this study indicated an improved duration of primary access patency in patients with AVGs maturation 6 months prior to HD initiation [7]. This statement suggested that it may be better to complete AVG placement and maturation as early as possible before HD initiation for the duration of primary access patency. However, this finding needs further evidence for the clinical implication.

Ankle-Brachial Index

The ankle-brachial index (ABI), defined as the ratio of the ankle systolic blood pressure (SBP) divided by the arm systolic blood pressure, was reported to be a reliable index for endothelial dysfunction and atherosclerosis. ABI <0.9 was not only an indicator for peripheral occlusive arterial disease but also represented for generalized atherosclerotic disease. Chen et al. hypothesize that an ABI <0.9 may be correlated with AV access dysfunction in HD patients on the basis of several shared pathological changes in AVF stenosis and cardiovascular atherosclerosis. They conducted an observational study of 225 HD patients, while the ABI was measured once in each patient 10–30 min before an HD session. During the mean follow-up period of 42.2 ± 42.8 months, patients with ABI <0.9 had an inferior AV access survival compared with those with ABI >0.9. Thus, this study concluded that screening HD patients by routinely measuring ABI may help to identify the high-risk population for AV access failure [8]. Further large-scale prospective trials are needed to strengthen the predicting value of ABI measurement for AV access failure.

Pulse Pressure

Pulse pressure (PP) has been shown to be a risk factor for coronary events and cardiovascular disease-related deaths. Previous literature has shown that both AV access malfunction and elevated pulse pressure are associated with chronic inflammation. To evaluate the predictive power of PP for AV access thrombosis, Chou et al. conducted a single-center retrospective observational study, enrolled 576 patients with AV access for HD. Patients' 3-month average blood pressure was used for analysis, and PP was defined as the difference between systolic blood pressure and diastolic blood pressure. Patients with PP >60 mmHg showed an inferior thrombosis-free survival compared with those with PP<60 mmHg. In multivariate analysis, the elevated PP was found to be independently associated with an increasing risk for AV access thrombosis, with a hazard ratio of 2.57 (95 % confidence interval: 1.5–4.4, $P=0.001$). Thus, this study concluded that high PP was associated with the development of vascular access thrombosis in chronic HD patients [9]. More interventional studies are needed to determine if treatment that decreases PP may decrease the risk of AV access thrombosis among chronic HD patients.

Indoxyl Sulfate

Indoxyl sulfate (IS) is one of a number of protein-bound uremic toxins that accumulate in patients with impaired renal function. Current conventional HD is ineffective at removing this toxin, as 90 % of IS is bound to albumin5 and the IS–albumin complex molecule is larger than the dialysis membrane's pore size. Evidences indicated that IS may induce vascular dysfunction and cardiovascular disease in CKD and HD patients [10]. Recently, Wu et al. conducted a prospective study that enrolled 306 HD patients undergoing percutaneous transluminal angioplasty (PTA) for dialysis access dysfunction [11]. After a median follow-up of 32 months, the authors demonstrated that absolute levels and tertiles of free IS were both independent predictors for AVG thrombosis after PTA. Clinical trials using preventive or therapeutic strategies are warranted to clarify the role of indoxyl sulfate in secondary prevention of graft thrombosis after PTA.

Asymmetric Dimethylarginine

Asymmetric dimethylarginine (ADMA) is widely considered as an endothelial nitric oxide synthase inhibitor and reduces nitric oxide bioavailability, correlated with endothelial dysfunction and the development of cardiovascular events in patients with uremia [12]. In 100 consecutive patients with dysfunctional AVFs, Wu et al. obtained baseline plasma ADMA levels before PTA and investigated the

predictive power for symptomatic restenosis of AVF after PTA [13]. During the 6 months after PTA, higher levels of ADMA had a significant higher restenosis rate. In multivariate analysis, plasma ADMA was found to be independently associated with an increased risk for recurrent symptomatic AVF stenosis. The author concluded that higher baseline ADMA before angioplasty predicts symptomatic AVF stenosis after PTA. Methods of modifying ADMA levels or improving endothelial dysfunction, such as L-arginine, statins, and blockade of the renin–angiotensin system, could be investigated as ways of preventing recurrent AVF dysfunction.

Endothelial Progenitor Cells

Accumulating evidence suggests that circulating endothelial progenitor cells (EPCs) reflect the repair capacity of the endothelium. However, studies of circulating EPCs in HD patients and its role with vascular access remodeling are scarce. In a prospective study, Wu et al. investigated the relationship between baseline-circulating EPCs and the subsequent development of restenosis after angioplasty of hemodialysis vascular access [14]. Quantification of EPCs markers was conducted immediately before angioplasty procedures for EPCs numbers assessment. A total of 130 patients were enrolled, and the result showed that circulating EPCs counts were independent predictors of target-lesion restenosis during the 1-year follow-up. This study suggested that circulating EPCs may play a role in inhibiting venous intimal hyperplasia after PTA. Clinical trial of modifying EPCs number or function is needed to clarify its potential role to prevent the development of AVF restenosis.

Matrix Metalloproteinases: 1, 3, and 9

Matrix metalloproteinases (MMPs) hydrolyze the extracellular matrix and play a central role in many biological processes, such as embryogenesis, normal tissue remodeling, wound healing, and angiogenesis. Tissue inhibitors of metalloproteinases (TIMPs) are specific inhibitors of MMPs that control the local activities of MMPs in tissues. Previous studies showed that genotype polymorphisms of some MMPs and TIMPs were associated with various cardiovascular disorders [15]. Lin et al. conducted a retrospective study to determine whether MMPs/TIMPs gene polymorphisms play a role in AVFs stenosis [16]. A total of 603 HD patients with AVFs were enrolled, and a significant association was disclosed between AVF failure and specific genotypes of MMP-1, MMP-3, and MMP-9. The unassisted patency of AVF at 5 years decreased significantly from 93.3 to 38.4 % for the composite high-risk MMP-1/MMP-3/MMP-9 genotypes. The authors speculated that high-risk genotypes of MMP-1, MMP-3, and MMP-9 possessed lower transcriptional activities and may result in more accumulation of extracellular matrix, and leading to AVF stenosis.

Heme Oxygenase-1

Heme oxygenase-1 (HO-1) is a stress-responsive protein that can be induced by various oxidative agents, including heavy metals, inflammatory mediators, ultraviolet radiation, endotoxin, heme, and hemoglobin. Moreover, HO-1 plays an important role in growth regulation, cell proliferation, cell death (apoptosis), and cell hypertrophy. Evidence shows that a longer guanidine thymidine dinucleotide [(GT)n] repeat in the promoter region of the HO-1 gene is associated with restenosis and increased vascular inflammation after PTA [17], susceptibility to coronary artery disease (CAD) [18], and the development of abdominal aortic aneurysms [19]. To evaluate its role in AVFs, Lin et al. conducted a retrospective study that included 603 prevalent HD patients [20]. The results showed that (GT)n repeats greater than or equal to 30 in the HO-1 promoter are associated with a higher frequency of access failure and poorer patency of AVFs. On the basis of these findings, the authors speculated that longer GT repeats in the HO-1 promoter might limit gene transcription and consequently offset the protective effect of HO-1 against vascular injury.

A Novel Therapy for AVF Maintenance: Far-Infrared Therapy

Given that the most common mode of AVF failure is by thrombosis, many investigators have conducted trials of medications for AVF patients that may reduce thrombus formation. Results of a Cochrane systematic review and a more recent large-scale randomized controlled trial generally favor antiplatelet therapy in the prevention of AVF thrombosis; however, these trials showed considerable heterogeneity in outcomes, and many had only very short follow-up periods [21, 22]. Far-infrared radiation (FIR) is an invisible electromagnetic wave with a longer wavelength than that of visible light. Infrared radiation transfers energy that is perceived as heat by thermoreceptors in the surrounding skin [23]. Animal studies also demonstrated that FIR improves skin blood flow [24, 25], leading to the use of FIR in the treatment of ischemic lesions and necrosis of the skin tissue as a result of trauma, diabetes, and peripheral arterial occlusive disease. In addition, some studies indicated that FIR therapy may improve endothelial function and reduce the frequency of some cardiovascular diseases [26–28].

Because vascular access usually is located in the superficial site of the upper extremities of HD patients, a series of

studies on FIR therapy were conducted as an alternative therapeutic modality for improving access flow and the function of the AVF in Taiwan. In a single-center randomized controlled trial [29], 145 HD patients with stable AVF function more than 3 months were enrolled and were randomly assigned to receive standard care ($n=73$) or FIR therapy ($n=72$). FIR radiator was set at a height of 25 cm above the surface of the AVF with the treatment time set at 40 min during HD three times per week. After a 1-year follow-up, FIR therapy significantly improved the access flow and survival of the AVF through both its thermal and nonthermal effects.

The therapeutic mechanisms of FIR treatment was demonstrated to be related to the anti-inflammatory effects, stimulated by the expression of HO-1, leading to the inhibition of tumor necrosis factor-α (TNF-α)-induced expression of adhesion molecules in endothelial cells as well as in HD patients [30–34]. The association of AVF patency was demonstrated to be related to the inducibility of HO-1 gene, which is determined by long guanidine thymidine dinucleotide [(GT)n] repeat in the HO-1 promoter [20, 31]. Therefore, the success rate of the FIR therapy in different length polymorphisms of the HO-1 gene was further evaluated. In this study [35], 280 HD patients using AVF as vascular access were randomly assigned to routine care or a thrice weekly FIR therapy. After a 1-year follow-up, FIR therapy and patients with short allele length polymorphism in the HO-1 gene promoter [(GT)n <30] were associated with improved outcomes, including access flow, unassisted patency rate, and cumulative patency rate of AVF. The study also showed that FIR therapy offered the best protective effect in those with S/S genotype of HO-1.

The application of FIR therapy on primary and secondary prevention of AVF failure was also evaluated. In a randomized controlled trial, a 40-min FIR therapy was scheduled three times weekly after the second day of AVF creation and was continued for 12 months in the treatment group. Before starting HD, patients received FIR therapy at either a nephrology clinic or at home. After starting HD, FIR therapy was performed during HD. After 12 months, FIR therapy significantly improved the access flow and decreased the risk of AVF malfunction [36]. Another randomized controlled trial evaluated the effect of FIR therapy on vascular access patency rate after successful percutaneous transluminal angioplasties. Of 216 participants analyzed, FIR therapy improves PTA-unassisted patency in patients with AVG, but not in patients with AVF [37].

A series of studies in Taiwan provided evidences to support the use of FIR therapy for the vascular access management in hemodialysis patients. A genetic background for the beneficiary effect has also been determined. However, these data were limited to a single-center study and a single ethnic group. Multicenter, randomized controlled trial with different ethnic groups is still needed to confirm the study results.

Economic Impact of Interventional Procedures for Vascular Access Malfunction

The annual inpatient hospital costs for dialysis patients in Taiwan had doubled from the year of 2000–2011. The average expenditure for a hospital stay was also increased by 27.8 %. Considering the limited source of health insurance fund, it's a critical issue to address how to decrease the admission rate and day of hospitalization. A retrospective study in Taiwan concluded that, under the current insurance payments in Taiwan, early vascular access creation at least 1 month before the initiation of HD is associated with lower inpatient medical expenses and shorter length of hospitalization [38]. According to the 2014 annual report on kidney disease in Taiwan, since the initiation of pre-ESRD program in 2006, 5.7 % of incident patients in 2007 were enrolled before hemodialysis, and the ratio had increased to 48.1 % in 2012. Patients participated in this program had a higher rate of vascular access preparation before HD than those did not (35 % and 18.1 % respectively in 2012). Therefore, a successful public health policy is beneficial for early recognition and vascular access preparation for pre-ESRD patients. However, whether the cost-effectiveness of this policy was worthwhile may need further analysis.

Conclusions

CKD and ESRD are highly prevalent diseases in Taiwan. Because of the full insurance reimbursement and easy accessibility of the medical services, HD remained the primary modality of renal replacement therapy. AVF is the most commonly utilized vascular access and is associated with less infectious complication then AVG or TDC. Several studies evaluated the risk factors of access failure in Taiwan. AVG, female, elderly, ABI lower than 0.9, and PP higher than 60 mmHg are associated with shorter vascular access survival. History of DM is a risk factor for AVG failure, and several genetic backgrounds of MMPs and HO-1 are independent determinants of AVF patency. Baseline levels of IS, ADMA, and circulating EPCs counts predict AVG restenosis after PTA. Series of clinical trials revealed a significant beneficiary effect of FIR therapy on AVF maturation and survival. The possible mechanism is associated with HO-1 polymorphism and its anti-inflammatory effect. A timely preparation of vascular access before HD initiation is associated with a shorter length of hospital stay. Considering the limited source of health insurance fund, the implement of pre-ESRD program increases the vascular preparation rate before HD and may lower the medical expenses.

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Ethical Issues in Hemodialysis

8

Thomas R. McCormick

Introduction

The history of hemodialysis is closely intertwined with the birth of bioethics. When Belding Scribner and Wayne Quinton joined in creating the arteriovenous shunt, it allowed repetitive hemodialysis treatment for the first time in human history. A gateway to vascular access that had eluded former generations was opened. Ironically, the problem of limited patient access to the kidney machines and issues of scarcity and cost led to a number of ethical issues that forever linked the history of hemodialysis with the birth of bioethics. Urgent questions arose pertaining to who should live. As issues of scarcity and cost were addressed, the "worth" of a human life was discussed in households across the nation. At the federal level, policies were initiated that had powerful ethical implications. The Medicare Act, Section 299I of Public Law 92–603, was passed on October 30, 1972, and has funded the treatment of hundreds of thousands of hemodialysis patients, while raising questions of distributive justice for underfunded patients suffering from other illnesses. Home hemodialysis is more economical, yet for-profit treatment centers have lobbied successfully for center-based hemodialysis. The advent of successful kidney transplantation has benefited many patients, yet many will die on a waiting list due to the scarcity of organs for transplant. Although the employment of artificial kidneys has the capacity to prolong lives, it also leads to quality of life problems that will arise eventually for every hemodialysis patient. We have made great strides in the science and technology of treating patients with kidney failure. We must continue our efforts to improve treatment modalities and not lose sight of the ethical challenges that accompanied the beginning of hemodialysis. These challenges, many contend, gave birth to the discipline we now call bioethics. This chapter provides a review of the ethical quandaries that emerged in establishing continuing treatment for patients with chronic renal failure. This author was privileged to know Dr. Scribner and some of his associates such as Dr. Christopher Blagg, as well as Dr. George Aagaard, former Dean of the Medical School, and Dr. John Hogness, former president of the University of Washington. These relationships allowed personal communications regarding ethical issues arising from the newly developed practice of chronic renal dialysis.

The Search for an Artificial Kidney

Death from kidney failure is a problem that has plagued human kind from earliest times. It was not until the advances in medicine and technology of the mid-twentieth century that physicians caring for patients with renal failure could imagine a machine substituting for a human organ. In the 1940s, with World War II raging, Nils Alwall in Sweden, Willem Kolff in the Netherlands, Gordon Murray in Canada, and Leonard Skeggs and Jack Leonard in the USA were simultaneously developing the earliest artificial kidneys—machines that could provide hemodialysis for patients in acute renal failure. At that time, there was no regulation of clinical research or experimentation, and the discipline of bioethics was yet to be developed. Kolff reported that although he was able to decrease his patients' urea levels, the first 14 all died [1]. His work was unquestioned by any authorities. Eventually, his treatment enabled a patient to survive from acute glomerulonephritis, and after the war, the research in developing an effective artificial kidney intensified. The process involved an arrangement that sent the patient's blood on one side of a semipermeable membrane with dialysate on the other, so that the toxins could be cleansed from the blood. Like any inventors, they had to find appropriate materials and construct a machine that would allow this process to take place without jeopardizing the patient's blood supply. Early inventors recalled that the tragic

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plight of particular patients inspired them to persevere in finding a solution.

These early efforts toward a mechanical solution to the problem of acute kidney failure occurred in a context where physicians primarily relied on dietary management. Patient care emphasized a diet low in protein, sodium, and potassium, accompanied by fluid management. This remains the basis for the contemporary care of a patient with chronic kidney disease. In the developing field of nephrology, there was a considerable anti-dialysis sentiment. J. G. Borst, a respected investigator in Amsterdam, advocated dietary management and gave a low priority to hemodialysis for patients in acute renal failure. As late as 1956, at the annual meeting of the American Society for Artificial Internal Organs (ASAIO), it was recognized by Dr. Danzig that strong opposition of dialysis was due to delaying the use of hemodialysis until desperate measures were required, which was by then often too late [1].

In those early days, the field of nephrology lacked any comparative studies into the most efficacious approach to patients with kidney failure. Such research might have helped to resolve this uncertainty. At that time, there was no operant bioethical imperative demanding that such studies be carried out, and physicians caring for patients in kidney failure were driven by clinical desperation. Research ethics was in its infancy. Gradually, it became apparent from clinical observation that hemodialysis in patients with acute renal failure was, indeed, a life-saving procedure. During the Korean War, 1950–1953, injured soldiers in the US Army with acute renal failure were saved by temporary hemodialysis. These successes helped solidify the growing opinion that hemodialysis could be accepted as a standard procedure.

In spite of the successes in treating patients with acute kidney failure, there was still no hope for patients diagnosed with chronic kidney failure. This problem was attributed to the limited number of vascular access points for multiple hemodialysis sessions. Each treatment required a cutdown to cannulate an artery. Once access for hemodialysis had been accomplished using the wrists and ankles, the number of suitable access points to the patient's vascular system diminished. Earlier attempts at providing a reusable access point had ended in failure. This was the challenging context in 1960, in which Dr. Belding Scribner carried out his work as a nephrologist at the University of Washington.

The Story of the Scribner-Quentin Shunt

Belding Scribner described to me his anguish in 1960 when he discovered that the renal failure in his young patient, Joe Saunders, was not acute, but chronic, and that he had no choice but to send him home to die (Fig. 8.1) [2]. Not long after this, Dr. Scribner diagnosed a very likeable young Boeing machinist, Clyde Shields, with chronic renal failure. In the night, following this tragic diagnosis, Scribner described his awakening at 4 a.m. with a mental picture of an external device, a U-shaped arteriovenous shunt, an indwelling device that could allow access to the circulatory system for ongoing hemodialysis. He quickly drew a sketch of this image on a pad at his bedside. The next morning, Scribner described his idea to Loren Winterscheid, MD, a surgeon, who recommended he check with medical supplies as the cardiothoracic surgeons were using Teflon tubing to enclose electrical wiring for heart devices such as pacemakers, due to its noninflammatory property. Scribner obtained the Teflon tubing and eventually learned that the "nonstick" property was actually the essential ingredient in making it work successfully, without clotting. Scribner and Wayne Quinton, an engineer, experimented with the tubing and learned to shape it by using a mandril heated to 300 °F. This allowed them to bend the stiff tubing which was then cooled with water so that it held the desired shape. Matching cannulas were made, one for the radial artery and one for the vein in the forearm. A U-shaped piece was also crafted and held in place with a Swagelok® (a plumbing device) so that between hemodialysis sessions, the blood could flow continuously between the artery and vein, keeping the site open.

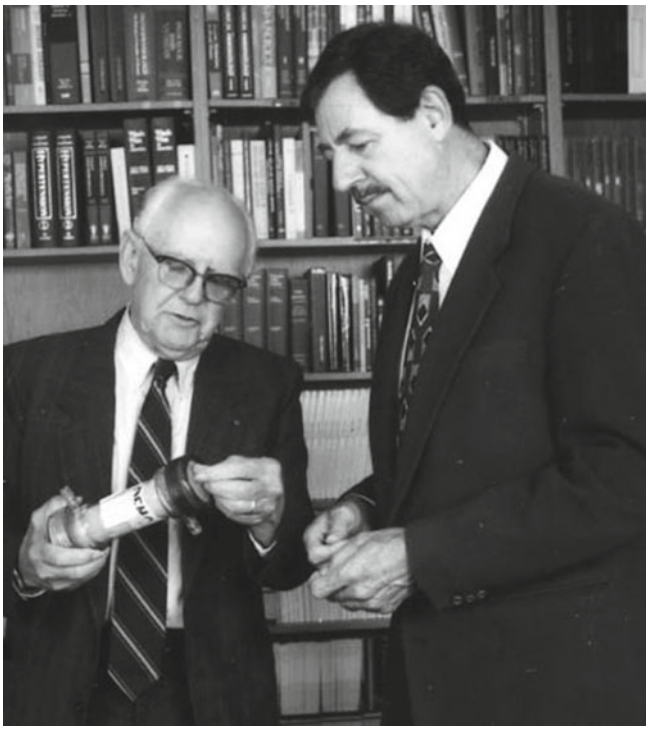

Fig. 8.1 Dr. Belding Scribner discusses the evolution of hemodialysis with Dr. McCormick at the University of Washington

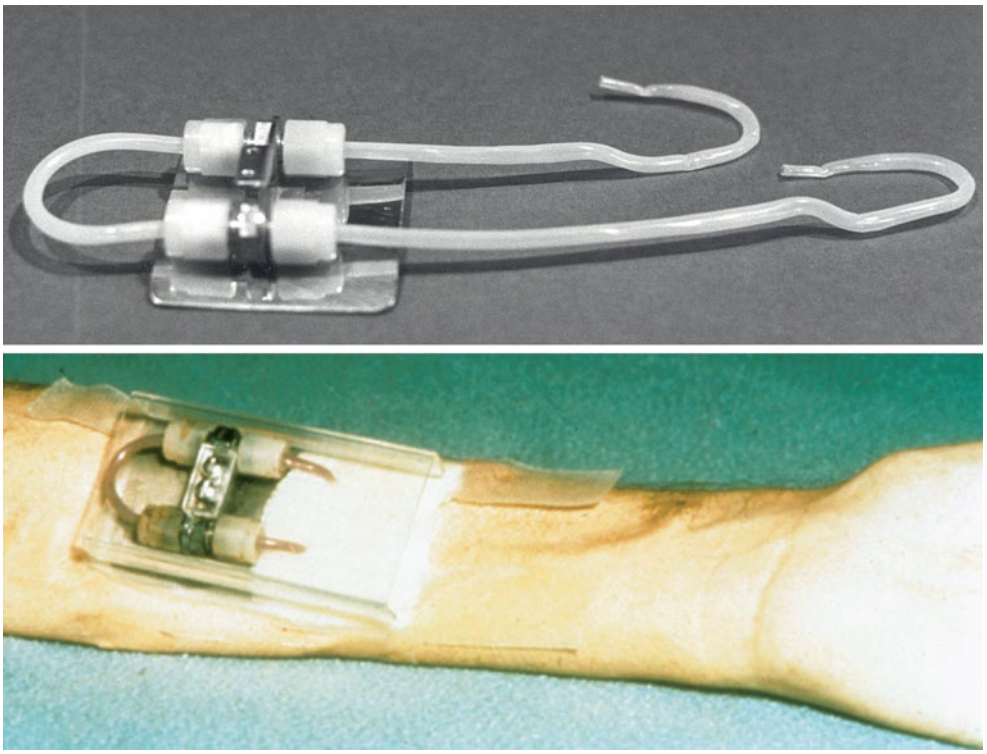

Fig. 8.2 *Top panel*: the Teflon arteriovenous shunt made of two thin-walled Teflon cannulas with tapered ends designed for long-term use in patients with "chronic renal failure." *Bottom Panel*: the Teflon shunt after implantation. Long Teflon arms and long subcutaneous tunnels were used to decrease the risk of infection. The shunt is attached to a "Swagelok® connector," a stainless-steel arm plate covered with a plastic protective cover. The arm plate anchors the cannulas to the arm and provides the means for easily changing the external circuit from bypass to dialyzer circuit. The rate of blood flow in this assembly is 100–200 ml. Patency of the blood artery and vein between dialysis sessions is maintained via an external arteriovenous fistula created by means of a Teflon-Silastic loop (Images used with permission from the Northwest Kidney Centers, Seattle, WA)

This arteriovenous shunt was made on the morning of March 9, 1960 (Fig. 8.2), and shortly thereafter installed at the wrist of the patient, Clyde Shields, a machinist, by a University of Washington surgeon, David Dillard, MD. That same afternoon, Clyde had his first hemodialysis session using the arteriovenous shunt as the access point to his circulatory system (Fig. 8.3). It worked. After the hemodialysis session, the loop was closed to allow normal circulation of blood. The shunt would provide access for all future hemodialysis sessions. A door had opened. For the first time, there was hope for patients with chronic renal failure. Clyde was able to return to his work as a machinist at an engineering company that provided work for the Boeing plant. He lived an additional 11 years following his initial treatment. He died, not from kidney failure, but from a myocardial infarction. During those years, Scribner's work continued, and the shunt was constantly improved by new innovations. Clyde Shields, the first long-term survivor, benefitted from these new and improved shunts during that time.

Seattle's Artificial Kidney Program

When it became clear that Mr. Shields was surviving because of the dialysis treatment, other patients were enrolled. Mr. Harvey Gentry was the next patient enrolled followed by Mr. Rollin Heming and in July 1960, Mr. Jack Capelloto. All were suffering from end-stage renal disease (ESRD), and all received hemodialysis at the University of Washington in Seattle. Scribner recounted his desire to admit additional patients to hemodialysis after the first four patients demonstrated that hemodialysis was effective. However, UW Hospital medical director, John Hogness, refused his request. Hogness believed that once a patient was admitted to chronic hemodialysis, there was an implicit moral imperative that the treatment should continue as long as needed. Hogness knew the university did not have the funds to provide this and felt that from an ethical standpoint, it was not possible to expand the university's program without a guarantee of funding. He encouraged continuing research aimed at improving this treatment regimen. The success in treating these early

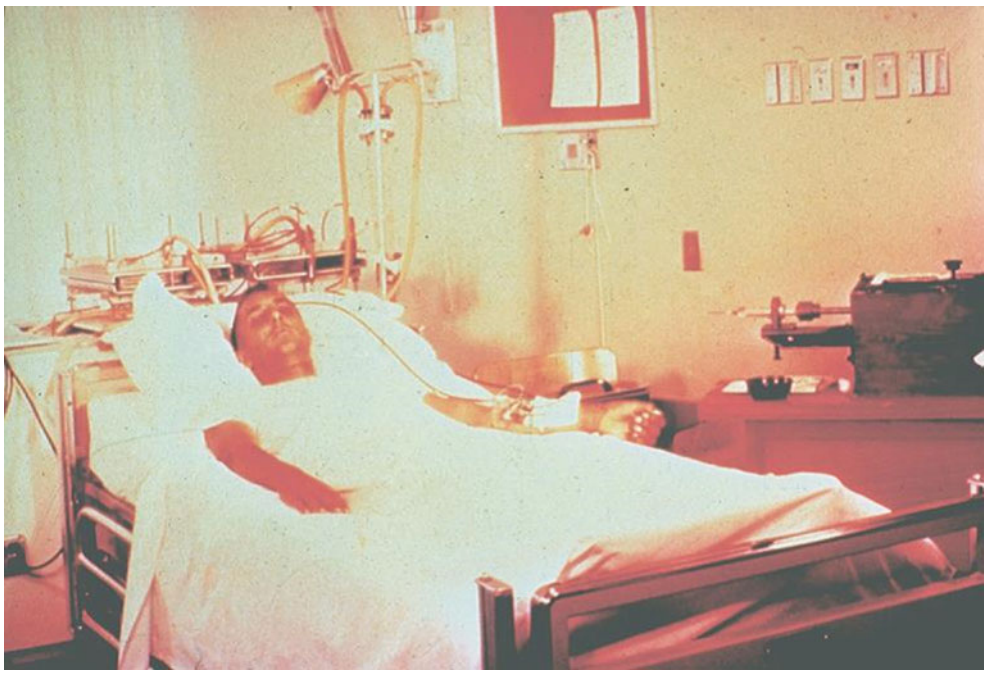

Fig. 8.3 Clyde Shields, Scribner's first patient to use the arteriovenous shunt. Note the Skeggs-Leonards dialyzers and the chest-type freezer behind Clyde and the heparin pump borrowed from the Physiology department (Images used with permission from the Northwest Kidney Centers, Seattle, WA)

patients with chronic renal failure was at first a closely guarded secret out of fear that overwhelming numbers of patients with end-stage renal disease (ESRD) would apply for hemodialysis, once it was discovered to be efficacious and before necessary provisions had been made.

Dr. Scribner described late-night seminars in his hotel room at the annual American Society for Artificial Internal Organs (ASAIO) meeting in Atlantic City, 1960. He and Quentin demonstrated to nine nephrologists the art of "tube bending" so they could return home, make their own cannulas, and enroll their ESRD patients in hemodialysis programs in cities across the country. Scribner actually brought Mr. Shields to Atlantic City as a living demonstration of the month-long success of his treatment. Dr. Shreiner, president of ASAIO, allowed a brief paper written by Scribner describing his technique in chronic hemodialysis to be published in the report on the ASAIO meeting, even though Scribner had not been on the program due to the late breaking nature of his discovery. Gradually, as word spread, nephrologists and nurses from throughout the USA flocked to Seattle, WA, to learn about hemodialysis.

Scribner recognized the financial problems in expanding the hemodialysis program at the University of Washington. Once a patient was accepted for dialysis, the patient would need treatment three times per week for the rest of his/her life. How was such treatment to be paid for? Scribner, with the support of the dean of the medical school, Dr. George Aagaard (1954–1964), appealed for assistance from the community. Dr. James W. Haviland, then president of the King County Medical Society, responded to Scribner's request for community support. He assisted through donations and a grant from the Hartford Foundation in establishing the world's first hemodialysis center. On January 1, 1962, the *Seattle Artificial Kidney Center (SAKC)* opened in the former nurses' quarters in the basement of Swedish Hospital. It was a nonprofit organization dedicated to the care of hemodialysis patients. The SAKC was a novel operation at the time as the task of hemodialysis was turned over to the nurses. Scribner never sought a patent on his invention as his goal was to keep the costs down and to provide hemodialysis for all who need it. Seattle became a leader in teaching patients and their families the methods of "home dialysis." This was more convenient for patients and more cost-effective. Dr. Christopher Blagg, a colleague with Scribner in the Division of Nephrology from 1963, became executive director of the newly renamed Northwest Kidney Centers from 1971 until 1998, a period of amazing growth in the treatment of dialysis patients [3].

The Ethics of Access

Bioethical issues were inherent in this new hemodialysis program. Chronic hemodialysis marked the beginning of an era in which machines could supplant the functions of human organs. Such machines were in limited supply. In 1960, there were only three hemodialysis machines in Seattle, so only a few patients could be accommodated for ongoing hemodialysis, raising the questions: Who should live when not all can live? What criteria should be used in selecting patients? The Seattle physicians attending to the hemodialysis patients felt they could determine who was medically eligible, but should

not have the responsibility for choosing among competing candidates. They appealed to the King County Medical Society for assistance. This led to the formation of an anonymous body of seven volunteer citizens who formed the *Admissions and Policies Committee of the Seattle Artificial Kidney Center* at Swedish Hospital. They had no special training and were given no guiding principles. They were to rely upon their own moral intuition. They were given a few exclusionary points. Children were to be excluded due to the many unknown aspects of the effects of hemodialysis on a growing child. Persons over 45 years of age were to be excluded as they were more likely to experience other comorbidities. Only citizens of the state of Washington could be included, as the university was a public university and supported by state tax dollars.

When Shana Alexander came to Seattle in the summer of 1961, she gathered information for an article that appeared in *Life* magazine, November 9, 1962. In her article she claimed: "These seven citizens are in fact a Life or Death Committee. With no moral or ethical guidelines save their own individual consciences, they must decide, in the words of the ancient Hebrew prayer, "Who shall live and who shall die; who shall attain the measure of man's days and who shall not attain it; who shall be at ease and who shall be afflicted." They do not much like the job" [4].

Alexander's article had broad readership and focused attention on the ethical difficulties of comparing the worth of one human being over another in a life and death situation. Would a "first come, first served" principle be more fair or a lottery that provided an equal chance for all participants? James Childress, ethicist-theologian, favored the idea of a lottery to choose among those who were medically qualified as the most just approach to preserving the dignity of all [5].

The Ethics of Cost

The cost of hemodialysis was another ethical issue. Since chronic hemodialysis patients would require treatment for the remainder of their lives, unless they could acquire a kidney transplant, the issue of cost loomed large. How much should the cost of treatment weigh in terms of the worth of a human life?

In today's economy, the cost of hemodialysis in a nonprofit institution such as Washington State's Northwest Kidney Center (NWKC) is approximately $30,000.00 per year. In the 1960s, the cost was about $10,000.00 per year for the average hemodialysis patient. In the "1960s," it was estimated that about 50,000 patients per year would need hemodialysis. Today, in the USA, as reported in the United States Renal Data System, there are 615,000 with ESRD [6]. Both the number of patients with ESRD and the costs of such treatment have far outstripped those early predictions. In addition, once the federal government guaranteed payment for hemodialysis, commercial for-profit enterprises entered the picture, contributing to rising costs of hemodialysis.

Another ethical issue revolves around current access to hemodialysis in patients who are undocumented immigrants. While it is unlawful for federal funds to be used to provide hemodialysis for undocumented immigrants, there is an allowance for state Medicaid funds to be used. The Alien Emergency Medical (AEM) is a federal program that allows state Medicaid to pay for hemodialysis services using state-only funds, without violating federal rules (since Medicaid is a state/federal program). Currently, about ten states, such as Washington, Ohio, and New Jersey, utilize AEM to provide regular hemodialysis for such patients, while in the other states that do not, undocumented immigrants with ESRD have no alternative but to go to the emergency department, in life-threatening distress, once every 7–10 days to get a treatment to stay alive, relying solely on the charity care of the hospital. For such patients, there is no social worker, dietitian, care management, or care coordinator. Their blood is cleansed just enough to stay alive, but they are always on the edge. Clearly, such a practice is not in the best interests of these patients and is an abrogation of the principle of beneficence, raising the question of "who should survive" afresh in a new generation of ESRD patients.

Hemodialysis Access in Intravenous Drug Users

An ongoing issue in vascular surgery arises when the hemodialysis patient is also addicted to injectable drugs. If the addicted person "shoots up" by using the fistula, there is a serious risk of infecting and destroying the site due to the use of unsterile needles. Some vascular surgeons refuse to surgically create a fistula in a drug-addicted patient. This usually leads to the installation of a central line in order to initiate hemodialysis; however the morbidity and mortality rate of patients using a central line for hemodialysis is significantly higher. Ethically, it is imperative that such patients are recognized as having a dual diagnosis, ESRD and drug addiction, and both problems need to be addressed simultaneously so that optimum treatment can be provided [7]. Discussion of this issue from a vascular surgeon's perspective is covered in Chap. 29.

Quality of Life

Quality of life is an issue for many patients on hemodialysis. Patients on hemodialysis in the USA receive 3.5–3.75 h of treatment three times each week. In Australia they dialyze 4 h, three times per week. Patients on peritoneal dialysis dia-

lyze every night. All patients are closely dependent upon the machines that cleanse their blood. However, no machine can completely replace the functions of a healthy kidney.

A University of Washington reporter, Julie Garner, reported on an experiment with a new kind of device, a wearable kidney machine:

> The prototype for the wearable artificial kidney (WAK) is familiar; it looks like a tool belt from a big box hardware store. It is battery-powered, weighs about 10 pounds, can dialyze patients continually while allowing mobility, and it only takes a pint of fluid to work. Researchers are hoping the continuous hemodialysis the device provides will improve the quality of life for kidney patients and keep them healthier. [8]

If current trials demonstrate the WAK is safe and effective, it could have a revolutionary effect on the quality of life for hemodialysis patients by providing freedom of movement for patients choosing this treatment format. It may also reduce some of the dietary restrictions that must accompany the traditional hemodialysis. (WAK is discussed in Chap. 44, portable and wearable dialysis devices for the treatment of patients with end-stage renal disease.)

Quality of life is also impacted by one's location and environment. In the past years, many patients chose to live in closer proximity to their local treatment center. Such moves, and restricted mobility due to the effects of the illness, often lead to social isolation and a lower quality of life as described by patients. Further, older patients on hemodialysis with comorbidities at times feel their quality of life has declined to the point that they wish to stop the treatment. A patient's request to stop the treatment should precipitate an important conversation with care providers so that efforts can be made to improve the patient's quality of life. When patient needs cannot be satisfactorily accommodated, a significant number of patients choose to stop hemodialysis. In the USA, such patients are provided with palliative care to minimize discomfort from the buildup of toxins in their bodies in their last days of life. Of patients on hemodialysis who die in a given year, approximately 14% die because they choose to stop hemodialysis [6].

End-of-Life Concerns

End-of-life support is an important factor in the last days of patients who choose to stop hemodialysis. Patients have the ethical and legal right to stop medical treatment they no longer desire [9]. Usually, the decision to stop treatment is based on patients' assessment that staying on hemodialysis is no longer meeting their goals. In many cases, these patients have advance directives in place and have discussed their preferences with family members. When a patient loses decisional capacity, the advance directive is seen as an extension of the patient's autonomy, by allowing the patient's choice to be acted upon by ceasing hemodialysis. In some cases, hemodialysis patients have, over time, become demented, and the family sees the continuation of hemodialysis as a greater burden than a benefit for their loved one and requests that hemodialysis be stopped and palliative care be initiated. Surrogate decision-makers have an ethical responsibility to represent the known values and wishes of the incapacitated patient. If these are unknown, then the ethical responsibility shifts to that of acting in accord with the best interests of the patient as assessed by the surrogate [10].

Conclusion

Viewed from the long history of medicine, hemodialysis for patients with chronic renal failure is a relatively new achievement. The development of rudimentary artificial kidneys in the "1940s" and "1950s" and the invention of the arteriovenous shunt in 1960 opened the door to this new treatment opportunity for patients facing ESRD. Creative vascular surgeons developed the internal arteriovenous fistula, providing a stable access point to the blood supply for ongoing hemodialysis. The advent of hemodialysis gave rise to a number of ethical issues: Who should live when there are not enough machines for everyone? Is it a morally sound practice to accept into treatment those who are judged by a utilitarian formula to be more valuable or useful to society than others? Would not the element of equal chance as introduced in a lottery system more appropriately recognize the equal worth of every human life? Unless the hemodialysis patient obtains a kidney transplant, hemodialysis will be a life-long treatment at a considerable cost to society. While patients in kidney failure qualify for federal assistance through Medicare, how do we as a society compare the needs of patients suffering from other illnesses such as cancer or heart disease? The principle of justice would have us treat similar cases similarly. What about the undocumented workers in need of hemodialysis? Acting on the "do-no-harm" principle, several states have found a way to provide compassionate care for such patients. In the early days of hemodialysis, patients with ESRD almost unilaterally desired this life-extending treatment. Today, many hemodialysis patients are elderly and have comorbidities such as cancer, diabetes, heart disease, or dementia. Guided by the principles of beneficence and nonmaleficence, clinicians and families must consider the proportionality of benefits and burdens for suffering patients. It is helpful when patients have the capacity to choose to withdraw from hemodialysis and have provided an advance directive stating their wishes. In other patients with dementia and other comorbidities, such decisions fall to the family who must represent the values of the patient or decide on the basis of "best interests" for their loved one. In all such cases, compassionate communication and competent palliative care are essential components of excellent

end-of-life care. Vascular surgeons and providers of hemodialysis are challenged by the hemodialysis patient who is also addicted to injectable drugs and must find solutions to both diagnoses in order to provide optimum care. On the horizon, scientists are likely to develop new innovations such as the wearable artificial kidney (WAK) that will hopefully provide greater freedom, mobility, and a better quality of life for patients in the future. In the early 1960s, the advent of hemodialysis coincided with the rise of the new discipline of bioethics. Many of the early ethical issues continue to challenge us. We have a scarcity of organs for transplants that could greatly improve the quality of life for many. We continue to seek solutions that balance the principles of beneficence and autonomy and justice. The ethical questions noted above that evolved with the advent of hemodialysis mean that hemodialysis and ethics will forever be inextricably bound by their common beginnings. Dr. Albert R. Jonsen, chair of the Department of Medical History and Ethics at the University of Washington's School of Medicine in the early 1990s, hosted a national bioethics conference. He called it "The 30th Anniversary of the Birth of Bioethics" [11]. Jonsen chose the innovation of the Scribner shunt and the questions that emerged from its use as the starting point for modern bioethics.

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Part II

Hemodialysis Access Planning

Timing of Hemodialysis Access

9

Mark R. Nehler

Kidney Disease Outcomes Quality Initiative

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) for vascular access states patients in need of long-term, permanent access for hemodialysis (HD) should undergo native arteriovenous fistulae (AVF) creation over other access types (e.g., grafts or central catheters (CVC)) [1]. This should be done preferably at least 6 months before the anticipated start of HD – typically chronic kidney disease (CKD) stages IV and V. Once patients are identified, three action items include avoid central venous catheterization (CVC), protect potential access sites and venous conduit, and maximize the creation of "useable" fistulae as the best long-term access choice. The guidelines emphasize targets for permanent HD access placement to include a rate of functional AVFs greater than 50 % in incident HD patients and at least 67 % in prevalent cases, with long-term CVC use in less than 10 % [2]. The Centers for Medicare and Medicaid Services embraced this idea with the development of the National Vascular Access Improvement Initiative (NVAII) and the Fistula First Breakthrough Initiative (FFBI) to disseminate these guidelines to the medical community [3]. In January 2013, performance goals limiting the number of patients in HD centers using a CVC for access without financial penalty began. It is important to remember that large portions of the access practice guidelines for KDOQI are not significantly based on level-one data.

Once the AVF is in place, it should be monitored by either nephrology or surgery, and if not maturing satisfactorily within 4–6 weeks, a fistulogram and intervention is recommended. Central to these initiatives is the presumption that preemptive HD access planning will increase the likelihood of fistula construction and successful maturation prior to initiating HD treatments. The actual results nationwide are more sobering. A recent study demonstrated only 52 % of end-stage renal disease (ESRD) patients saw a nephrologist prior to onset of HD, and only 17 % of incident patients had a functioning AVF at onset [4]. The importance of the preemptive access concept is emphasized in a recent report [5]. Even when controlling for other risk factors, starting HD with a CVC increased long-term mortality significantly regardless of the ultimate form of access. Given the obvious disparity between FFBI goals and actual achievements in incident patients and the potential benefit from the same, it is useful to examine the factors involved to see if they are modifiable.

Patient Population

CKD afflicts 14 % of the US general population [6]. Patients with CKD are classified into one of five stages according to the presence of kidney damage/glomerular filtration rate. The prevalence of stages III–V CKD has grown by 40 % in the last decade. There is a significant racial disparity in the rate of ESRD incidence – Hispanics are 1.5 times the rate as non-Hispanics, and African-Americans are 3.5 times the rate of whites. Just as the population is aging, the incidence of patients with ESRD who are over 65 has risen over 30 % in the last decade. As will be seen in the risk factors affecting successful placement of an AVF, these racial and age disparities have impact on the success of FFBI [7].

Mortality is another issue that clearly impacts the efficacy of preemptive HD access. Table 9.1 demonstrates the most recent data for expected survival in years for patients with ESRD compared to age-matched controls. The population over age 65 on HD has an abbreviated life expectancy that is similar to a number of different malignancies. The top causes of death in ESRD patients (Table 9.2) include cardiac causes as the top two, followed by sepsis and withdraw of dialysis. The latter two can clearly be influenced by type of access or complications of the same. The large contribution to mortality of withdraw of dialysis in the older ESRD cohort also has implications

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Table 9.1 Mean life expectancy in years for prevalent USRDS dialysis and transplant population compared to controls 2012

	ESRD patients, 2012								
	Dialysis			Transplant			General U.S. population, 2010		
Ages	All	M	F	All	M	F	All	M	F
0–14	22.3	23.2	21.3	61.0	60.1	62.5	72.9	70.5	75.3
15–19	19.3	20.6	19.0	48.7	47.9	50.0	59.5	57.1	61.7
20–24	17.0	17.7	16.1	44.7	44.0	45.9	54.7	52.4	56.9
25–29	14.9	15.5	14.1	40.7	40.0	41.8	50.0	47.8	52.0
30–34	13.4	13.8	12.7	36.8	36.1	37.9	45.2	43.1	47.2
35–39	12.0	12.3	11.5	32.8	32.1	33.9	40.5	38.5	42.4
40–44	10.5	10.6	10.2	28.9	28.2	30.0	35.9	33.9	37.7
45–49	8.9	9.0	8.7	25.1	24.4	26.2	31.4	29.6	33.2
50–54	7.6	7.6	7.6	21.6	20.9	22.7	27.2	25.4	28.8
55–59	6.5	6.4	6.5	18.3	17.7	19.3	23.1	21.5	24.5
60–64	5.5	5.4	5.6	15.4	14.8	16.4	19.1	17.7	20.3
65–69	4.6	4.5	4.8	12.9	12.4	13.8	15.5	14.2	16.5
70–74	3.9	3.8	4.1	10.8	10.4	11.5	12.1	11.0	12.9
75–79	3.3	3.2	3.5	9.1	8.7	9.7	9.1	8.2	9.7
80–84	2.7	2.6	2.9	[a]	[a]	[a]	6.5	5.8	6.9
85+	2.2	2.1	2.4	[a]	[a]	[a]	3.4	3.0	3.5
Overall	6.6	6.6	6.6	18.6	18.0	19.5	22.2	20.7	23.4

Data Source: Reference Table H.13; special analyses, USRDS ESRDS Database; and Table 7 in National Vital Statistics Reports, Deaths: Final Data for 2010. Expected remaining lifetimes (years) of the general U.S. population and of prevalent dialysis and transplant patients. Prevalent ESRD population, 2012, used as weight to calculate overall combined–age remaining lifetimes
USRDS Reports
Abbreviation: *ESRD* end-stage renal disease
[a]Cell values combine ages 75–85 and over

Table 9.2 Unadjusted annual mortality rates per 1,000 by cause of death in prevalent USRDS dialysis patients 2010–2012

Hemodialysis	0–19	20–44	45–64	65–74	75+
Acute myocardial infarction	0.6	2.5	6.2	10.1	12.9
Hyperkalemia		0.6	0.5	0.6	0.8
Pericarditis		0.1	0.1	0.1	0.1
Atherosclerotic heart disease		0.3	1.6	2.8	5.0
Cardiomyopathy	0.3	0.8	1.9	4.0	6.9
Cardiac arrhythmia	0.8	1.8	3.6	5.6	7.9
Cardiac arrest	6.6	18.9	36.6	54.6	74.1
Valvular heart disease		0.3	0.4	0.8	1.5
Pulmonary edema		0.4	0.5	0.7	1.1
Congestive heart failure	1.1	0.8	2.4	5.5	10.8
AIDS					
Cachexia		0.4	1.5	3.8	9.8
Cerebrovascular disease	1.1	2.7	4.4	5.9	7.5
GI hemorrhage		0.3	0.7	1.2	2.0
Other hemorrhage	0.3	1.0	1.4	1.8	2.6
Septicemia	1.4	4.7	10.4	15.0	19.5
Pulmonary infection	1.4	0.7	1.8	3.8	8.2
Viral infection		0.1	0.2	0.1	<0.05
Other infection	0.6	0.9	1.7	2.0	2.9
Malignant disease	1.9	1.0	4.8	9.8	11.6
Withdrawal from dialysis/uremia	3.0	2.7	9.1	23.6	56.0
Other cause	6.1	7.2	11.2	16.5	23.2
Unknown cause	7.8	15.8	29.1	44.2	64.6

Data source 2014 ADR Reference Tables. Table H. From http://www.usrds.org/reference.aspx
USRDS reports
GI gastrointestinal

on quality of life. In summary it is clear that in many older patients with ESRD, HD is often palliative in nature with modest results of the same, which calls into question the efficacy of preemptive access in all patients within this subgroup.

Success of AVF Creation

Much of the literature on AVF placement has reported rather disappointing results with most series demonstrating maturation failure rates of 40–45 % [8–11] [12] with a single recent series slightly better at only 30 % [13]. Added to that, some patients undergoing AVF placement in the preemptive strategy may never require HD and are exposed to unnecessary morbidity. Risk factors for failure of AVF maturation are often not modifiable. This includes advanced age, female gender, diabetes, and nonwhite race. The size of the vein and the creation of upper versus forearm AVFs (likely interrelated) have some potential modification in planning with targeting a certain extremity/vein, etc. Current recommendations for acceptable vein diameter range from 2.5 to 3 mm with veins 4 mm or greater having the best chance of AVF success [14]. If, however, the plan was to only perform AVFs on younger nondiabetic white males with large veins, the fraction of patients undergoing AVF would be minimal, and although maturation success would be much higher, the percent of incident patients using an AVF at HD onset would remain very low.

These contributions can be seen in the regional variability of prevalent AVF usage in the FFBI data. Regions such as Colorado, Oregon, New Hampshire, Rhode Island, and Washington are at or above the target of two thirds prevalent AVF usage. Conversely, regions such as South Carolina, Virginia, District of Columbia, Alabama, and Arkansas are only slightly above 50 % prevalent usage. It would seem safe to assume that much of these differences are due to non-modifiable issues within the respective populations they are caring for rather than any inherent skill set differences between the providers. However, none of these issues are addressed in the current guidelines or performance metrics.

The major morbidity of AVF creation is lack of maturation and failure to mature for use, necessitating additional procedures as stated above. Other issues include steal in 1–8 % of patients [15, 16] arm edema due to unmasked central venous stenosis, and rarely ischemic monomelic neuropathy [17]. All of these require secondary procedures up to and including abandoning the access. The incidence of these complications increases with age and diabetes.

The Morbidity of Central Catheters

Published reports about late referral for vascular access evaluation demonstrate poor global outcomes such as increased CVC use; increased morbidity, such as line sepsis and central venous stenosis; and ultimately increased mortality [5, 18, 19]. Recent United States Renal Data System (USRDS) data demonstrated markedly increased rates of admissions for infection in patients with CVCs compared to either AVG or AVF (Table 9.3). Although the rate of infection in AVG patients was larger than AVF patients, it is markedly less than in patients using a CVC.

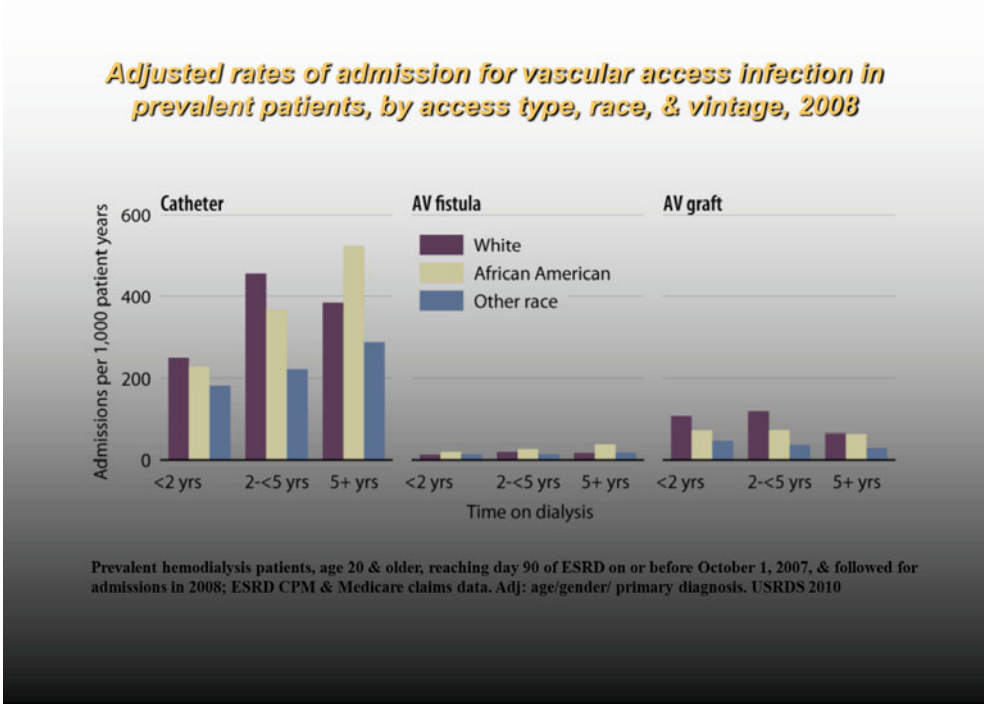

Table 9.3 Adjusted rates of admission for vascular access infection in prevalent patients by access type, race, and vintage 2008
USRDS reports

A large review of access and mortality in the Fresenius dialysis database [20] demonstrated that the mortality rates of patients with CVC access were markedly greater than AVG or AVF patients adjusted for other risk factors. Patients who were female, African-American, and also had onset of HD for less than 1 year were much more likely to be using CVC access. A recent national review mirrors the findings of the Fresenius study [5]. There is no argument regarding the morbidity and mortality of CVC. What is not proven is whether preemptive AVFs would reduce this and also whether an increased placement of AVGs would also be beneficial given the poor results with AVFs in certain patient and anatomic scenarios.

Results of Preemptive Dialysis Access

Study Design

The study [21] was a retrospective review from the vascular surgery practices at the University of Colorado at Denver (Denver Veterans Affairs Medical Center and University of Colorado Hospital) and the Portland Veterans Affairs Medical Center. Consecutive patients with late-stage CKD who underwent preemptive AVF creation (AVF prior to onset of HD per the NVAII and FFBI and in accordance with KDOQI principles) between January 2003 and December 2007 were entered into a registry database. Patients were excluded if they had a previous vascular access procedure (e.g., fistula, graft, or catheter) or were receiving hemodialysis treatments or initiated the same within 1 week of the vascular access consultation.

Baseline demographics and comorbidities were collected. Technical operative data included preoperative vein mapping and type of AVF created. Preoperative vein mapping data included the cephalic and basilic veins above and below the elbow. Adequate vein size for AVF creation was qualified as greater than or equal to 2.5 mm per the recommended guidelines by Silva et al. [14]. The radiocephalic AVF was considered as the first-line option if the cephalic vein size was adequate.

The primary objectives were to determine the efficiency of a preemptive AVF strategy by examining over time success of predicting the need for HD and success of AVF maturation/use. To accomplish this, patients were stratified into one of four subgroups (groups A–D) over the follow-up period: those on HD using their fistulae (group A, ideal result), those not on HD with patent fistulae (group B, near ideal), those on HD with a secondary access type (failed fistulae; group C, succeeded in predicting HD but failed in AVF maturation and function), and those not on hemodialysis with an abandoned AVF due to death, refusal of HD, kidney transplant, or fistulae failure (group D, failed on both goals).

Patient-related outcomes determined over the follow-up included incidence of hemodialysis initiation and all-cause mortality. Fistula-specific outcomes assessed were mean maturation time (i.e., time interval from creation to first cannulation), cumulative functional patency at 6 and 12 months, mean number of interventions per fistula, most frequent complications, and total AVF abandonment over time.

Results

Demographics

The study cohort included 150 late-stage CKD patients (85 % male, median age 63 years) referred for first-time AVF creation over a 4-year period at the combined sites (Portland Veterans Affairs Medical Center, Denver Veterans Affairs Medical Center, and University of Colorado Hospital). Table 9.4 lists baseline demographics and clinical characteristics of the study group. Most patients were Caucasian (66 %) with African-American (15 %) and Hispanic (11 %) comprising the largest two minority groups.

The majority of patients referred were CKD stage IV. Over two thirds of patients were diabetic, and the major-

Table 9.4 Demographics of 150 chronic kidney disease patients undergoing preemptive arteriovenous fistula construction

Variable	*N*	Percent
Smoking		
Current	36	23 %
Former	75	48 %
Never	45	29 %
Diabetes	104	69 %
Hypertension	100	67 %
Median BMI	30	–
CKD		
Stage III	7	5 %
Stage IV	108	73 %
Stage V	34	23 %

Reproduced with permission from Kimball et al. [21]
BMI body mass index, *CKD* chronic kidney disease

ity smoked. Consistent with the high incidence of diabetes in this population patients were frequently obese with a median BMI of 30. A total of 142 patients (92 %) underwent preoperative vein mapping. One hundred and fifty AVFs were created (54 % in upper arm and 46 % in the forearm). The majority of forearm AVFs were constructed at the Portland Veterans Affairs Medical Center, and most basilic vein transpositions were constructed in Denver (Table 9.5).

Patient-Related Outcomes

At a median follow-up of 10 months (Figs. 9.1 and 9.2), 74 (49 %), patients were receiving HD and 48 of the 74 (65 %) were using their AVF (Group A), while 26 of the 74 (35 %) were not due to AVF failure (Group C). Thirty-four (23 %) patients never initiated HD treatments, but had a patent AVF (Group B), and 42 patients (28 %) never initiated HD and abandoned their AVF (Group D). Thirty-four (23 %) of all patients had died.

Fistula-Specific Outcomes

Mean maturation time of all AVFs that were cannulated was 285 days (median 185 days, range 30 to 1,265 days). Cumulative functional patency for all AVFs was 19 % and 27 % at 6 and 12 months respectively with a mean number of two interventions per AVF (range 1–10). The top five complications encountered were maturation failure for cannulation (15 %), focal stenosis requiring intervention (13 %), inadequate flows on HD (9 %), steal syndrome (9 %), and thrombosis (8 %). A time-dependent, cox proportional-hazard model found no influence from patient and operative predictor variables on time to AVF abandonment (Table 9.6). Upper extremity fistulae were abandoned less often than forearm fistulae during the short term (<2 years), although this comparison was not statistically significant over the entire time interval (Fig. 9.3; $p > 0.872$). The overall AVF abandonment incidence was 51 %.

Discussion

Preemptive AVF placement in the present series demonstrated that predicting HD needs at 10 months was only 50 %. Mortality was quite high that calls into question a preemptive strategy. Of the patients on HD, two thirds were using their index AVF for access. However, in terms of functional patency for all 150 AVFs, the results were quite poor at 6 and 12 months. Reasons for these results include size criteria for vein and the usual factors that make AVF maturation difficult.

Do these results justify a preemptive AVF access strategy? In comparison to other prophylactic treatment strategies in vascular surgery – asymptomatic abdominal aortic aneurysm (AAA) repair [22] – and asymptomatic carotid

Table 9.5 Type of preemptive arteriovenous fistula constructed

AVF type	N	Percent
Forearm	72	48 %
Upper arm	78	52 %
Brachial cephalic	58	74 %
Basilic vein transposition	20	26 %

Reproduced with permission from Kimball et al. [21]
AVF arteriovenous fistula

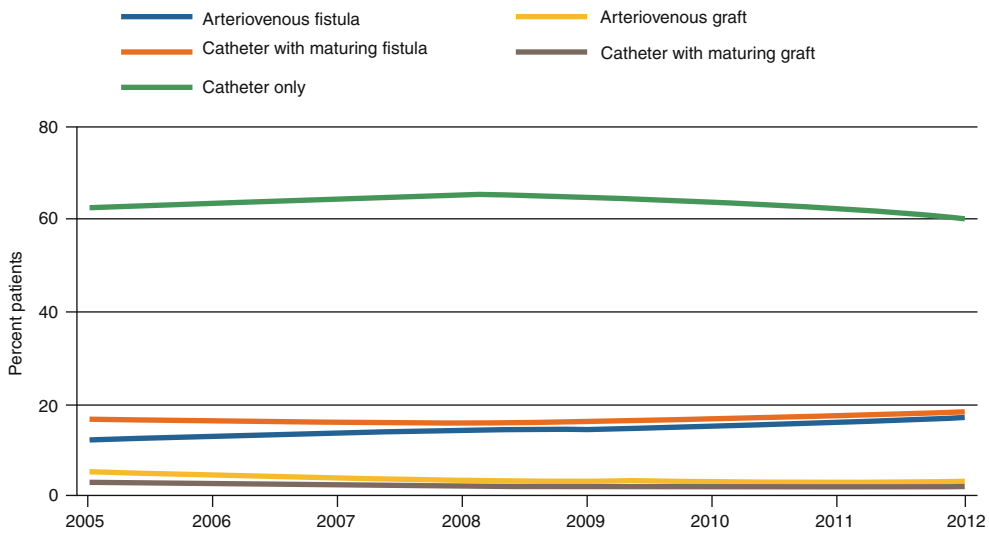

Fig. 9.1 Access for initiating hemodialysis in the USRDS data from 2005 to 2012 (Data source: vol 2 Fig. 3.13 VA use among HD patients at initiation of ESRD treatment, from the ESRD Medical Evidence Form (CMS 2728); time trend from 2005 to 2012)

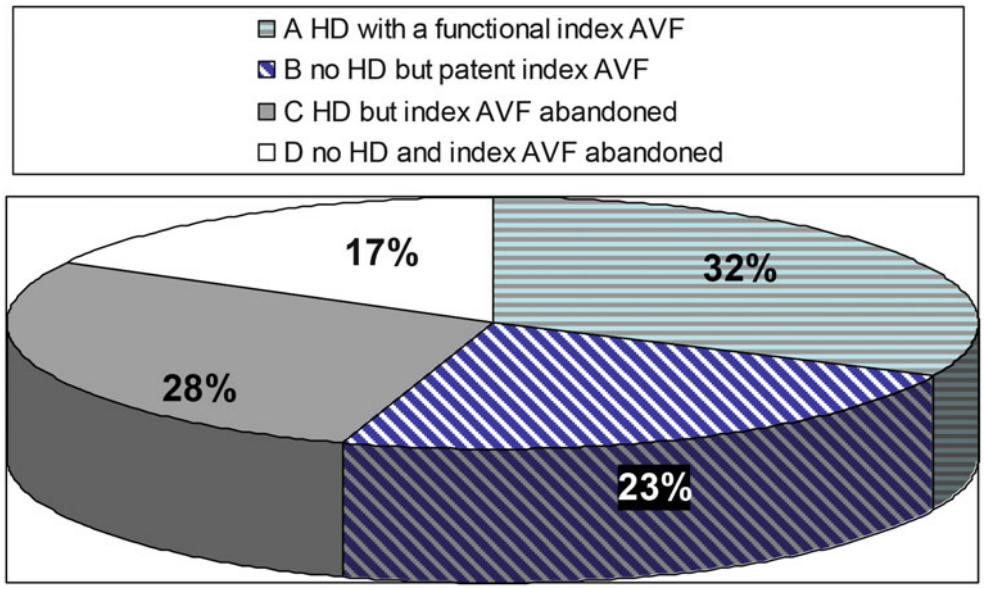

Fig. 9.2 Clinical fate at a mean of 10 months of 150 chronic kidney disease patients undergoing preemptive arteriovenous fistula construction (Reproduced with permission from Kimball et al. [21])

Table 9.6 Patient and operative predictor variables on time to AVF abandonment

Strata	Test	Chi-square	DF	Pr>chi-square
Gender	Log-rank	0.5065	1	0.4767
Race	Log-rank	0.3751	1	0.5402
Smoking	Log-rank	0.5717	1	0.4496
Institution	Log-rank	3.9371	2	0.1397
Age75	Log-rank	0.0163	1	0.8984
BMI30	Log-rank	0.1938	1	0.6598
Procedure	Log-rank	2.5937	5	0.7623

Reproduced with permission from Kimball et al. [21]

revascularization [23], the strategy success in the current series is lower. Even taking into account that the natural history of many patients with asymptomatic AAA and carotid stenosis is to remain so – the long-term success of the revascularizations is markedly better than the success rate of AVFs. Only half of the preemptive AVF population benefit from the procedure with intermediate term patency, and another half actually progress to HD during near-term follow-up. However, the argument can be made that the perioperative risk of the AVF is less than AAA repair or carotid revascularization.

Comparing the hypothetical benefits in preemptive AVF construction with operative management of small AAAs prior to the major randomized trials [22] is instructive. The assumption for small AAAs was that all patients became worse operative risks over time. Furthermore, it was established that small AAAs would grow over time and that rupture risk was related to increased size. Therefore, it made intuitive sense to operate on good risk patients with small AAAs provided the repair could be done with a small perioperative mortality risk. These assumptions however were not confirmed when tested in randomized trials using open [22] or endovascular [24] techniques despite excellent technical success.

Preemptive AVF construction is similar in many ways. The assumption is that patients become worse access candidates over time as potential vein sites are exhausted with intravenous lines. It is established that CVCs have significant septic and thrombotic morbidity [25], and once patients initiate HD with a CVC, they have increased mortality rates [5] and are often reluctant to agree to surgery for a better access option. Patients with CKD stages IV and V have a high rate of requiring near-term HD [26], and the maturation time for AVFs is often measured in months not weeks. Therefore it makes intuitive sense to construct AVFs preemptively on patients with late-stage CKD.

However, there are some major issues with this argument. As stated above, global success of AVF construction in the vast majority of recent reported series [7–12, 27] is modest – 50 %, despite preoperative assessment per KDOQI – including one randomized trial. One major principal of prophylactic vascular care is to focus on good risk patients with a life expectancy that justifies the up-front morbidity and potential mortality of the procedure. However,

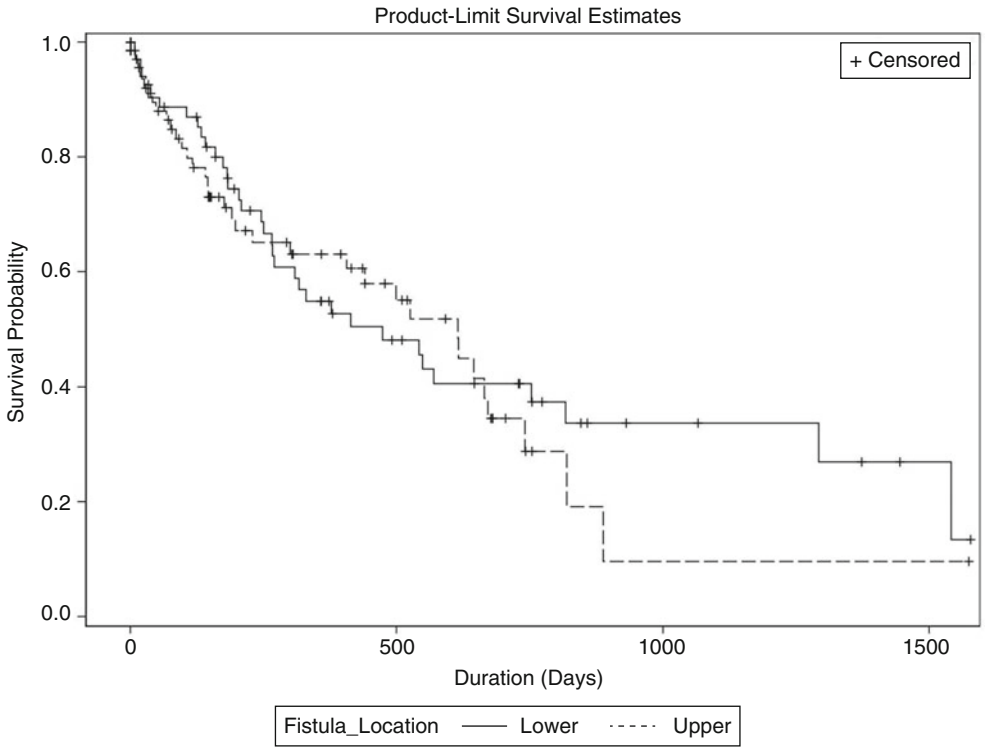

Fig. 9.3 Freedom from abandonment of 150 preemptive arteriovenous fistulae comparing upper arm and forearm (Reproduced with permission from Kimball et al. [21])

KDOQI does not focus on good risk patients. Unfortunately, the mortality rate of a modern renal failure population is substantial – especially older patients [28]. The quality of life of many older patients on HD is questionable – withdraw of HD is a major cause of death in the United States Renal Data report. Just as patients are reluctant to undergo surgery for an AVF once they have CVC access on HD, they are also often reluctant to undergo surgery for an AVF when their CKD does not yet require HD.

Potentially as relevant to the discussion of preemptive AVF construction is compliance with the plan. Is getting a population of ESRD patients willing to comply with a preemptive AVF realistic? The track record to date would indicate no. There would be much less AAA repairs if older patients were not willing to get a screening ultrasound (US); however, large trials indicate 80 % will [29, 30]. But an US is significantly less invasive than an attempt at an AVF. The current modest compliance with screening colonoscopy for colorectal cancer is instructive of the realities. Large trials demonstrate widely variable compliance rates [31]. It is safe to assume that the compliance of preemptive AVF in patients with ESRD is never likely to be great, especially since poor compliance with other conditions (diabetes, hypertension) is often responsible for the ESRD [6].

Another issue that impacts the performance of preemptive AVF creation is reimbursement models in the United States. In Europe the initiation of HD with an AVF is much higher [32]. In the United States, patients only become eligible for Medicare Part A coverage for ESRD after HD initiation [33]. Preemptive AVF placement is not covered retroactively unlike renal transplantation [34]. Implementing a similar retroactive coverage for preemptive AVF placement has been advocated.

Finally, the argument for preemptive AVF construction would be much stronger if the success rate of the procedure was improved. Although there is no general agreement, perhaps our criteria for acceptable venous conduit are not stringent enough. In this study veins 2.5 mm or greater were considered usable for AVF construction as recommended by Silva et al. [14]. However, this differs from the best report on lower extremity venous bypass, the Prevent III trial [35]. In that study venous conduit of <3.5 mm was considered high risk [36], and those grafts had worse patency rates and greater number of interventions compared to grafts constructed with venous conduit ≥3.5 mm. A recent report on AVF construction demonstrated that veins ≥4 mm had much better maturation rates [13]. Unfortunately, in our practice very few patients would qualify for an attempt at preemptive AVF construction if those criteria were used – but 3.5 mm vein requirement could be a compromise. One of the authors in the present report uses ≥3 mm rather than 2.5 mm as the size for acceptable venous conduit for AVFs.

Regardless of changes in strategy, the plan for preemptive AVF placement for all patients is not realistic. Many patients would likely be better served with an AVG and focus on reducing the need for CVC rather than increasing the percent of AVFs. Certain patient populations (obese, female, African-American) have poor AVF maturation rates. It would seem a reasonable compromise to focus preemptive AVF placement in the population most likely to have successful maturation

to make the risk-benefit ratio justifiable. Ultimately, the compliance is likely to be modest for preemptive AVF, regardless of the focus.

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Preoperative Considerations and Imaging

10

Ted Kohler

Creation of adequate dialysis access is the most critical component of renal replacement therapy. Proper site selection can provide years of maintenance-free dialysis, whereas selection of a suboptimal site leads to multiple procedures, high cost, inadequate dialysis, and even a shortened life span. Thoughtful, thorough preoperative planning is the first step in this process. The choice of procedure depends on the individual's goals of care and will be very different for a young person at the beginning of his or her illness than for an elderly patient who has suffered for decades with multiple prior hospitalizations. For some, peritoneal dialysis is the best option. It is well tolerated, more gentle than hemodialysis, and can be done at home and in the evening. However, it requires a willing and compliant patient with a stable, clean home environment and suitable abdominal anatomy. For patients with a short life expectancy, a tunneled catheter may provide the most ready access with sufficient long-term patency. For most, the best access is a native arteriovenous fistula in the nondominant upper extremity. The choice of access is discussed elsewhere. This chapter will discuss patient evaluation with an emphasis on preoperative ultrasound imaging.

Goals

The purpose of the preoperative evaluation is to identify the most appropriate access for each individual. A team approach is best, including the patient, nephrologist, surgeon, sonographer, social worker, and dialysis provider, all of whom have a unique perspective that needs to be considered when choosing the optimal renal replacement therapy. The primary concern is to provide a functional access with as few interventions as possible. When vascular anatomy allows and the need for access is not immediate, autogenous fistulas are preferred, starting as peripherally as possible on the nondominant upper extremity. The goal is to avoid the need for central catheters for bridging while fistulas are being created and to avoid prosthetic grafts in patients who are likely to require renal replacement therapy for a prolonged time.

Preoperative vessel imaging has been credited with enabling an increased use of fistulas in lieu of prosthetic grafts. The proportion of patients on dialysis with a functioning autogenous fistula in the United States has increased significantly over the past decades from only about 20 to over 40 % in response to the Centers for Medicare and Medicaid Services (CMS)-sponsored AV Fistula First Breakthrough Initiative and the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines [1]. The current goal is to have 65 % of patients on hemodialysis using native fistulas. The initiatives include early referral for access planning, protection of potential upper extremity veins, increased awareness of the advantages of this approach, the use of alternative procedures such as transposition fistulas, quality assurance program, and the routine use of preoperative vessel mapping.

Data on which the KDOQI guidelines were based are now dated, with more recent studies showing that prosthetic grafts can function as well as or better than autogenous fistulas and are the appropriate first access in many patients. The push to use more native veins has resulted in attempts to use smaller veins and, as a result, an increase in the rate of failure to mature, which results in increased cost, the use of central venous catheters, and the need for multiple procedures. For this reason, a number of authors have argued that the fistula first initiative should be moderated with an emphasis on function rather than a strict prohibition of grafts [2]. This is particularly the case when a bridging graft can be placed in the forearm where it can be used quickly and reliably while saving the upper arm vein for later use, potentially maturing the basilic vein in the process.

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Table 10.1 A detailed history is the first step in dialysis access preoperative assessment

History assessment	Relevance
Dominant arm	Use of nondominant arm is preferred to minimize negative impact on quality of life
History of previous central venous catheter	Associated with central venous stenosis
History of pacemaker use	Risk of central venous stenosis due to pacemaker wires
History of severe congestive heart failure	Access may alter hemodynamics and cardiac output
History of diabetes mellitus	Associated with small vessel disease in the upper extremity
History of anticoagulant therapy or any coagulation disorder	Abnormal coagulation may cause clotting or problems with hemostasis of access
Presence of comorbid conditions such as malignancy and coronary artery disease that limit the patient's life expectancy	Morbidity of placement and maintaining access may not justify their use in some patients
History of arterial or venous peripheral catheter	Possible damage to target vasculature
History of heart valve disease or prosthesis	Rate of infection associated with specific access type should be considered
History of previous arm, neck, or chest surgery or trauma	Prior trauma may limit target access sites
Anticipated kidney transplant from a living donor	Central venous catheter may be sufficient
History of vascular access	Limits available access sites, reasons for prior failure may influence future dialysis access planning

Adapted from Vascular Access Work Group [1]

Preoperative History

The preoperative evaluation begins with a detailed history (Table 10.1). Hand dominance must be noted since fistula placement can result in disability from vascular steal, edema, or neuropathy. Note should be made of prior central catheter access, which may cause stenosis that reduces venous outflow from the ipsilateral extremity. The same is true of pacemakers, internal defibrillators, and peripherally inserted central catheters (PICC lines). An associated central vein stenosis may preclude the use of the ipsilateral extremity for access placement unless the stenosis can be treated or bypassed with a hybrid approach such as a HeRO™ device. A history of anticoagulant use or thrombotic episodes should be noted and investigated to determine if the patient has a hypercoagulable state. Prior trauma may affect either the venous or arterial anatomy or may result in poor function of the otherwise dominant extremity, thereby making it the preferred location for access. Stroke may have a similar effect. Skin conditions, either chronic infections or inflammatory disorders such as psoriasis or eczema, if inadequately treated, prohibit access placement due to an increased risk of infection.

The choice of access is heavily influenced by factors affecting goals of care such as social support and life expectancy. Another important consideration is how soon access is needed. It has been recommended that patients be referred for access placement when in late stage 4 renal failure, which means an estimated glomerular filtration rate of less than 20–25 mL/min [3]. Because creation of a functional native fistula could take several months, patients who need access within weeks may be better served by a prosthetic bridge graft. Conversely, arteriovenous fistulas may be attempted even with marginal veins in patients who are 6 months or more away from requiring renal replacement therapy.

Physical Examination

The preoperative examination is most useful when the surgeon participates directly. Each patient has unique needs and physical considerations that greatly influence the choice of access site. For some, the need to preserve the dominant extremity may lead the surgeon to consider the possibility of using a brachial vein in the nondominant arm. The examiner may find that a "failed" prior fistula is actually still patent but has not matured due to inadequate inflow or steal from large vein branches. Suspicion of inadequate radial inflow may stimulate a closer look at the diameter and length of the forearm cephalic vein, which could be proximalized to a loop brachiocephalic fistula. The surgeon has the most insight into what constitutes an acceptable vein and artery.

Physical examination should include the cardiovascular system, looking for evidence of congestive heart failure (Table 10.2). Note should be made of the strength, sensation, and functionality of the upper extremities. If one limb is nonfunctional, it may be the better choice for fistula creation. Chronic skin conditions that may increase the risk of prosthetic graft infection should be noted. Elderly patients with thin forearm skin may be better served with an upper arm access [3]. Obese extremities pose an increased risk of infection, and vessel depth may require a more involved procedure to superficialize the vein. Arterial examination should note the strength and symmetry of the brachial, radial, and

Table 10.2 Physical examination of the arterial and venous system as part of the preoperative surgical evaluation

	Exam	Relevance
Arterial assessment	Character of peripheral pulses, supplemented by handheld Doppler evaluation when indicated	An adequate arterial system is needed for access; the quality of the arterial system will influence the choice of access site
	Results of Allen test	Abnormal arterial flow pattern to the hand may contraindicate the creation of a radiocephalic fistula
	Bilateral upper extremity blood pressure	Determines suitability of arterial access in the upper extremities
Venous assessment	Evaluate for upper extremity edema or differential in arm size	Indicates venous outflow problems that may limit usefulness of the associated potential access site or extremity for access placement
	Examination for collateral veins	Collateral veins are indicative of venous obstruction
	Examination for evidence of previous central or peripheral venous catheterization	Use of central venous catheters is associated with central venous stenosis. Previous placement of venous catheter may have damaged target vasculature
	Examination for evidence of arm, chest, or neck surgery/trauma	Vascular damage associated with previous surgery or trauma may limit access sites
	Tourniquet venous palpation with vein mapping	Palpation and mapping allow selection of ideal veins for access

Adapted from Vascular Access Work Group [1]

ulnar arteries. An experienced examiner can determine if these vessels have normal compliance or are stiff due to calcific disease. Blood pressure must be measured in both extremities. A significantly lower blood pressure (10–15 mm Hg difference in resting systolic pressure) indicates a central arterial stenosis that may prevent adequate inflow. Examination of the anatomic snuff box at the base of the thumb between the extensor hallucis longus and the extensor pollicis brevis may reveal an adequate vein and a strong pulse in the adjacent radial artery branch for creation of a fistula, the distal most location for a functional fistula.

The Allen Test

The Allen test helps determine the integrity of the palmar arch, which is quite variable, connecting the radial and ulnar artery supply (Fig. 10.1). The value of this information is uncertain for fistula creation at the wrist, but an incomplete arch poses a risk of hand ischemia if the radial artery is ligated or inadvertently occluded. On physical examination, the test is performed by occluding the radial and ulnar arteries by compression while the patient's fist is clenched and then released. The hand becomes blanched and should rapidly become hyperemic on release of the radial artery (Fig. 10.2). Radial insufficiency is indicated if the palm remains blanched for at least 5 seconds after release of radial compression [4, 5].

A more quantitative assessment can be made using a continuous-wave Doppler placed over the palmar arch, while the radial and then the ulnar artery are occluded. Decrease in strength of the Doppler signal with radial or ulnar occlusion is an indication of an incomplete palmar arch. The hyperemic response may also be used to assess adequacy of flow. To test this response, the hand is clenched for 2–3 min and then released. If inflow is normal, hyperemia results in increased diastolic flow. Reactive hyperemia can be quantified by calculating the resistive index:

$$\left(\mathrm{PSV}-\mathrm{EDV}\right)/\mathrm{PSV}$$

where PSV is the peak systolic velocity and EDV the end-diastolic velocity. In one study, the arterial resistive index during reactive hyperemia was significantly lower in successful fistulas than in those that failed within 24 h (0.5 ± 0.1 versus 0.7 ± 0.2) [6]. Another approach is measurement of digital pressures with and without radial compression. A digital pressure less than 60 % of systemic pressure indicates an increased risk of symptomatic steal when a fistula is placed. Some laboratories use photoplethysmography (PPG) to assess the vasculature of the hand. PPG detects the amount of blood in the skin. The waveform is nearly identical that of arterial pressure. For preoperative testing, the PPG is used with a digital cuff to measure blood pressure in the thumb (Fig. 10.3) [4]. The normal waveform has a rapid upstroke with a sharp peak and dicrotic notch in the downslope. Thumb pressure should be above 80 mmHg and should not drop more than 30 % with radial compression. A dampened waveform and low pressures indicate an abnormal ulnar artery or palmar arch.

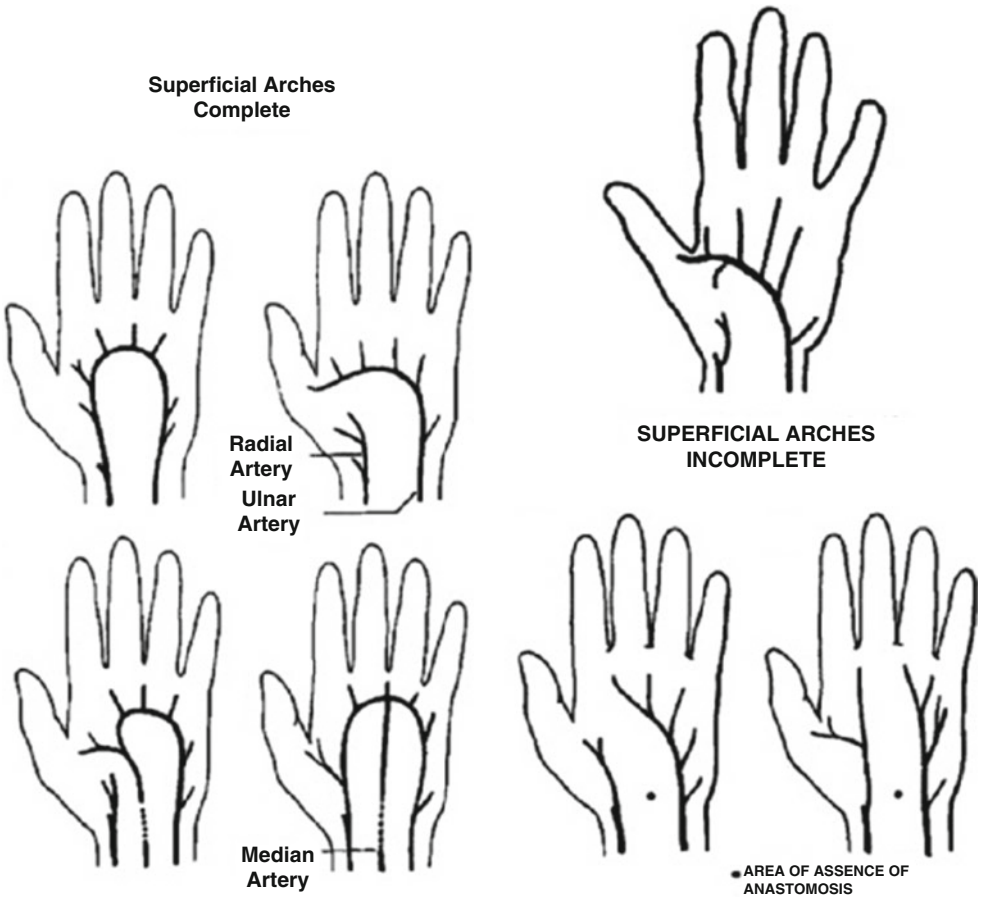

Fig. 10.1 Variations in vascular anatomy of the palmar arch. (used with permission from 17)

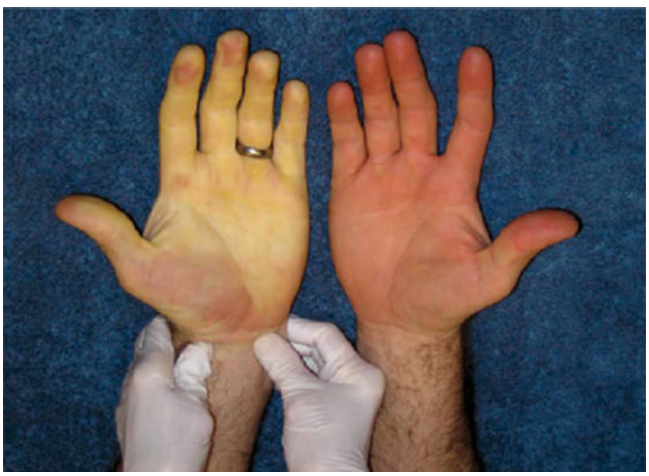

Fig. 10.2 The allen test, Blanching of the Hand with Compression. Allen test shows open left hand with radial and ulnar artery compression producing pallor of the hand and fingers. (used with permission from 4)

In a study of 287 patients undergoing cardiac surgery, 85 % had a normal Allen test as assessed by simple compression and observation. The remaining 43 underwent duplex scanning of the radial and ulnar arteries; only five were abnormal (2 % of the total group). All of these patients had their radial artery harvested with no adverse consequence to the hand [7]. Although renal failure patients are likely to have more diffuse and calcific disease of their upper extremity arteries than patients undergoing cardiac surgery, this study suggests that a simple Allen test in conjunction with duplex scanning can safely identify patients who will tolerate loss of radial artery perfusion to the hand.

Normal, healthy upper extremity arteries can supply fistula flow while continuing to adequately perfuse the hand. Steal occurs when the inflow is diminished due to central arterial stenosis or stenosis of the brachial or forearm arteries, which is particularly prominent in diabetic patients with renal failure. If there is uncertainty regarding the arterial inflow or the presence of stenosis of distal arteries that will be used for fistula creation, an arteriogram should be obtained.

Examination of the Veins

Normal venous anatomy of the upper extremity is shown in Fig. 10.4. When considering potential fistula sites, it is useful to keep in mind that a successful fistula needs to fulfill the rule of sixes at maturity: the vein should be at least 6 millimeters in

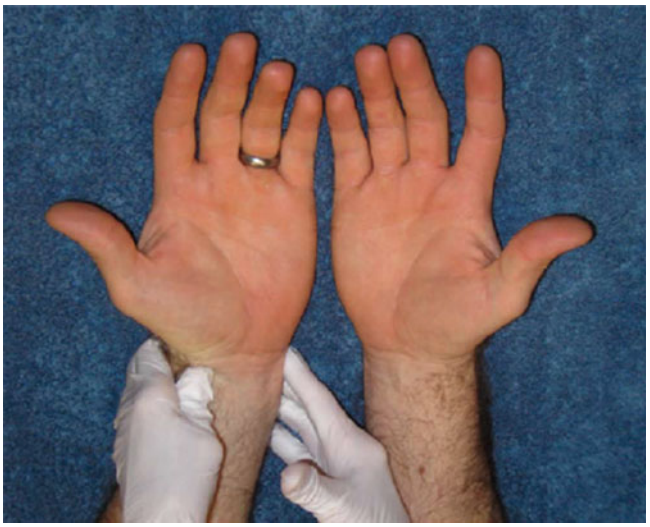

Fig. 10.3 The normal allen test. Allen's test shows open left hand with release of ulnar artery compression while radial artery compression is maintained. Note return of normal color to the hand. (used with permission from 4)

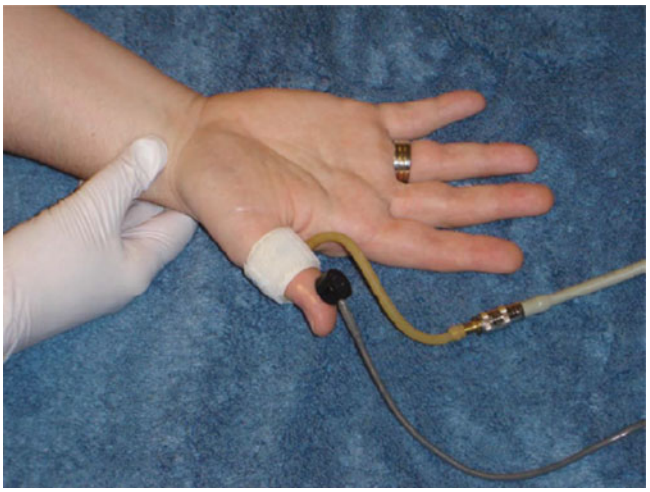

Fig. 10.4 A digit blood pressure cuff and photoplethysmograph (PPG) are used to measure changes in the thumb pressure and volume pulses with and without manual compression of the radial artery. (used with permission from 4)

diameter (generally 2.5 mm or better at creation); vein depth should be no more than 6 mm; and flow should be at least 600 cc/min. In addition, there should be a length of at least 10 cm of accessible vein for ease of access and adequate separation between the inflow and outflow needles to prevent recirculation. Therefore, the examiner needs to determine if the vein is of adequate diameter, is either not too deep or transposable to a superficial location, and is of adequate length.

Physical examination of the veins should be done with the patient in a comfortable environment and preferably well hydrated. Note should be made of prior venipunctures, which may cause synechiae in the vein or scaring of the wall that prevents adequate vessel dilation. Prominent veins on the chest wall, neck, or shoulder should raise suspicion for central venous obstruction, as does hand or forearm edema. Veins may be particularly difficult to examine if the patient has recently finished dialysis and is relatively volume depleted. The extremity is examined in a dependent position. Veins that are not prominent may be dilated by application of a tourniquet and repeated clenching and relaxation of the fist. Ultrasound vein mapping may not be necessary if the examination reveals a 4 mm or larger superficial cephalic or basilic vein in the forearm that is collapsible and can be traced to the elbow or a similar cephalic vein in the upper arm that extends from the elbow to the shoulder. Even in these cases, however, the office examination is enhanced by duplex ultrasound, which confirms vein diameter, patency, lack of thrombosis or stenosis, communication with more central veins, and adequate size and quality of the proposed inflow artery [8]. Occasionally, veins that were not adequate when measured preoperatively become large and dilated in the operating room following regional anesthesia. These veins may be prone to spasm and can sometimes disappoint when used as a fistula. The examiner should not overlook the basilic vein in the forearm, which is often preserved and can be used as a transposition fistula.

The clinical practice guidelines published by the Society of Vascular Surgery recommend the use of a tourniquet for vein mapping [3]. Some advocate two tourniquets, one above the elbow to occlude the deep veins and one below to occlude the superficial veins. Clinicians should be aware that this distended diameter may not predict success of the fistula as well as the non-distended diameter. Jayaraj and coworkers found that two-thirds of fistulas created with veins that were at least 3 mm in diameter without application of a tourniquet functioned successfully at 6 months, whereas only one-sixth of those that achieved this diameter only with the use of a tourniquet were successful [9]. Forearm veins should be examined even if the radial and ulnar arteries are stenotic since a proximal inflow source can be used, for example, by using a loop forearm brachiocephalic fistula or creating retrograde fistula using a proximal radial artery [10].

Vessel Imaging

Physical examination is not adequate to locate the most suitable vein in many patients, particularly those who are obese or elderly. Venography or magnetic resonance angiography, which will be addressed in depth in a subsequent chapter, can provide more detailed anatomic information, particularly regarding the central veins. However, venography only visualizes the veins and carries a risk of phlebitis and nephrotoxicity and adds significant cost [11]. Duplex scanning can evaluate both veins and arteries and

is now recommended as the modality of choice for preoperative imaging, although its cost-effectiveness and efficacy have not been proven [11, 12]. The duplex scanner combines B-mode imaging with a pulsed Doppler to allow acquisition of velocity information from specific locations within the visualized vessels. The image can be used to measure vessel diameters and to detect calcification of arteries or thrombus in veins, which prevents them from collapsing when compressed. Velocity waveforms are useful to detect stenosis, which is associated with an increase in velocity and poststenotic turbulence. Low arterial velocities indicate insufficient flow. Velocity and direction of flow can be displayed on the image using a color scale. This mode of imaging makes it possible to more rapidly locate vessels and areas of flow disturbance.

Central veins are difficult to evaluate with ultrasound, which cannot penetrate the bone or air cavities. However, duplex scanning often can detect central vein stenosis or obstruction from absence of spontaneous phasic flow, incompressibility, lack of augmentation with distal compression of the extremity, and lack of flow on color imaging (Figs. 10.5 and 10.6) [13]. Large collateral veins may also be seen in cases of chronic obstruction. When the patency of the central veins is in doubt, a venogram via puncture of the antecubital vein or magnetic resonance imaging may be warranted. In a retrospective review of hemodialysis patients with suspected central vein stenosis, 8 % had indeterminate duplex studies due to artifact from bones or indwelling catheters. In the remainder, duplex scanning had a specificity of 97 % and sensitivity of 81 % as compared to venography [13].

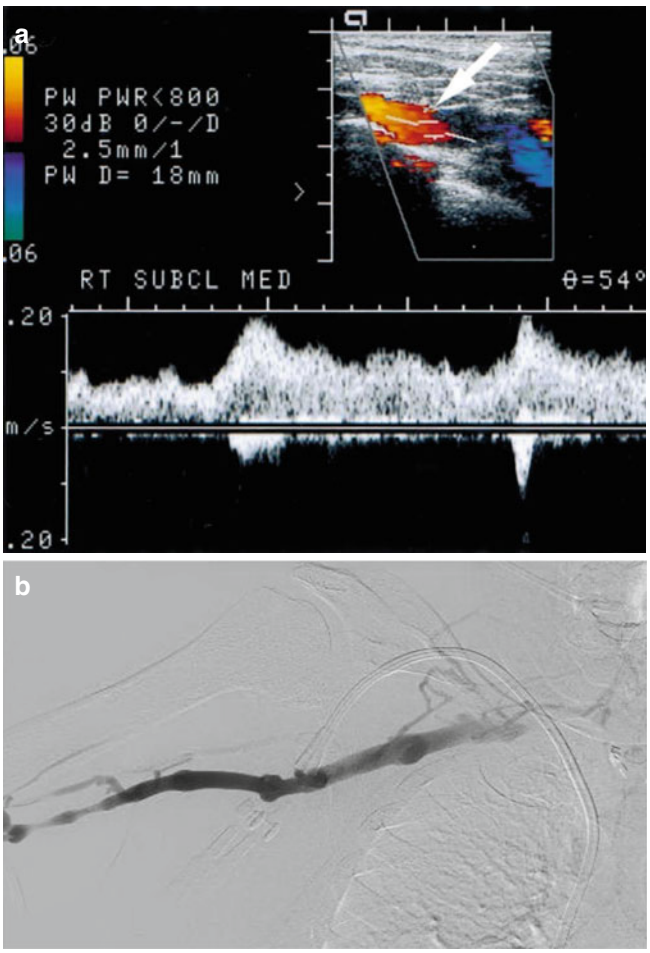

Fig. 10.5 Duplex detection of central venous stenosis. Preoperative US mapping in a 49-year-old man. (**a**) Longitudinal US scan of a patent subclavian vein (*arrow*). The Doppler waveform shows abnormal respiratory phasicity, with monophasic flow that does not decrease to baseline with inspiration. These findings are suggestive of central brachiocephalic venous or superior vena cava stenosis or occlusion. (**b**) Corresponding anteroposterior venogram shows 50% stenosis of the brachiocephalic vein (*arrowheads*) compared with the normal-caliber subclavian vein (*arrows*). (used with permission from 18)

Arterial Imaging

Normal peripheral artery waveforms are triphasic, with a forward component in systole followed by a reverse component as flow is deflected from the periphery and then a third forward flow component. Stenosis dampens this waveform, which becomes monophasic with significant stenosis (Fig. 10.7). At the site of stenosis, velocity increases to accommodate flow through the narrower channel. A doubling of velocity indicates a flow-restricting stenosis. These critical lesions have low-velocity and blunted waveforms proximal and distal to the site of stenosis. It is recommended that arteries should be at least 2 mm in diameter for a native fistula or graft. Calcification of the arterial wall can be evaluated on the ultrasound image (Fig. 10.8). Renal failure patients, many of whom are diabetic, are particularly prone to having calcification of the upper extremity arteries, a condition made worse due to secondary hyperparathyroidism. This process may involve the entire extremity including the digital arteries. Resulting stenosis makes the extremity susceptible to ischemia when a fistula is placed. Calcification also makes it more difficult to suture the vessels and may prevent the artery from dilating sufficiently to provide the amount of flow required for dialysis.

Arterial anatomy can be variable. The most common variant is a high takeoff of the radial artery. This variant, and any others, should be noted since knowledge of these anomalies can avoid confusion at the time of surgery. The surgeon may choose not to use such a radial artery as inflow for a fistula at the wrist if it is the dominant arterial inflow to the hand.

Venous Imaging

Duplex scanning can be used to determine if veins are patent or thrombosed both by detecting flow within them and

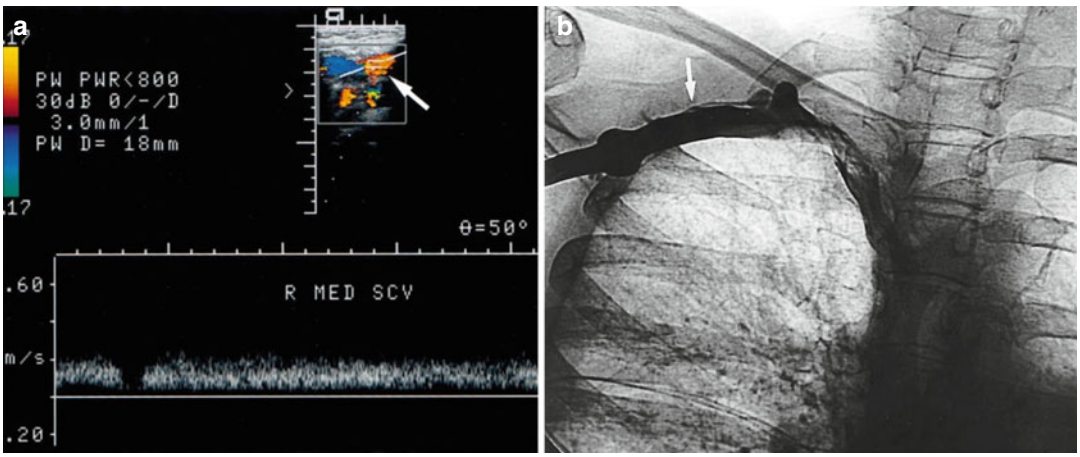

Fig. 10.6 Duplex scanning of central vein stenosis. Preoperative US mapping in a 49-year-old woman. (**a**) Longitudinal US scan demonstrates a patent subclavian vein (*arrow*) with abnormal respiratory phasicity, and monophasic flow that does not decrease to baseline, on the Doppler waveform. These findings are suggestive of central venous stenosis or occlusion. **b** The corresponding initial anteroposterior venogram of the subclavian vein (*arrow*). (used with permission from 18)

assessing their ability to fully collapse when compressed by the scanhead. Venous webs or scarring should be noted as should areas of sclerosis (wall thickening). Vessel diameters are best measured on longitudinal (long axis) view to avoid overestimation by oblique imaging of cross sections (Fig. 10.9). The scan should include central veins (Fig. 10.10), which may be stenotic due to prior catheterization, venipuncture, or thrombosis. Both deep and superficial veins of the upper extremity should be imaged, assessing for patency, diameter, and depth (Fig. 10.11). The basilic and cephalic veins should be imaged in the upper arm and forearm. The brachial veins at the elbow are of interest in patients being considered for a prosthetic forearm bridge graft. Some authors advocate a minimum vein diameter of 2.0 mm; most require at least 2.5 mm. In any case, the larger the vein, the greater the chance of success. The minimum diameter found along the entire length of the vein should be considered, not just the diameter at the proposed operative site. One study of 158 patients undergoing first-time dialysis access creation found that vein diameter was the prime predictor of access maturation; by multivariate logistic regression, age, gender, diabetes, and body mass index had no additional effect on outcome [14]. If dialysis is not likely for many months, there is little harm and much potential benefit in attempting a wrist fistula using a small diameter vein, perhaps as small as 2 mm. This approach has a negligible risk of harm to the artery or hand but results in more failures to mature and thus more subsequent procedures. Bridge grafts require slightly larger veins of 4 mm minimum diameter to supply adequate flow to maintain patency.

Table 10.3 outlines a recommended approach to preoperative vessel imaging. All potential veins should be mapped, including diameter, patency, depth, and areas of stenosis, thrombosis, or sclerosis (wall thickening). Note should be made of the location of vein branches that are 1 mm or greater in diameter as these may prevent maturation of the fistula by diverting flow. Assessment of vein depth is important because veins that more than 6 mm from the skin surface are difficult to cannulate unless they are quite large. Such deep veins may need to be superficialized at the time of fistula creation or some time later when it is known to have adequately matured. Because venous anatomy is variable, the examiner should be alert to possible duplicate systems or unusual locations of the major upper extremity veins. At the elbow, the antecubital vein, which connects the cephalic and basilic veins, should be included in the imaging. The anatomy of this vein is particularly variable and can be very important as it may provide the major outflow for a forearm cephalic vein that does not extend centrally into an adequate sized vein above the elbow. Also variable is the location at which the basilic vein joins the brachial vein in the upper arm. The examination should note this location as well as the size of the brachial vein which it joins since this vein is often used to extend the length of a transposed basilic vein fistula. In this case, it is useful to know if there is a second brachial vein of good caliber since using the brachial vein for the fistula could result in significant edema if it is the main outflow vein for the extremity.

Venous Imaging Technique

The patient should be examined in a semirecumbent position with the extremity slightly dependent, preferably at least 30 min after being in a warm environment, and well

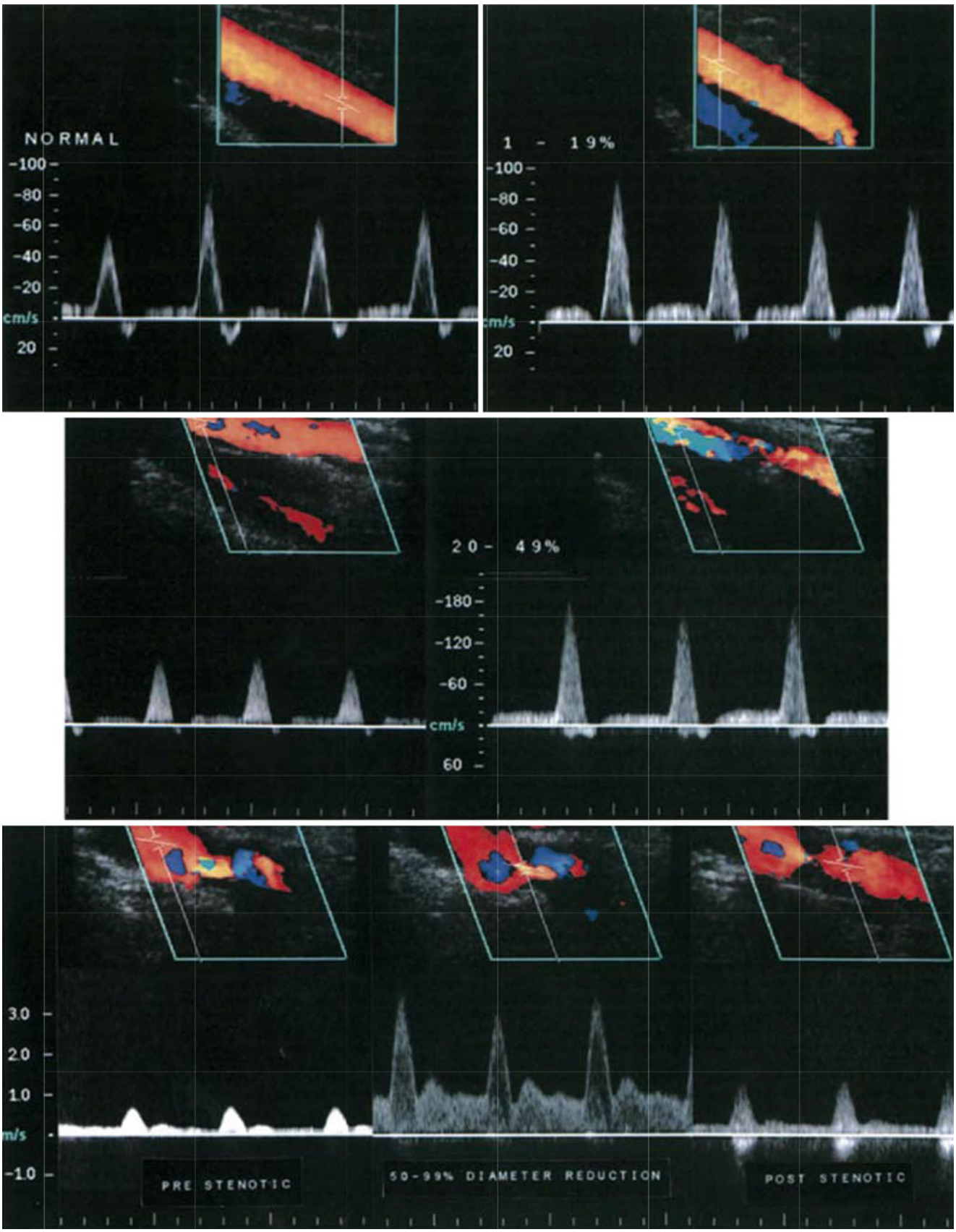

Fig. 10.7 Arterial velocity waveforms. Typical arterial doppler velocity waveforms. The normal waveform is triphasic. As the degree of stenosis increases, the waveform becomes dampened and monophasic and the peak velocities increase. Clinically significant lesions (greater than 50% narrowing) have a doubling of velocity as compared to a normal adjacent segment and the velocities are diminished proximal and distal to the stenosis. (used with permission from 19)

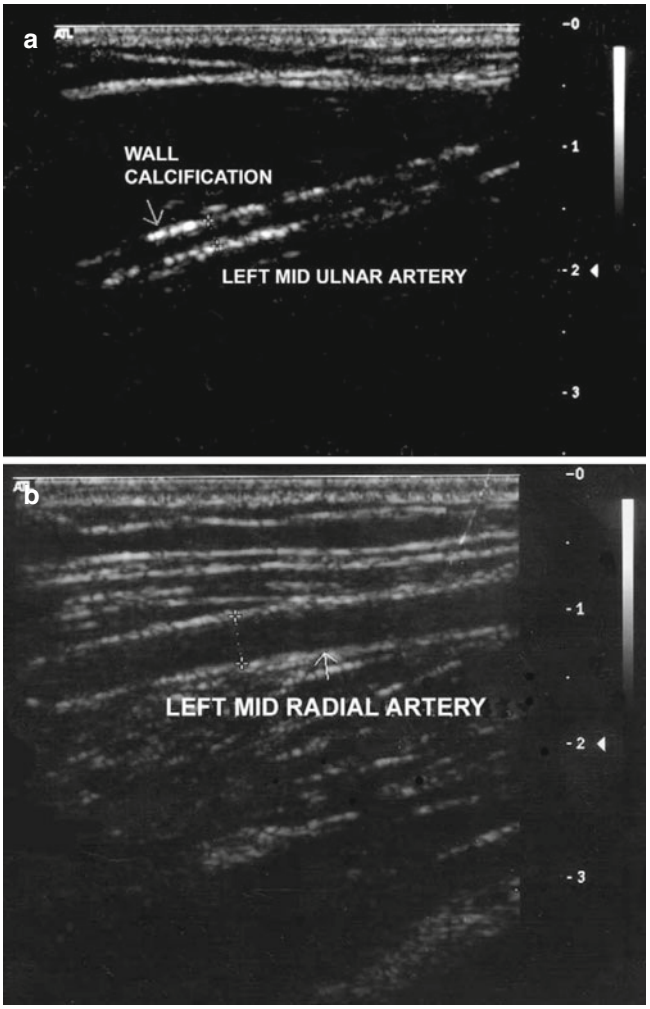

Fig. 10.8 Ultrasound detection of arterial calcification. (**a**) Demonstration of wall calcification (*arrow*) of the ulnar artery. (**b**) Ultrasonography image of a normal radial artery (*arrow*) in the same patient. (used with permission from 7)

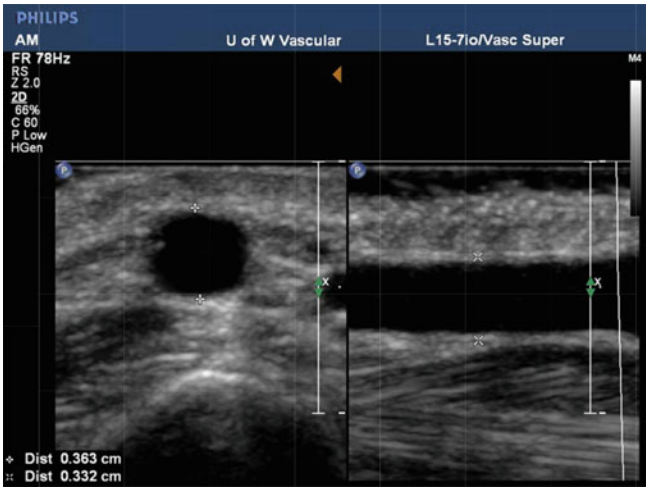

Fig. 10.9 Measurement of vein diameter. (used with permission from 20)

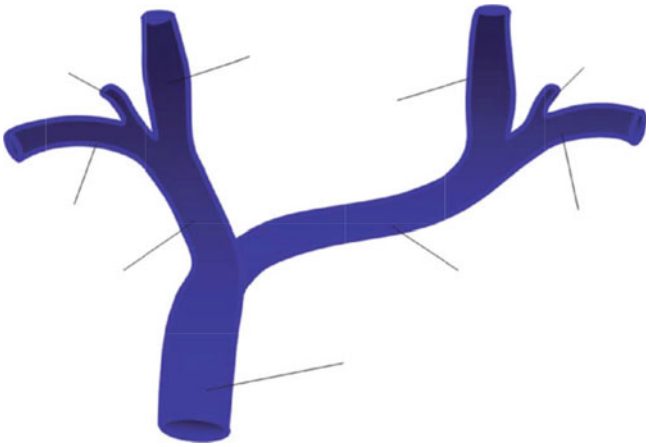

Fig. 10.10 Central venous anatomy. Anatomy of the upper extremity central veins. (used with permission from 20)

hydrated to promote vein distention. Heating pads, warm blankets, the use of warmed ultrasound gel, and exercise of the extremity can be helpful for optimal vein dilation. If the veins are too constricted, it may be necessary to bring the patient back at another time. Constricted veins have a "doughnut" appearance on ultrasound due to the thickened wall. In the operating room, the surgeon should reassess veins that were insufficient on preoperative examination that may dilate with anesthesia (regional or general) and hydration. Superficial veins should be examined with a relatively high-frequency probe (10–12 MHz) for optimal visualization. Some examiners routinely use a tourniquet, although as previously mentioned, veins that only dilate to adequate size with the tourniquet may not function as well as those whose diameter is adequate without this maneuver. For this reason, the examiner should always indicate when a tourniquet has been used. Percussion of the forearm veins, as is done prior to venipuncture, is a useful maneuver.

Routine Preoperative Duplex Imaging

Several authors have demonstrated that the routine use of preoperative duplex scanning changes the planned procedure in as many as 30% of cases, either using a vein rather than a prosthetic or using a different vein (Fig. 10.12) [15]. Allon and coworkers reported an increase in fistula rate from 34 to 64% with preoperative duplex scanning [8]. There is little doubt that preoperative duplex scanning gives the surgeon useful information, but there is not yet clear evidence that it results in an improved rate of fistula maturation. In a 2013 review of the literature, only three randomized trials were found comparing

Table 10.3 Preoperative vein mapping protocol obtained in the vascular lab

Central venous mapping
Scan the innominate, subclavian, and axillary veins to evaluate for patency and flow pattern
Superficial venous mapping
Scan the cephalic vein from the wrist to shoulder, noting any anatomic anomalies and evidence of phlebosclerosis. Diameter should be carefully documented throughout the entire course of the vein. Map and mark the vein
Scan the basilic vein from its origin to its confluence with the brachial vein near the axilla, noting any anatomic anomalies and evidence of phlebosclerosis. Diameter should be carefully documented throughout the entire course of the vein. Map and mark the vein
Document patency and size of the median cubital vein. Map and mark the vein
If no acceptable vein is found, proceed to the contralateral arm
Arterial mapping
Obtain bilateral brachial systolic blood pressures and Doppler waveforms
Scan the brachial, radial, and ulnar arteries, documenting any evidence of atherosclerosis, abnormalities, or anomalies (e.g., high bifurcation of the brachial), and any stenosis, which must be confirmed with spectral waveform analysis
Allen's test may be performed if the veins are acceptable
If abnormal (digit pressure drops to <80 mmHg or a >30 % drop with compression of the radial artery), proceed to the next limb area. If normal, measure ipsilateral first and third finger pressures (if not already done)
If neither upper extremity is acceptable, proceed to the lower extremity

Adapted from Lok [16]

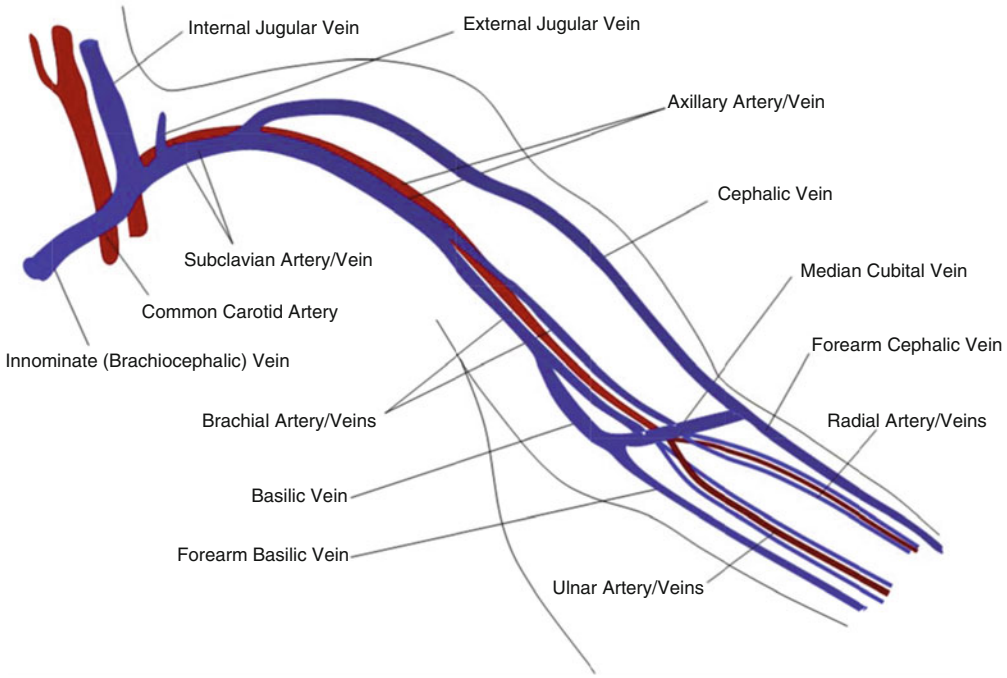

Fig. 10.11 Peripheral venous anatomy. (used with permission from 20)

preoperative duplex ultrasonography to clinical examination [11]. Meta-analysis revealed a nonsignificant trend toward more successful arteriovenous fistulas with preoperative duplex scanning. Two of these three trials showed benefit; one showed none. In all cases, the outcome was not access function but merely a thrill or bruit within 24 h.

In our own practice, although we routinely use preoperative duplex scanning, we ultrasound the patients in the operating room immediately prior to access surgery to confirm adequacy of the proposed artery and vein and to assure our understanding of their anatomy.

Patients Who Have Had Prior Access

With each access failure, the challenge of finding an appropriate location for the next fistula or graft becomes more challenging. Distorted anatomy can make the examination

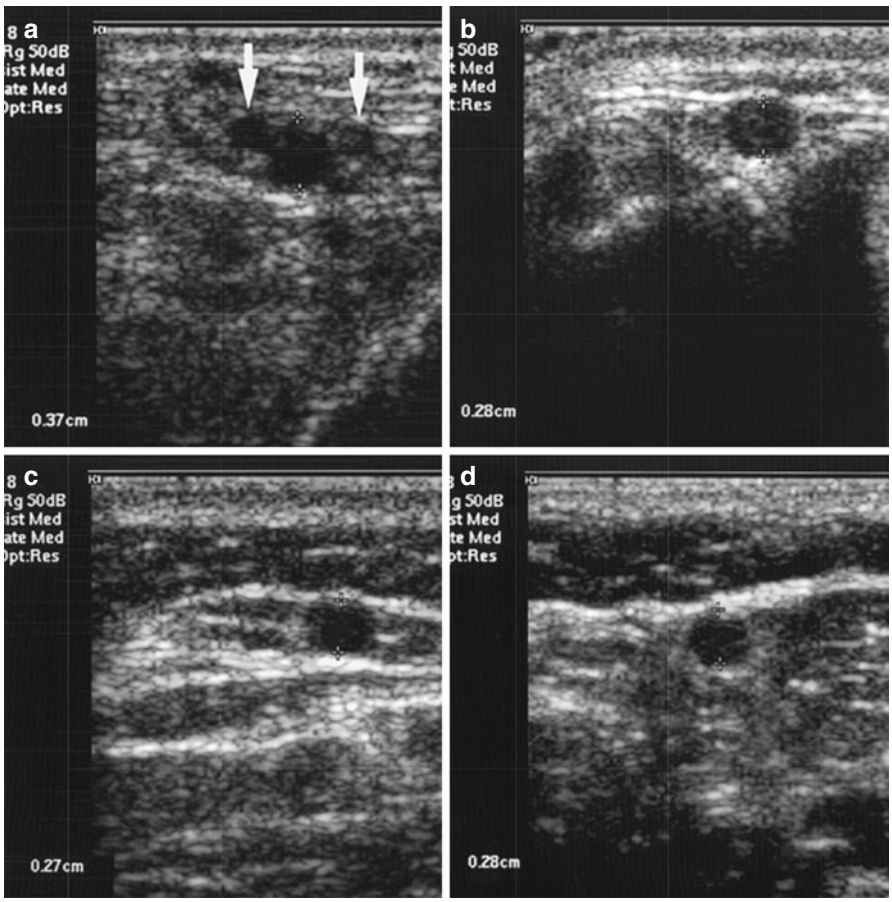

Fig. 10.12 Ultrasound detection of an adequate peripheral vein not visible on physical examination. Preoperative US mapping in a 50-year-old man with a nonpalpable cephalic vein in the wrist who was scheduled to receive a forearm graft. After US mapping, a successful forearm arteriovenous fistula was placed. (**a**) Transverse US scan demonstrates adequate diameter of the left radial artery at the wrist. The arrows point to small adjacent radial veins. (**b**–**d**) Transverse US scans of the cephalic vein in the (**b**) wrist, (**c**) middle forearm, and (**d**) antecubital area. (used with permission from 18)

difficult, particularly if details of prior procedures are not available. The examiner should always return to first principles and reevaluate all possible sites for access, starting in the forearms. There may be an overlooked basilic vein in the forearm, or an upper arm cephalic vein that was inadequate on a prior examination may have matured as a result of increased flow from a forearm fistula. Deep veins and central veins must also be reexamined. They may have developed stenoses or thrombosis in the interval since the prior examination as a result of a prior fistula, which can cause stenosis, possibly due to hemodynamic factors or reinfusion of blood with procoagulant and proinflammatory factors that have been activated by the dialysis system. Other patients may have had vein injury due to tunneled catheters that were used while waiting for a more permanent access to mature. When no suitable location is found in the nondominant extremity, the dominant extremity should be examined, unless the patient is dependent on this extremity for essential activities, in which case other sites should be considered first. If neither upper extremity has suitable veins for access creation, but the brachial arteries are adequate (there has been no problem with arterial steal), then the central veins should be reassessed for potential use of a hybrid graft-catheter, such as the HeRO™ device. This device uses the brachial artery for inflow into a prosthetic graft which is connected to a central catheter for outflow.

Another option is the use of the femoral vein and artery for creation of access in the thigh. In this case, the ankle-arm index should be measured bilaterally. With the patient supine, the blood pressure cuff is placed just above the ankle, and a handheld, continuous-wave Doppler is used to detect return of flow as the pressure in the inflated cuff is released. This procedure is performed using both the dorsalis pedis and posterior tibial artery. Blood pressure is measured in both upper extremities using the cuff above the elbow and detecting flow at the brachial or radial artery below. The ratio of the higher ankle pressure to the higher brachial pressure gives an indication of whether or not there is arterial occlusive disease in the extremity. The normal index range is 0.9–1.2. Values below this indicate arterial occlusive disease and above indicate abnormally stiff arteries due to medial wall calcification. If the index is abnormal, compromise of the lower extremity blood supply by a groin fistula could result in steal and limb threat. In many cases the tibial vessels will be calcified, leading to false elevation of the ankle pressures or completely incompressible vessels. This finding does not necessarily indicate stenosis of these vessels and should be followed by toe-brachial pressure measurements and duplex scanning to

determine the extent, if any, of arterial obstructive disease. Lower extremity examination should include documentation of the extent of calcification of the common and superficial femoral arteries and the patency of the profunda femoris artery. The accompanying veins should be assessed for patency and normal phasicity to assure that there is no local or more central venous stenosis or occlusion. The size and patency of the saphenous vein should also be determined, although the use of this vein for creation of a fistula has been disappointing.

Summary

The goal of the preoperative evaluation of patients for dialysis access requires input from the entire team, including the patient, nephrologist, surgeon, dialysis provider, and social worker. The examiner should start with establishing the long- and short-term goals of care, which will dictate the type of access. The history should determine hand dominance and the presence of comorbidities that may affect access function. Physical examination starts with evaluation of extremity function and the integrity and health of the skin. The experienced examiner can determine if there are arteries and superficial veins that are clearly suitable candidates for fistula creation, but duplex scanning is confirmatory and may locate superior vessels. Its use is becoming routine. The success rate of fistula creation is highest when using noncalcified arteries at least 2 mm in diameter and veins at least 2.5 mm in diameter. Because success correlates with vein diameter, larger veins should be used when delays due to failure of the fistula to mature cannot be tolerated. Evaluation of patients with prior failed fistulas should begin with a search for veins that may have been overlooked in prior examinations and then should move to secondary locations, such as the femoral vessels.

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Strategies of Arteriovenous Dialysis Access

11

Bao-Ngoc Nguyen and Anton Sidawy

According to the report from United States Renal Data System in 2014, there were more than 600,000 patients with end-stage renal disease who were on hemodialysis (HD) and 80 % of these patients initiate hemodialysis with a central venous catheter (CVC) [1]. The mortality associated with using a CVC for dialysis is significantly higher than dialysis using an arteriovenous fistula (AVF) or an arteriovenous graft (AVG) [2]. The risk of death in the first year with CVC use is greater than 50 % [3]. As a result, early preparation for long-term dialysis access placement such as an AVF or an AVG is highly recommended. It is undisputable that the outcomes of a functional AVF are much better than those of an AVG because of better long-term patency, lower frequency of infection, and required intervention to maintain patency [4, 5]. In 2003, the Fistula First Initiative called for a 65 % prevalence of dialysis patients using an AVF by 2009. As a result, AVF placement increased from 24 to 52 % between 2000 and 2008 [6]. Nevertheless, increasing AVF placement and reduction of AVG use did not translate to an improvement of overall patient outcomes because the reported rates of non-maturation of fistula also increased from 25 to 60 % [6–8]. Because most patients referred for long-term access are already on HD via a CVC, higher rate of fistula failure leads to prolonged catheter-dependent time and catheter-associated complications [7, 9], thus negates the potential long-term benefit of AVFs over AVGs. As a matter of fact, Disbrow and associates observed that for patients who were referred for first-time long-term access and were already on HD via a CVC, those who had AVF splaced had doubled catheter days compared to those with AVGs without any added benefit toone- or 2-year secondary patency or the number of interventions needed to maintain patency [10]. As a result, in 2006, an update from the Kidney Disease Outcomes Quality Initiative (KDOQI) reevaluated the concept of "fistula first at all costs" and recommended that a functional fistula should be the goal and emphasized that "individualizing patient care" or "patient first" should be the focus [11]. This approach requires thoughtful preoperative strategies for each and every patient who needs long-term dialysis access.

In order to address this complex decision-making process regarding the best long-term access for each dialysis patient, Allon and associates suggested an individualized approach based on the following four factors: (1) initiation of dialysis, (2) patient's life expectancy, (3) history of previous failed dialysis access, and (4) the likelihood of fistula non-maturation [12] (Fig. 11.1). Based on this algorithm, a patient whose life expectancy of less than 2 years and has prior failed access would benefit more from an AVG rather than an AVF unless the risk of fistula non-maturation is less than 25 %. On the other hand, if he/she has a good life expectancy and no prior history of failed access, a fistula should be considered first unless the risk of fistula non-maturation is greater than 75 %. For those patients in between these two extreme categories, the choice between fistulas and grafts is best made with the "patient first" and "catheter last" philosophy.

Life expectancy is important in the decision-making process because elderly patients who initiate dialysis in their 70s are more likely to die from their comorbidities which minimize potential long-term benefits of AVFs over AVGs. The survival for patients who are greater than 75 years old and on HD is 53.5 % at 1 year and decreases to as low as 2.4 % at 5 years [13, 14]. Whereas a mature fistula is superior to a graft, an immature fistula resulting in prolonged catheter dependence is inferior to a working graft. Therefore, an AVG may be a more sensible choice for this patient population with short life expectancy. This issue was addressed in a study by Desilva and associates who analyzed the data from the US Renal Data System on pre-dialysis vascular access placed on elderly patients. The authors found that although grafts had a slightly higher mortality compared to fistula for patients from 67 to 79 years old, the difference

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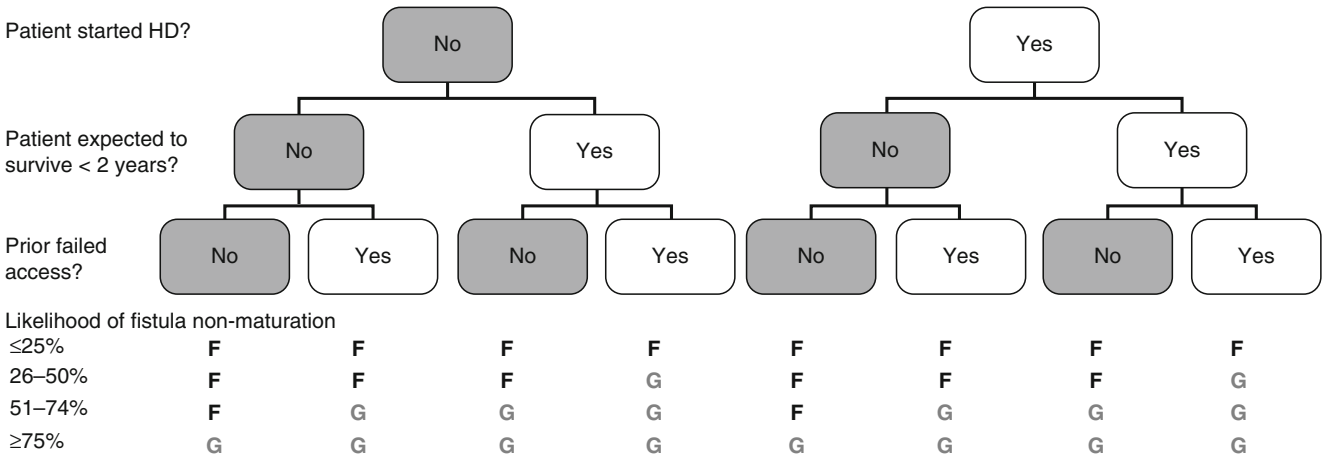

Fig. 11.1 A suggested algorithm for individualized approach regarding the most appropriate dialysis access for each patient. The four clinical factors used to make the decision are the initiation of dialysis, patient life expectancy, history of previous failed access, and likelihood of fistula maturation (From Allon and Lok [12])

was not significant for the patients over 80 years old [15]. Drew and associates studied elderly patients who were on HD via a CVC also confirmed that the overall advantages of an AVF over an AVG were less among patients older than 60 years old, particularly women with diabetes [16]. Therefore, fistula is not necessarily the first choice for elderly patients because there was no clear benefit in terms of mortality over the grafts in the octogenarians and nonagenarians [15].

The likelihood of fistula non-maturation is another important factor in the decision-making process of the best access for dialysis patients. The reported rate of fistula non-maturation in multiple series varies widely between 9 and 70 % [17–21]. The location of the fistula is one factor that affects maturation. Whereas the average rate of maturation for a distal radiocephalic fistula is 55 %, that of a brachiocephalic or brachiobasilic fistula is closer to 90 % [20]. Older age, female sex, African-American, and vascular morbidity have been shown to associate with higher risks of non-maturation [8, 17, 22, 23]. The decision-making process would be easier if there is a reliable way of predicting the probability of fistula failure based on a patient's preoperative characteristics. Lok and associates built a model to predict the risk of fistula non-maturation based on the four patients' preoperative characteristics such as age, coronary artery disease, peripheral vascular disease, and race [22]. Patients with each of these parameters were at higher risks for fistula non-maturation and were assigned a risk score (Fig. 11.2). The total score could range from 0 to 10.5 and was stratified into four different groups of low (24 %), moderate (34 %), high (50 %), and very high (69 %) risk for fistula non-maturation (Fig. 11.3). The authors recommended a different alternative to AVF in the "very high risk" group but would consider AVFs for the first three groups with the understanding that more preoperative work-up and postoperative intervention are needed for the moderate and high-risk groups (Fig. 11.4).

Using the algorithm from Allon et al., the risk model of fistula non-maturation from Lok et al., and the guidelines from the Society for Vascular Surgery [24] as the foundation for this chapter, we will now discuss the individualized strategy regarding the most suitable upper extremity access for each patient based on the availability of the superficial veins in the arms. The strategy for lower extremity and other complex hemodialysis access in the unusual locations (i.e., the chest and the abdomen) is discussed in details in other chapters.

Cephalic Vein in the Forearm Is Adequate

The radiocephalic fistula is a very good configuration because it requires minimal dissection and provides a very reliable access that is free of complications for multiple years. The disadvantage of this configuration is a relatively greater risk of primary failure and interventions required to promote maturation, especially in elderly, female, and diabetic patients [25, 26]. Nevertheless, it is worth the attempt in young and pre-dialysis patients even in equivocal cases because even if it fails, it does not affect the creation of a secondary access at more proximal sites. Although some studies have demonstrated little association between the vessel size and the likelihood of fistula maturation [27], most centers require a minimum arterial diameter of 2 mm and a minimum venous diameter of 2.5–3 mm [28]. When diameter of the vein is less than 2 mm, only 16 % of fistula matured compared to 76 % when the diameter is greater than 2.5 mm [29].

Variable	Points score	Variable definitions
Age > 65 yrs	+2	Age at time of fistula creation
PVD	+3	Documented lower extremity revascularization, digit or extremity amputation, history of claudication and ischemic extremity changes or gangrene
CAD	+2.5	Documented coronary stenosis by angiography or history of myocardial infarction or previous coronary revascularization by angioplasty, stenting, or bypass surgery
White	–3	Not of black, Asian, aboriginal, or other non-European descent
Baseline score	+3	All patients are given baseline score of 3
Total		Sum of scores

The total score could range from 0 to 10.5.

Fig. 11.2 A scoring system based on four major preoperative parameters for each patient (From Lok et al. [22])

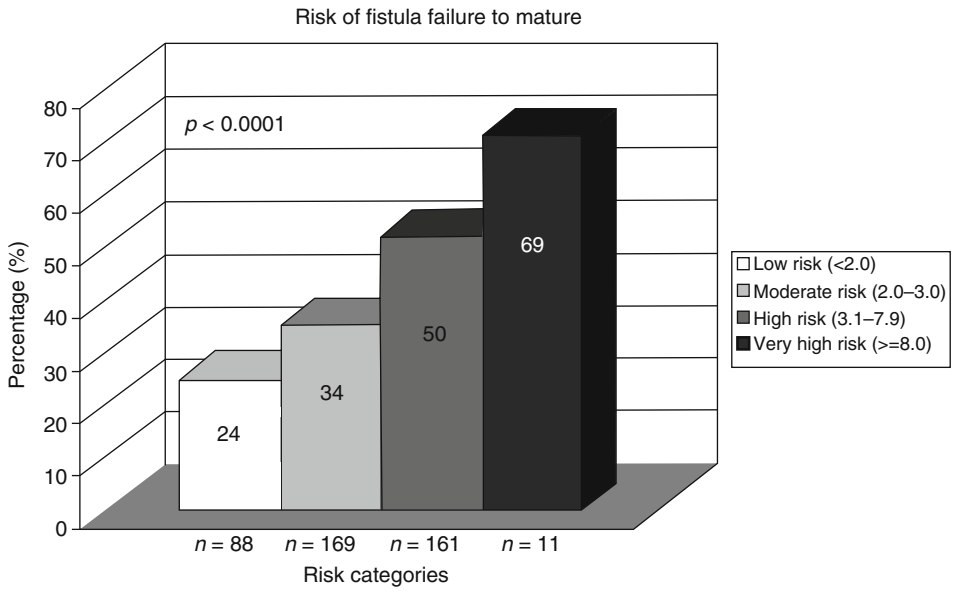

Fig. 11.3 Risk categories of fistula non-maturation (From Lok et al. [22])

Score	Risk category[b]	Clinical application[c]
<2.0	Low risk: 25%	PE[d] ± duplex ultrasound; create AVF
2.0–3.0	Moderate risk: 35%	PE,[d] duplex ultrasound ± venogram; create AVF
3.1–6.9	High risk: 50%	Arteriogram + venogram and appropriate preoperative intervention as necessary; create AVF with very close postoperative monitoring (*e.g.*, weekly or biweekly), and anticipate the need for aggressive intervention to facilitate maturation
≥7.0	Very high risk: 70%	Consider another form of permanent access (*e.g.*, graft); continue to avoid catheter use

Fig. 11.4 An example use of the predicted risk categories of fistula non-maturation (From Lok et al. [22])

Cephalic Vein in the Forearm Is Inadequate

When the cephalic vein in the forearm is not suitable for a fistula (or there is a failed forearm radiocephalic fistula), vein mapping or physical examination should measure the caliber of the basilic vein in the forearm as the next potential conduit. Although the basic vein needs to be transposed and requires more dissection, the primary and secondary patency rates of AVF from the basilic vein (54.7 and 76.7 %) are comparable to that of the cephalic vein (49.3 and 71.3 %) [30]. The rate of maturation failure is between 20 and 24 % [31, 32]. When the radial artery is greater than 2.5 mm and basilic vein diameter is greater than 3.5 mm, the cumulative patency of radio-basilic fistula is 93 % after 1 year, 78 % after 2 years, and 55 % after 3 years. Utilizing the basilic vein in the forearm helps preserving the proximal veins of the upper arm for future access which is essential in the younger patient population.

When neither the cephalic nor the basilic vein in the forearm is a good option, and the cephalic vein in the upper arm is available, a dilemma exists between a forearm AVG or an upper arm AVF as the next best alternative. Brachiocephalic AVFs have a maturation rate as high as 90 % [33]. As a matter of fact, in order to maintain a high fistula creation rate without increasing catheter-dependent time, some surgeons favored brachiocephalic fistula over forearm fistula unless a patient's anatomy is ideal for a radiocephalic fistula [33, 34]. This approach is especially sensible in elderly patients where site preservation for future accesses is not as relevant as for the younger patients. Whereas only 26 % of patients with forearm fistulas were able to avoid CVC with initiation of dialysis, 43 % of patients with upper arm fistulas were able to do so because of better maturation rate and shorter maturation time [35].

Although brachiocephalic AVFs have a high success rate and respectable long-term patency, the risk of complication such as arterial steal is not insignificant [36, 37].As a result, using the proximal radial artery instead of the brachial artery as the source of inflow was suggested as a better alternative. The proximal radial artery has larger caliber and is generally less calcified/diseased than the radial artery at the wrist level; therefore, it should provide adequate arterial inflow and at the same time lower the risk of arterial steal syndrome with brachial artery fistulas. The long-term patency of proximal radiocephalic AVF could be as high as 80 % at 42 months with no ischemic complications [38]. There are several reported configurations for proximal forearm fistula construction such as side-to-side anastomosis between the proximal radial artery and median antebrachial vein or end-to-side anastomosis between the medial antecubital vein and the proximal radial artery [39] (Fig. 11.5). The mean time to maturation of the radio-median cubital vein or radiocephalic AVF at the elbow was 26 ± 5.2 days [39]. Failure rate was as low as 2.5 % with similar patency to brachiocephalic AVFs. Furthermore, using the median cubital vein allows arterialization of both the cephalic and basilic veins for venous outflow [39]. Another reason that makes the proximal radiocephalic AVF an attractive alternative is the delay of the need to proceed to a more proximal location while still preserving the option for future placement of a brachiocephalic fistula [40].

Although the KDOQI guideline recommended brachiocephalic AVF before forearm AVG, there is currently no randomized controlled trial comparing the outcomes of these two types of access. The configurations of the forearm AVG could be either straight or loop dependent on the sources of arterial inflow. If the radial pulse is palpable and has good quality, a straight forearm AVG from the radial artery to the antecubital vein is a good option. A retrospective study by Lee and associates reported that for patients with previously failed forearm AVFs, upper arm AVFs had higher failure rate than forearm AVGs (44 vs. 20 %), required more interventions for maturation and longer catheter dependence (131 vs. 34 days), and had more episodes of CVC-associated bacteremia (1.3 vs. 0.4 per patient) [41]. Survival was better for AVF when primary failures were excluded but similar when primary failures were included [41]. As expected, AVFs were only more advantageous over the AVGs once they became functional, due to less required intervention to maintain patency. Proponents of "forearm AVG first" also emphasize that the presence of a forearm AVF could promote dilation of the upper arm veins to allow a future construction of a brachiocephalic AVF once the forearm AVG fails [42]. As a matter of fact, forearm AVGs have been used as a "bridging" strategy to allow earlier cannulation and avoid CVCs for patients with late referral for long-term access placement, with the understanding that an AVF will be placed in the future upon the impending failure of the AVG. Nevertheless, in order for this "bridging" strategy to work, the venous

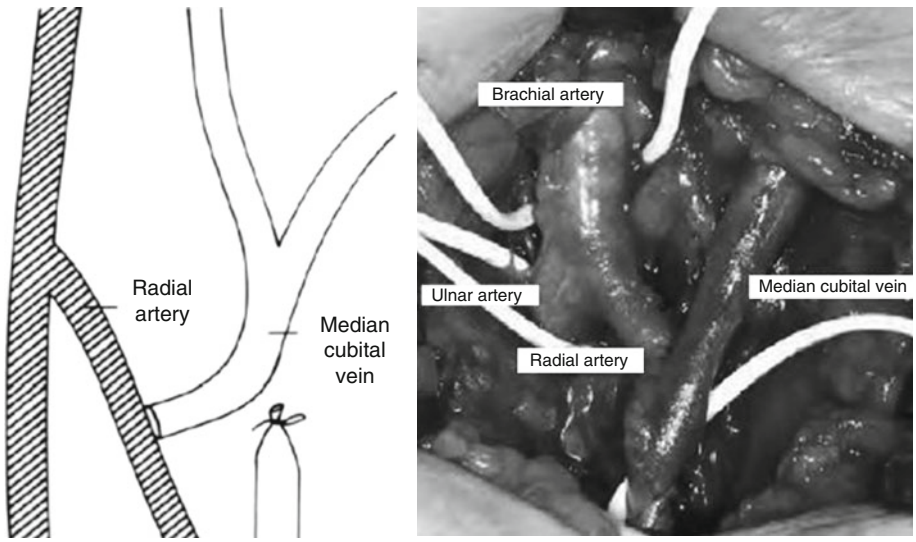

Fig. 11.5 Proximal radial-median cubital fistula (From Kumar et al. [39])

anastomosis of the AVG should not cross the elbow, and repeated angioplasties or thrombolysis to salvage the AVGs should be avoided to prevent damaging the outflow veins.

Cephalic Vein in the Entire Arm Is Inadequate

When the cephalic vein in the entire arm is no longer available for a fistula conduit, the next viable option is either a forearm AVG or a brachiobasilic-transposition fistula (BBAVF). Although a BBAVF has the advantage of less complication such as infection and thrombosis (a 1-year patency of 69 % [43]), this configuration should not be an automatic first choice for every patient because of higher perioperative morbidity such as arm swelling, pain, bleeding, and higher steal than other fistula. In contrast, a forearm AVG is technically easier to construct, requires less time to cannulation, and has higher success rate after reintervention. When a BBAVF was compared to forearm loop AVGs (PTFE) in a randomized controlled trial for patients with no options for radiocephalic or brachiocephalic AVF, Keuter and associates reported significantly better patency and fewer interventions in the BBAVF group compared with the PTFE group and concluded that BBAVF is the preferred choice for vascular access [44]. However, although another randomized controlled trial by Morosetti and associates also confirmed superior long-term outcomes of BBAVF over forearm AVGs, they required longer hospital admission time, total intervention time, and mean interval to maturation. The authors concluded that BBAVF should be reserved for patients with good life expectancy but AVGs should be used for patients with compromised clinical conditions [45] such as vein diameter of less than 3 mm [46], elderly patients especially women with diabetes due to twofold higher risk of non-maturation for every decade increase in age [47, 48].

Superficial Veins in the Forearm Are Not Available

Finally, if there is no superficial vein available, the general guidelines recommend a forearm loop graft first for site preservation before placing a brachial-axillary AVG. The potential venous outflow sites for forearm AVGs are the median antecubital vein, the cephalic vein, and the basilic vein at the elbow. For upper arm AVGs, the cephalic and basilic veins as well as the deep veins (brachial and axillary) can be used [49]. Although the larger caliber of the venous outflow of the brachial-axillary AVG would suggest better outcomes than forearm AVGs, there is no evidence confirming this assumption. Indeed, the patency of forearm AVGs is similar to that of upper arm AVGs [49]. Therefore, unless the venous outflow at the level of the elbow is suboptimal, forearm AVGs should be attempted first before proceeding to the brachial-axillary configuration.

In conclusion, although AVFs should still be considered for each patient, "fistula first at all costs" is not the current practice. Patient's access history, life expectancy, and risks of AVF failure should be taken into consideration. The modern approach favors individualized strategy with "patient first" and "catheter last" which means sometimes that a functional AVG is a better alternative than a failed AVF. The selective use of AVGs could be a sensible option in elderly patients with multiple comorbidities, short life expectancy, and high risk for AVF failure who depend on CVCs for HD. In younger patients with late referral for long-term access, forearm AVG placement as a "bridging" strategy could shorten or avoid the time of CVC dependence and allow arterialization of the upper arm veins in order to prepare for AVF placement at the time of impending graft failure rather than salvaging AVGs multiple times and ruining the outflow veins [50]. Nevertheless, a patient who is about to embark on a potentially life-changing process of hemodialysis needs more than a good vascular surgeon because even the best surgical strategy could not replace the caring and thoughtful medical and emotional support from a multidisciplinary team of the primary care physicians, nephrologists, transplant surgeons, and supporting staff of an excellent dialysis center.

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12 Anesthesia and Perioperative Management Considerations for the Patients Undergoing Hemodialysis Access Procedures

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Introduction

Patients with end-stage renal disease (ESRD) have an adjusted all-cause mortality rate that is 6.4–7.8-fold higher than the general population, and chronic kidney disease (CKD) is an independent risk factor for postoperative death and cardiac events [1]. Procedures to establish hemodialysis access are common in this patient population that carries a high degree of comorbidities. This chapter will describe the essentials of anesthesia management for hemodialysis access surgery.

Preanesthesia Preparation

Preanesthesia Clinic

Safe and effective anesthesia management starts with appropriate preoperative evaluation. This is most efficiently performed in a preanesthesia clinic where it is essential to identify the comorbidities that are common to patients with chronic kidney disease (CKD) or end-stage renal disease (ESRD). The main role of the preanesthesia clinic visit is to identify correctable problems and optimize the management of the comorbid conditions.

Cardiovascular disease is the most frequent cause of death in patients with ESRD [2]. Table 12.1 summarizes the comorbid conditions commonly seen in patients with ESRD. Once identified, measures should be taken to medically optimize the comorbidities in order to minimize the risk of surgery and anesthesia. Current guidelines recommend checking a baseline electrocardiogram (ECG) in patients who have risk factors for or documented cardiovascular disease [3].

Hypertension is common in this population, and good control should be achieved to minimize perioperative instability. Additionally, the patient should be instructed to schedule hemodialysis the day prior to the surgery, as well as counseled on what to do regarding their regular medications. It is somewhat controversial, but in general, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are not given on the day of surgery because of the risk of significant hypotension at induction of anesthesia.

In the patient with diabetes, a balance must be achieved between best controls of blood glucose while minimizing the

Table 12.1 Comorbid conditions in incident HD dialysis patients starting dialysis between 2003 and 2008

Comorbidity	Number	Percentage (%)	Median age (years)
Angina	1845	16.9	71.3
MI in past 3 months	339	3.1	70.7
MI > 3 months ago	1304	11.9	70.8
CABG/ angioplasty	837	7.7	69.0
Cerebrovascular disease	1,177	10.8	71.1
Diabetes (not listed as PRD)	977	9.1	70.9
COPD	855	7.9	70.8
Liver disease	329	3.0	60.0
Claudication	957	8.7	70.6
Ischemic/neuropathic ulcers	410	3.7	62.6
Angioplasty/vascular graft	411	3.8	71.4
Amputation	248	2.3	61.3
Smoking	1629	15.3	61.2
Malignancy	1457	13.3	72.0

Modified from Trainor et al. [4]

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risks of hypoglycemia. While insulin doses should be tailored to each individual patient, basic guidelines can be followed:

- Night before the procedure:
  - Neutral Protamine Hagedorn (NPH)/Levemir and mixed insulins: 100 % of usual dose
  - Lantus: 80–100 % of usual dose
- Morning of the procedure:
  - NPH/Levemir: 50 % of usual dose
  - Lantus: 80 % of usual dose
  - Mixed insulin: 33 % of usual dose
  - Regular/short-acting insulin: HOLD

Routine labs may also be helpful in the preoperative setting to rule out major metabolic derangements, including a complete blood count, a chemistry, and a coagulation panel with repeat evaluation of pertinent labs on the morning of the procedure.

Same-Day Evaluation

Most procedures to create hemodialysis access are outpatient procedures with patients arriving 1–2 h prior to the planned procedure start. The preanesthesia interview in the preoperative holding area is one of the most important phases in preparing the patient for the administration of anesthesia. The anesthesia team should review the preanesthesia evaluation completed in the preanesthesia clinic and confirm that the patient's general condition has not changed since the preanesthesia clinic evaluation. Intravenous access and blood pressure monitoring should be avoided in the arteriovenous (AV) access arm. Obtaining peripheral venous access may be difficult, and SonoSite may be necessary to identify and guide access. In those patients with an indwelling catheter, it may be accessed, although this is avoided in general due to fear of increased infectious complications.

Special Considerations: Patients with Chronic Kidney Disease Versus End-Stage Renal Disease

In patients with CKD who are not yet on hemodialysis, it is important to elicit information regarding the volume and regularity of urine production with special attention to those who report a recent drop in volume or frequency. This may indicate a recent worsening of their renal function which may necessitate closer attention to potassium changes or fluid management during the procedure. For patients with ESRD on dialysis, it is important to establish when the patient underwent dialysis last. Ideally, the patient should have hemodialysis 12–24 h prior to the procedure, as the patient should ideally be completely or near completely at a normal physiological status and baseline dry weight at the time of anesthetic administration and the procedure. Close attention should be paid to establishing the correct "dry weight" for the patient, i.e., the weight at which they are euvolemic. If the patient is above their dry weight preoperatively, they risk pulmonary edema and poorly controlled hypertension perioperatively. If under their dry weight, they may become profoundly hypotensive during anesthesia [4]. Additionally, the regularity at which the patient has recently undergone dialysis is also important because a single session of dialysis may not normalize the patient that has missed more than one session, particularly with regard to fluid status. Similarly, it is important to ask if the patient tolerated the last hemodialysis session. If the patient did not tolerate the last hemodialysis session, the session was terminated prematurely or the patient skipped a regular session because of feeling ill; this warrants further investigation along with an assessment of laboratory abnormalities that may necessitate canceling or rescheduling the procedure.

Preoperative Laboratory Data

Verification of certain laboratory data is critical to check on the day of the procedure as these patients are subject to day-to-day changes.

Potassium

Patients with CKD or ESRD often have higher serum potassium levels than patients without renal dysfunction. Hyperkalemia is essential to diagnose and treat because it can be life-threatening due to the effect of increased potassium on electrical activity of the heart. Therefore, hyperkalemia may produce ECG changes, starting with peaked T waves and progressing to P wave widening and flattening, and as the PR segment lengthens, the P waves disappear. There are no recommendations for absolute levels of preoperative potassium levels that are considered safe; thus there is variability between hospital protocols in terms of which procedures need to be canceled and rescheduled based on findings of hyperkalemia on the day of the procedure. It is worth noting that the serum potassium level is closely related with serum pH; thus if the patient is acidotic, reevaluation of serum potassium level must be considered after pH is corrected. At our institution, a potassium level higher than 6.0 mmol/L prompts a discussion between the anesthesiologist and surgeon regarding the need for urgent hemodialysis prior to the procedure. One additional consideration is that venous potassium levels can sometimes falsely be higher than arterial levels, and obtaining an arterial blood sample may be useful in confirming the correct true potassium level [5].

Occasionally, some patients have a lower preoperative potassium level (<3.5 mmol/L). A lower potassium level is not as dangerous for the patient as much as higher potassium levels. Therefore, correction is required only if it is associated with frequent cardiac arrhythmias or with significant ECG changes such as QT prolongation. It is extremely difficult to correct hypokalemia in a patient with ESRD, and a nephrologist or cardiologist should be involved in the process to avoid overcorrection and possible cardiac effects.

Blood Glucose Levels

Often, patients with CKD and ESRD have concomitant diabetes mellitus and often present with hyperglycemia on the morning of the procedure. For mild hyperglycemia, intravenous regular insulin may be administered to bring down the glucose level, and the procedure can often proceed once the glucose level is brought down. However, for more severe derangements in glucose, each institution must determine what level of hyperglycemia is too high to be normalized for a same-day procedure, and these patients must be treated and rescheduled for their procedures.

Hemoglobin and Hematocrit

Most patients with CKD and ESRD are also affected by chronic anemia due to lower erythropoietin activity as well as the effect of toxic metabolites of uremia on the bone marrow. In general, this anemia does not need to be corrected because it is well tolerated by patients due to the gradual progression of anemia. There are no definite guidelines as to the hematocrit level below which blood products should be transfused, but previous studies have reported increased intraoperative complications in patients with end-stage renal disease and preoperative hematocrit levels ranging from 20 to 26 % [6]. Vascular access operations usually are not associated with significant surgical blood loss, and therefore, slightly more liberal criteria may be utilized for transfusion. Beyond specific objective criteria, such as hematocrit, transfusion should be considered if the patient is symptomatic or has significant comorbidities such as history of coronary artery disease and/or cerebrovascular disease. The decision to transfuse must be weighed carefully as transfusion of blood products may increase the patient's potassium level [7] as well as induce antibody formation which may decrease a patient's chances of successful renal transplantation in the future [8].

Coagulation Panel

Patients with CKD and ESRD are predisposed to coagulopathy due to underlying platelet dysfunction, decreased coagulation factors, and/or fragile capillary vessels. Additionally they may have uncontrolled atrial fibrillation, cerebrovascular and/or peripheral vascular disease requiring chronic therapeutic anticoagulation, or chronic antiplatelet therapy. Patients are usually instructed to hold oral anticoagulants prior to the procedure but if this is not carried out, this may add limitations to or necessitate canceling/rescheduling the procedure. In the case of a prolonged bleeding time or international normalized ratio (INR), regional nerve block may be contraindicated and therefore not done to avoid bleeding complications with hematoma formation and nerve compression.

Choice of Anesthesia Method

The type of anesthesia chosen is an integral part of the decision-making process for vascular access construction. The aims of anesthesia for vascular access operations are essentially the same as those for other surgical procedures:

- Keep the patients comfortable (reduce pain) as much as possible.
- Optimize conditions for the surgeon.
- Minimize risk of anesthetic complications (e.g., perioperative cardiac events).
- Optimize postoperative state – avoid prolonged sedation and minimize the strong postoperative analgesic medications.

Anesthetic methods include local anesthetic (LA) infiltration provided by the surgical team in combination with monitored anesthesia care (MAC) and sedation provided by the anesthesia team, regional anesthesia (RA), and general anesthesia (GA). Any of the three methods are acceptable for dialysis access creation. However, the patient's medical condition, anatomic location of the operation (the wrist/forearm, antecubital fossa, and upper arm), and the surgeon's preference should be considered when selecting the anesthesia method.

In terms of selecting anesthesia method as it relates to anatomic location, some generalities can be applied. Local anesthesia with monitored anesthesia care (MAC) and sedation can be considered suitable for the procedures performed at the wrist and the antecubital fossa. Regional anesthesia is a viable option for procedures performed at the antecubital fossa and distal upper arm. General anesthesia should be considered when procedures involve the proximal upper arm and for arteriovenous graft (AVG) and transpositions which require tunneling.

Local Anesthesia

Infiltration of local anesthesia in the surgical field by the surgeon provides the most physiologically stable of the anesthetic methods and is therefore used in patients who have

severe comorbidities such as recent myocardial infarction, severe coronary artery disease, or chronic obstructive pulmonary disease. The specific local anesthesia selected depends on the surgeon's preference, but many surgeons prefer 1 % lidocaine as the onset is faster compared to other local anesthesia. The maximum dose of lidocaine has been reported up to 3 mg/kg. Local anesthesia alone is not well tolerated as some patients can get agitated. However, this can be overcome by sedation provided by the anesthesia team. A drawback to local anesthesia is the lack of an effect on the flow characteristics of the artery, in contrast to regional and general anesthesia. Additionally, in patients with low bicarbonate values, the onset of action of local anesthetics may be delayed and the duration of effect may be shorter possibly due to low protein binding [9, 10].

Regional Anesthesia

Regional anesthesia of the upper extremity requires brachial plexus block. This is potentially safer in the fragile patient population and offers many advantages over other anesthetic methods, including intraoperative hemodynamic stability and good postoperative analgesia. Brachial plexus block by supraclavicular approach has been shown to dilate the veins and arteries in the ipsilateral extremity, reduced the incidence of arterial spasm during and after the surgery, and significantly decreased the rate of immediate arteriovenous fistula (AVF) failure postoperatively when compared to those that were performed with local anesthesia [11–13].

There are several methods to approach the brachial plexus block approach including inter-scalene, supraclavicular, infraclavicular, and axillary blocks. Complications of regional anesthesia include infection, hematoma, local anesthetic toxicity, and nerve injury. There are also complications that are specific to each approach, such as total spinal anesthesia, Horner syndrome, diaphragmatic paralysis, and pneumothorax. Although there is currently little published data, the use of ultrasound certainly appears to make this procedure less difficult and decrease the incidence of these complications [9]. Platelet count and coagulation profile should be checked before performing regional anesthesia and antiplatelet agents such as clopidogrel should have been stopped sufficiently in advance to minimize hematoma formation [14]. It is important to note that blockade adequate for regional anesthesia as the sole method of anesthesia may be technically difficult and time-consuming and successful overall anesthesia may require supplementation with local anesthesia by the surgeon. Additionally, there has been some criticism of this method of anesthesia due to the possibility of masking steal syndrome or ischemic monomelic neuropathy. Most blocks will last 6–8 h with some variation based on individual patients and the local anesthetic chosen for the block. If the patient is deemed to be high risk for ischemic steal syndrome, this should be considered carefully before a block is performed, although it is not an absolute contraindication [15].

General Anesthesia

Almost all patients with CKD and ESRD have multiple risk factors for general anesthesia due to the inherent nature of the comorbidities of these that have led to the renal insufficiency. Previous reports indicate that approximately 25 % of the patients who undergo renal replacement therapy have ischemic heart disease, 10 % have cerebrovascular disease, and 12 % have peripheral vascular disease [10]. For these reasons, general anesthesia is avoided when possible, but this may not be feasible, especially for patients with a history of psychological disorders or those who need more complicated procedures, such as an upper arm transposition or graft placement which may not be amenable to regional anesthesia. Modes of general anesthesia delivery include general endotracheal anesthesia (GETA) and laryngeal mask airway (LMA). There are some advantages of GETA over LMA. It provides a more secure airway and $PaCO_2$ is more easily controlled, avoiding the alkalosis that can contribute to decreasing the potassium level rapidly. However, the usage of LMA does not require muscle relaxants which can delay emergence from general anesthesia at the conclusion of the case.

During anesthesia induction, hemodynamics should be stabilized with the prompt use of narcotics. However, blood pressure does drop significantly after induction due to lower vascular compliance and/or lower cardiac reserve function. In these cases, vasoactive medications, such as ephedrine and phenylephrine intravenously as a bolus or a continuous infusion, should be utilized to keep the perfusion pressure adequate. For the pain control during the surgery, the use of LA by the surgeon can reduce the quantity of inhalational anesthetics and narcotics.

Intraoperative Management

Potassium Level

With the administration of any types of anesthesia, potassium may rise to a critical level suddenly. Therefore, close attention should be paid to ECG changes. Even minor changes of the QRS complex or the height of the T wave should prompt an immediate blood sample to check the potassium level so that treatment to lower the potassium can be initiated promptly if necessary.

If hyperkalemia is suspected/confirmed, immediate action should be taken. Immediate administration of calcium (10 ml of 10% calcium chloride) with a bolus dose of insulin (5–10 units while checking serum glucose simultaneously) should be followed by a continuous infusion of dextrose 10% in water (D10W) with 5–10 units of regular insulin per 25–50 g of glucose. After this, sodium bicarbonate (50–100 mEq) and furosemide (if the patient still can make urine) should be administered. Other methods to decrease the serum potassium level include increasing the respiration rate (if GA). Frequent checks of the potassium level should be performed until it is normalized.

Heparin

The surgeon will request heparin prior to clamping the artery. It is important to verify the dose of heparin and flash the lines to confirm the administration.

Oxygenation Status

In cases of local, regional, or general anesthesia with an LMA, the patient may require a high dose of sedatives. This can challenge the maintenance of a patent airway leading to hypoxia. In this situation, there should be a pause in the procedure to obtain a secure airway by using an oral or nasal airway or GETA. Inserting an airway instrument alone is sometimes enough to stimulate the patient to move suddenly which is one reason that the procedure should be paused.

Postoperative Anesthesia Care

Anesthesia management continues until the patient is discharged from postanesthesia care unit. It should be noted that potassium level may increase suddenly even in the perioperative period. Therefore, the recovery nurse should pay close attention for ECG changes, and sometimes a recheck of serum potassium is indicated. Occasionally, the timing of the next hemodialysis session may need to be accelerated, especially for the patient who may have missed a session prior to the procedure. This decision is made in consultation with the nephrologist.

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Part III

Creating Hemodialysis Access

Hemodialysis Access Catheters

13

Christopher R. Ingraham and Karim Valji

Introduction

According to recent data from the United States Renal Data System (USRDS), greater than 60 % of patients with end-stage renal disease (ESRD) will initiate dialysis by a central venous catheter (CVC) [1]. Approximately 20 % of dialysis patients at any point in time are dialyzing via a CVC [2]. Given the prevalence of central venous catheters for dialysis access and the problems associated with such devices, it is imperative that every health-care provider who works with dialysis patients be thoroughly familiar with dialysis catheter selection, options for placement, and management of device-related complications.

Choice of Dialysis Catheters: Tunneled or Non-tunneled?

Excluding the emergent setting, venous catheters are the least acceptable method for dialysis. They should be avoided whenever possible and only considered a reasonable means for long-term renal replacement in exceptional circumstances. Particularly for reasons of infection (see below), Kidney Dialysis Outcomes Quality Initiative (K/DOQI) Vascular Access Workgroup guidelines recommend less than 10 % overall catheter prevalence in the dialysis population [1, 3].

Non-tunneled hemodialysis catheters are indicated for inpatient use only in several situations when a permanent dialysis access or peritoneal dialysis catheter is not in place or not usable [4].

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- Acute kidney injury with expectation of rapid recovery of renal function.
- Patients requiring dialysis with known or suspected active bloodstream infection. If the patient improves clinically and blood cultures have been verified to be negative at 48 h, the catheter should be removed and a tunneled dialysis catheter placed if needed.
- Patients who are hemodynamically unstable or have a medical condition requiring emergent dialysis (e.g., pulmonary edema, severe hyperkalemia, severe acidosis) where faster, bedside placement is more practical than being transferred to a procedure suite or operating room for line placement.
- Patients with an uncorrectable coagulopathy or severe thrombocytopenia.

According to current K/DOQI guidelines, the maximum duration of dialysis treatment through a temporary line should be less than 1 week [3, 5]. Temporary dialysis catheters have been shown to be associated with increased rates of infection as early as 2 weeks post-placement [6]. If a patient is expected to require dialysis greater than 1 week, a tunneled catheter would be then the appropriate choice. Temporary dialysis catheters should be placed in the internal jugular (IJ) or common femoral (CF) vein. Per K/DOQI guidelines, the latter site is only suitable in bedbound patients [5].

Tunneled hemodialysis catheters should be placed in all other patients without a permanent and functional method for dialysis (e.g., arteriovenous fistula (AVF) or arteriovenous graft (AVG), peritoneal dialysis catheter). Tunneled catheters are always favored over non-tunneled catheters for ESRD patients. Infection rates are approximately 2.9 per 1000 catheter days for tunneled central catheters, versus 15.6 for non-tunneled internal jugular (IJ) catheters, and 20.2 for non-tunneled femoral vein catheters [6]. K/DOQI guidelines advocate for the *temporary* use of tunneled central venous catheters as a primary method for dialysis access. However, in certain patients who have no other options for access, the long-term use of a tunneled catheter may be the patient's only option.

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Catheter Site Selection

The operator has multiple potential options for venous access including the internal jugular (IJ) vein, external jugular (EJ) vein, subclavian vein (SCV), common femoral (CF) vein, and inferior vena cava (IVC). Current K/DOQI guidelines recommend placement in the following order of preference: right IJ, right EJ, left IJ, left EJ, SCV, CF vein, and finally translumbar or transhepatic IVC [5].

The IJ vein is the ideal location for catheter placement. There is a significantly lower rate of stenosis following IJ dialysis catheter placement (10 %) when compared to the subclavian vein (50 %) [7–10]. Despite K/DOQI guidelines, many experienced practitioners reserve EJ insertion for patients without usable IJ or femoral veins and prefer the femoral over the subclavian veins. The SCV is rarely chosen for access given that a stenosis in this location would be detrimental to future creation of an upper extremity fistula or graft on that side. However, SCV entry may be reasonable if the ipsilateral arm will no longer be a potential site for permanent dialysis access creation, such as in the case of upper extremity veins that are inadequate for access creation, or there is axillary venous stenosis or occlusion.

Right IJ vein access is preferred over left IJ vein access due to improved long-term function and perhaps lower rates of infection [11, 12]. When a catheter is placed in the right IJ vein, the catheter follows a straighter course through the central veins before terminating in the right atrium. A left IJ catheter comparatively requires two turns at the left brachiocephalic junction and at the SVC (Fig. 13.1). Thus, patency rates are higher in right-sided catheters [11]. Infection rates are perhaps lower when placed on the right for unknown reasons. It is proposed that left-sided catheters require frequent adjustments during dialysis to improve flow, one of which is manipulating the catheter at the skin exit site (i.e., pushing or pulling gently on the catheter to change position), and these additional manipulations may increase rates of infection [11]. Catheter placement should be avoided on the side ipsilateral to a maturing upper extremity dialysis access [5].

Compared with neck placement, potential problems associated with femoral vein catheters include higher infection rates, more discomfort, sometimes limited mobility, possibly an increased likelihood of deep vein thrombosis (DVT), and potential venous stenosis, which could pose a problem if the patient were to undergo renal transplantation in the future [5, 13, 14].

Catheter Placement Technique

If sedation is planned during the procedure, the patient should be evaluated for sedation based on the institution's sedation guidelines (e.g., body mass index, American Society of Anesthesiologists (ASA) score). Anesthesia guidelines typically recommend that a patient be NPO 6 h prior to the planned procedure to minimize the risk of aspiration. Laboratory values, including a recent platelet count and coagulation screen should be obtained. Transfusion may be necessary to minimize bleeding risks. If the patient's laboratory values cannot be corrected or emergent dialysis is needed, non-tunneled line placement should be considered. Non-tunneled line placement can be performed expeditiously, at the patient's bedside, and does not require the creation of a subcutaneous tunnel—an additional potential site of bleeding in an uncorrected patient.

Antibiotic prophylaxis is not routinely recommended prior to central venous catheter placement per recommendations from the Centers for Disease Control based on a recent study in oncology patients [15]. However, intravenous (IV) antibiotics are advisable during tunneled dialysis catheter exchanges for catheter dysfunction [16].

Non-tunneled dialysis catheters are typically placed at the patient's bedside. Local anesthesia with 1 % lidocaine is often adequate for anesthesia and patient comfort. Additional sedative medications to enhance patient cooperation and comfort are left to the operator and nurse's discretion. Given that live fluoroscopy is not readily available when line placement is performed at the bedside, a portable chest radiograph is required post-placement to verify catheter position (Fig. 13.2) and to assess for complications such as pneumothorax [5].

Placement of tunneled dialysis catheters should be performed in an interventional radiology (IR) or surgical suite (OR) with live fluoroscopy readily available. Since a tunneled catheter is intended for long-term use, every attempt should be made to avoid kinking of the catheter at the vein entry site and to position the catheter tip in the right atrium. Live fluoroscopy allows for real-time, minor adjustments in line position and allows for optimal, safe placement that is intended to be durable. Although it is possible to perform tunneled line placement at the patient's bedside, the authors do not recommend placement of a tunneled line without the use of fluoroscopy. Similar to a non-tunneled hemodialysis catheter placement, the patient is positioned supine on the procedural table. Most of these procedures can be performed with minimal or moderate sedation for patient comfort and cooperation. Occasionally, monitored sedation (or even general anesthesia) delivered by the anesthesiology service is necessary for severely ill or uncooperative patients.

Strict adherence to sterile technique is mandatory to minimize the risk of short-term infectious complications [4, 17]. Required measures include wide skin preparation with 2 % chlorhexidine gluconate with alcohol, draping the entire procedural site and patient, and appropriate sterile equipment

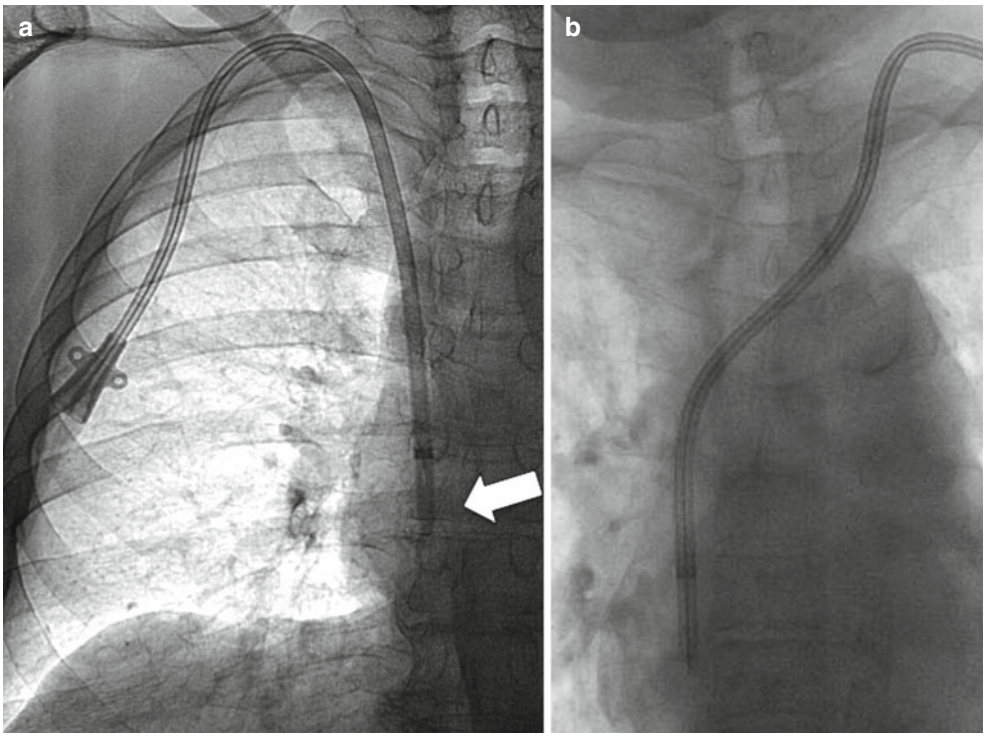

Fig. 13.1 A tunneled internal jugular hemodialysis catheter. (**a**) Right internal jugular hemodialysis catheter. Note the smooth transition of the catheter as it courses over the right clavicle without kinking. The tip of the catheter is in the right atrium (*arrow*), consistent with K/DOQI recommendations. (**b**) Left internal jugular hemodialysis catheter. Note how in caparison to the right internal jugular catheter, the left internal jugular catheter takes two turns, one at the left brachiocephalic junction and another at the superior vena cava

worn by the operators, including a mask, hat, gown, and gloves. Povidone-iodine with 70 % alcohol is an acceptable alternative antiseptic solution [18].

Ultrasound-guided venous access is standard of care per K/DOQI and the American Society of Diagnostic and Interventional Nephrology (ASDIN) guidelines [5, 19]. Ultrasound allows for continuous needle visualization during vessel entry, essentially eliminating the risk of arterial puncture or pneumothorax [20]. In the hands of an experienced operator, ultrasound assistance will minimize the number of skin punctures required to successfully enter the vein [5]. Multiple punctures into the target vessel and resulting hematoma formation have both been associated with an increased risk of venous stenosis and/or thrombosis [4, 5]. It is desirable to confirm vein patency prior to draping the patient. Many of these patients have undergone multiple venous access procedures and are thus at some risk for venous thrombosis.

The internal jugular veins are typically superficial and slightly lateral to the common carotid artery. The femoral vein is medial to the common femoral artery and identified by its large size. Unlike the artery, a patent vein should be completely compressible with the ultrasound transducer. Color Doppler can also provide assistance in distinguishing the vein from artery and confirming vein patency (Fig. 13.3).

Once the patency and location of the vein are verified, a skin site is chosen for access. In the case of a non-tunneled line, access into the vein can be from a lateral or superior approach, given that a tunnel does not need to be created and there is much less risk of the catheter kinking at the venotomy site. For *non-tunneled catheters*, the ideal skin entry site is within a few centimeters of the clavicle. This location will minimize patient discomfort from the external portion of the device. *For tunneled catheters*, a skin entry site is chosen as close to the clavicle as possible to minimize catheter kinking within the tunnel.

The skin and subcutaneous tissues are anesthetized with 1 % lidocaine. A small skin nick is made with a #11 scalpel, followed by blunt dissection of the subcutaneous tissues with a small curved clamp to accommodate future passage of the dilators and the catheter. With constant direct sonographic visualization, a 21-gauge micropuncture needle is advanced into the IJ vein. A lateral approach to the vein allows for constant visualization of the entire needle. With a superior approach, only portions of the needle will be visualized. Entry into the vein may only be noted by release of tenting of the anterior vein wall. Blood may or may not

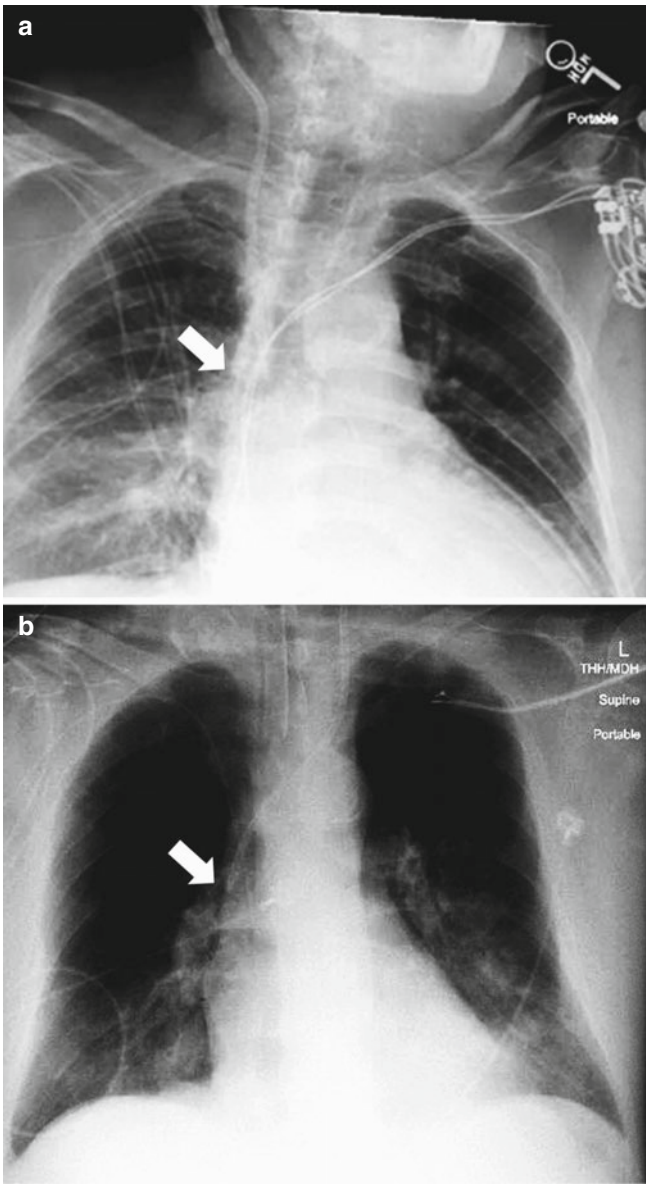

Fig. 13.2 Post procedure chest x-ray demonstrating placement of non-tunneled hemodialysis catheter in critically ill patients terminating in the central SVC (*arrows*). (**a**) Right internal jugular catheter (**b**) left internal jugular catheter

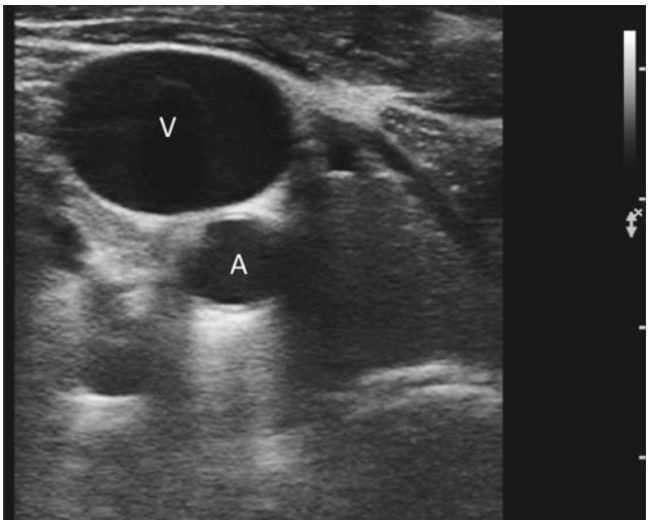

Fig. 13.3 Gray-scale ultrasound image demonstrating the right internal jugular vein (RIJV) and its relationship to the common carotid artery (CCA) under the sternocleidomastoid muscle (SCM). Notice that the vein lies superficial to the artery, free of thrombus, and is completely compressible

drip out of the needle once the vein is entered. If no blood appears at the needle tip, aspiration with a saline syringe can be attempted to verify venous entry. Under fluoroscopic guidance, a 0.018" wire is then advanced through the needle toward the right atrium. The needle is then exchanged for a micropuncture sheath. The wire tip is positioned in the middle of the right atrium (for tunneled hemodialysis catheters) or cavoatrial junction (for non-tunneled hemodialysis catheters, if fluoroscopy is used). The microwire is clamped at the catheter hub, the wire is withdrawn at the length of the hub system, and the wire is re-clamped and removed. The measured length from tip to clamp represents the intravascular length. This measurement is also used to select the appropriate "tip to cuff" catheter length (see below). Once the wire and inner dilator of the micropuncture sheath are removed, a 0.035" wire is advanced centrally. Ideally, the wire is directed into the IVC. The patient's cardiac rhythm should be observed to assess for ectopy. If the guidewire does not follow the expected course of the venous system, the wire should be withdrawn and contrast injected through the microcatheter to exclude vascular anomaly, venous occlusion, or inadvertent arterial entry (when fluoroscopy is used).

For *non-tunneled hemodialysis catheter placement*, a variety of catheters are commercially available (e.g., 13.5 Fr Mahurkar temporary dialysis catheter, Covidien, Dublin, Ireland). The functional catheter length (e.g., 15 cm, 20 cm) must be no longer than the measured or estimated (when fluoroscopy is not available) intravascular distance. Once a catheter length is chosen, the subcutaneous tissues are serially dilated, and the catheter is advanced over the wire until the hub is flush with the skin. The catheter is secured in place with sutures and both lumens are flushed with heparin solution (1000 units/mL). A portable radiograph is obtained to document the

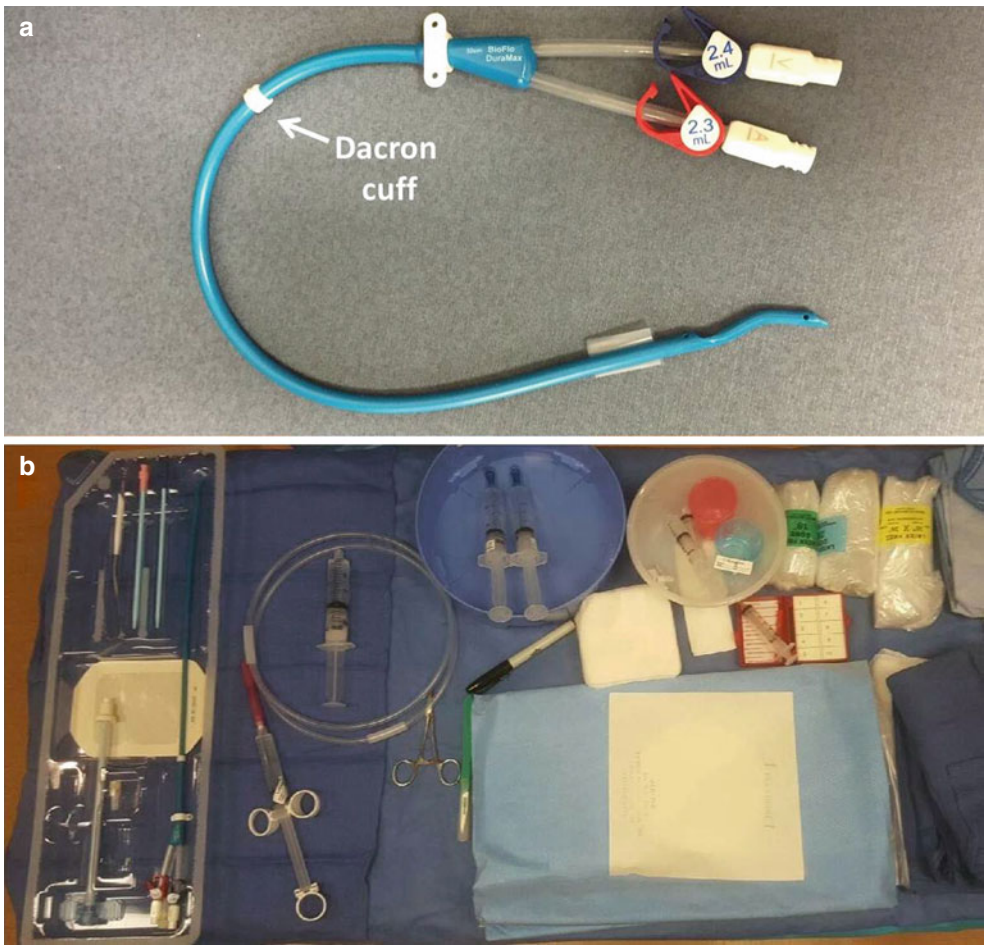

Fig. 13.4 An example of a tunneled hemodialysis catheter (**a**) and the set up associated with placement of the line (**b**)

position of the catheter tip and to assess for potential complication, such as pneumothorax. The ideal catheter tip location for non-tunneled catheters is the inferior aspect of the SVC [5], just central to the cavoatrial junction (Fig. 13.2).

For *tunneled dialysis catheters*, a variety of catheters are commercially available. No particular catheter has been consistently shown to be superior to any other device. All catheters have a dual lumen, have high flow configuration, and are composed of kink-resistant material. Typical catheter diameters range from 13 to 14.5 Fr and have variable lengths, typically 19 cm, 23 cm, or 28 cm. The endholes can be symmetric or asymmetric, with lumens that are staggered, non-staggered, or split. A synthetic fabric (Dacron) cuff embedded on the catheter shaft will, over time, cause a fibrous reaction that secures the catheter to the tissues and provides a mechanical barrier to spread of infection from the exit site (Fig. 13.4). The labeled catheter length "tip to cuff" must be greater than the measured intravascular distance. This is due to the Dacron cuff being located at least a few centimeters away from the vascular entry point. After venous access has been obtained, the operator then forms the subcutaneous tunnel, which is typically about 7 cm in length from the venous access site to skin exit site.

After application of 1 % lidocaine for local anesthesia at the chosen skin site, a stab incision followed by blunt dissection is made. Blunt dissection of the subcutaneous tissue in the tunnel facilitates subsequent passing of the tunneler and prevents kinking of the catheter. With the catheter attached to the tunneling device (metal or plastic), the tunneler is advanced through the subcutaneous tissues to the venous access site. The entire catheter is then pulled through the tunnel until the Dacron retention cuff is within the tunnel.

Dilators are then advanced under fluoroscopic guidance over the wire at the venous access site to accommodate the peel-away sheath. The peel-away sheath is then advanced

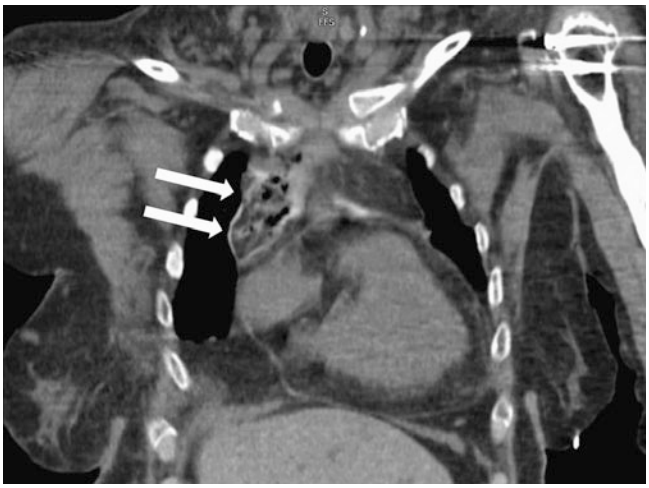

Fig. 13.5 Non-contrast computed tomography imaging showing contrast, fluid, and air bubbles near the medial aspect of the left innominate vein (*arrows*), consistent with a site of previous extravasation during an attempted placement of a left internal jugular tunneled hemodialysis line

over the wire under fluoroscopic guidance into the right atrium. These steps should be performed under fluoroscopy to assess adequate wire length and position before dilator or sheath advancement. Failure to advance these devices properly and safely can result in central vein or mediastinal injury (Fig. 13.5). With the patient suspending respiration (to avoid air embolism), the inner dilator and wire are removed from the peel-away sheath and the catheter is rapidly advanced into the sheath. The sheath is then peeled away from the catheter, leaving only the catheter behind. Using fluoroscopy, the catheter tip is adjusted so that it ideally terminates in the middle of the right atrium (Fig. 13.1). This is the standard location of the catheter tip recommended by K/DOQI [5]. Because the catheter tip will typically migrate about 3 cm cephalad with the patient upright, the ultimate catheter position (just inferior to the cavoatrial junction) will allow unimpeded blood flow during dialysis and extend the functional life of the catheter.

The catheter is then secured to the skin at the exit site using sutures, and the small skin incision overlying the venotomy site is closed with a single absorbable suture or skin glue (e.g., Indermil, Covidien). Both catheter lumens are then flushed with heparin solution (1000 units/mL).

Similar steps are followed for placement of external jugular (Fig. 13.6), subclavian, and femoral vein catheters. Ultrasound can be used and is recommended for venous access at any of these locations [5]. For tunneled femoral catheters, long devices (e.g., 55 cm tip to cuff) allow for tip positioning in the right atrium (Fig. 13.7). In the case of a tunneled line, the tunnel pathway will depend on the location of vein entry and surrounding soft tissues. The tunnel exit site should be several centimeters away from the venous access site and in a location which is easily accessible to the dialysis staff. In the case of a tunneled femoral line, the tunnel is frequently created several centimeters inferior or lateral to the venous access site.

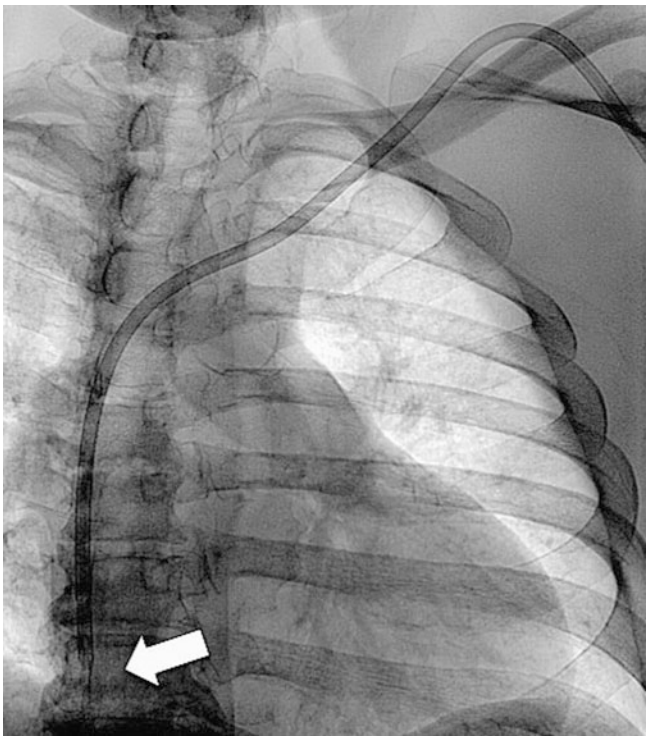

Fig. 13.6 A tunneled left EJ hemodialysis catheter. Note the smooth transition of the catheter as it courses over the left clavicle without kinking. The tip of the catheter is in the right atrium (*arrow*), consistent with K/DOQI recommendations

Alternative Sites for Access in the Challenging Patient

Patients who have been on chronic hemodialysis for many years are prone to central venous obstructions due to the occasional or frequent need for indwelling catheters. In rare cases, all potential thoracic and femoral venous sites for subsequent catheter placement are exhausted. In this situation, consideration can be given to translumbar or transhepatic IVC access [21–24]. These two procedures require advanced imaging techniques for placement and are typically performed in interventional radiology.

Translumbar Hemodialysis Line Placement

Prior imaging should be obtained to confirm patency of the vena cava. With the patient prone or in the left lateral decubitus position, the IVC can be entered superior to the right iliac crest, approximately 8–10 cm lateral to the midline [21, 22]. Although access can be obtained with blind advancement of a long 18-gauge needle using bony landmarks,

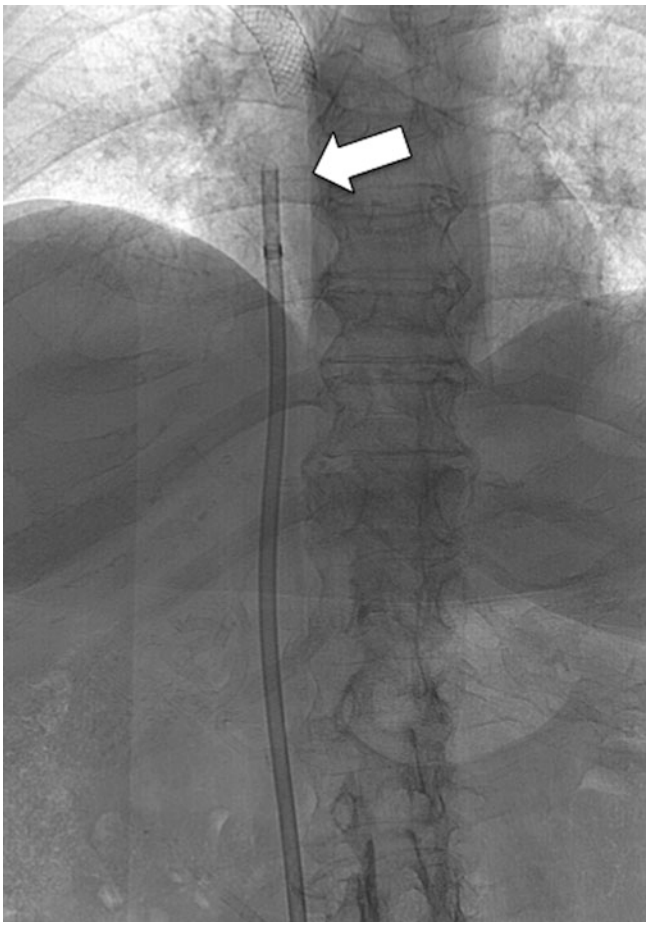

Fig. 13.7 A right common femoral vein hemodialysis catheter. Note the tip of the catheter is in the right atrium (*arrow*), consistent with K/DOQI recommendations

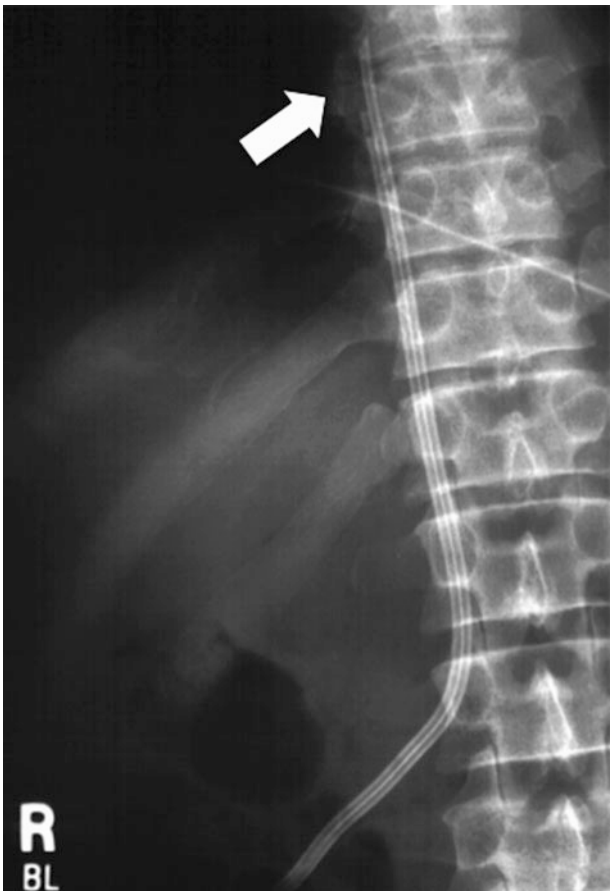

Fig. 13.8 A translumbar hemodialysis catheter. Note: the tip of the catheter is in the right atrium (*arrow*), consistent with K/DOQI recommendations

imaging-guided needle insertion (CT, US, or C-arm CT) is preferred. To avoid a sharp angle of entry into the IVC, slight caudocranial angulation of the needle is recommended. Once blood can be easily aspirated from the access needle, contrast injection will confirm entry into the caval lumen. Insertion of a stiff guidewire is important to facilitate placement of the peel-away sheath. The remainder of the procedure is similar to thoracic placement described above. A skin exit site on the lateral abdomen near the costal margin is preferred for patient comfort and ease of access. The ideal position for the catheter tip is at the IVC/atrial junction (Fig. 13.8).

Transhepatic Hemodialysis Line Placement

A transhepatic approach to the right atrium can also be considered in the challenging patient [23, 24]. Percutaneous access into a peripheral hepatic vein is achieved using a technique similar to that used for percutaneous transhepatic cholangiography or biliary drain placement. The procedure is performed on a standard fluoroscopy table with the patient supine or with a wedge under the patient's right side. After appropriate local anesthesia is administered, an access point in the region of the midaxillary line below the tenth rib is chosen to avoid the lateral pleural reflection. The operator directs a 21-gauge needle (Accustick set, Boston Scientific, Natick, MA, USA) under fluoroscopy toward the 12th thoracic vertebral body. After the needle is passed several centimeters centrally, the inner stylet is removed and contrast is connected to the needle hub. While slowly withdrawing the needle under fluoroscopy, contrast is injected very gently until a hepatic vein is visualized. The number of passes required to enter a hepatic vein is variable, though a recently published series documented an average of two passes [24]. Once a hepatic vein is visualized, a 0.018" wire is advanced centrally and the needle is removed. An Accustick sheath is then advanced over the wire. A stiff 0.035" Amplatz wire (Boston Scientific, Natick, MA, USA) is inserted through the sheath and into the right atrium. The remainder of catheter placement follows standard technique. The ideal position for the catheter tip is at the IVC/atrial junction (Fig. 13.9).

A recent review of 22 patients with transhepatic dialysis catheters demonstrated a low procedural complication rate,

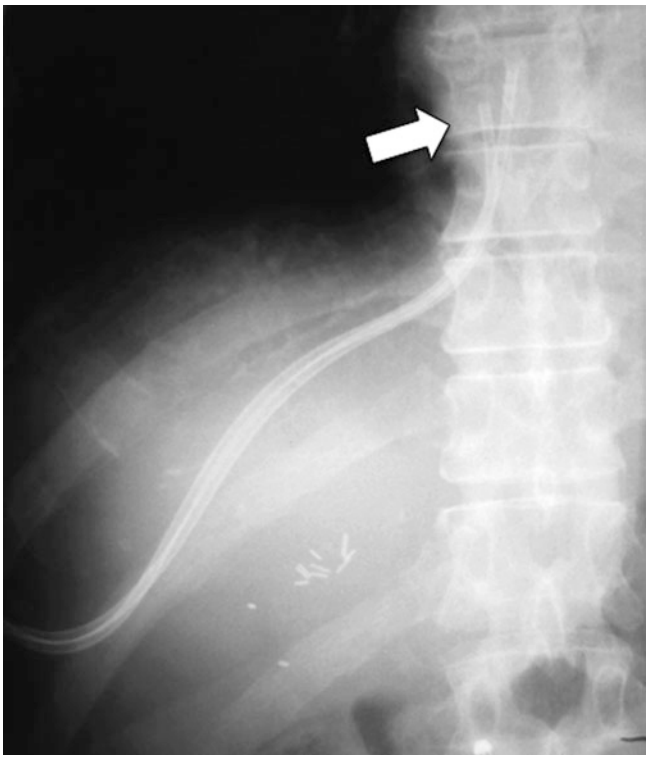

Fig. 13.9 A transhepatic hemodialysis catheter. Note: the tip of the catheter is in the right atrium (*arrow*), consistent with K/DOQI recommendations

with a calculated infection rate of 0.22 per 100 catheter days [25]. In this series, the mean cumulative catheter duration time (which included all exchanges of a patient's transhepatic catheter) was 506.2 days, and the mean time in situ of each catheter alone was 87.7 days. Although an alternative to translumbar IVC placement, multiple series have reported higher rates of complications associated with transhepatic catheters, including bleeding, thrombosis, and catheter migration [24, 25]. Respiratory motion is thought to be the likely etiology for the high rate of kinking and catheter dislodgement [24, 25]. Although historically this method of catheter placement was reserved for temporary use, its use has been suggested as an alternative for longer-term access [26].

Catheter Management

Once placed, all catheters are covered with a sterile dressing which also covers the catheter skin exit site. Dressing changes are recommended every 2 days for non-tunneled hemodialysis catheters and weekly for tunneled hemodialysis catheters, if the catheter exit site is clean and dry [27]. Before handling or touching the catheter, guidelines require that the operator perform hand hygiene and wear clean gloves [18, 20]. All catheters must be clamped when removing or replacing catheter caps or hubs. Using a separate antiseptic pad (e.g., Site Scrub, Bard Medical, Murray Hill, New Jersey, USA) for each hub, the hub must be thoroughly cleaned prior to and after use [18]. Prior to dialysis use, each lumen is aspirated with a sterile syringe until blood is obtained. When dialysis is complete, the catheter and hubs are again cleaned and then flushed with heparin solution (1000 units/mL).

Catheter Removal

Removal of both tunneled and non-tunneled catheters should include removal of any suturing devices in place and cleaning of the catheter exit site with antiseptic solution. Gentle traction is frequently adequate for removal of a non-tunneled catheter. For tunneled catheters, the Dacron cuff is frequently embedded in the surrounding soft tissues in the subcutaneous tunnel. This may require more forceful but controlled traction to release the cuff from the surrounding tissues. For catheters that are difficult to remove with traction alone, blunt dissection of the tunnel around the cuff via the catheter exit site may be required after administration of lidocaine for local anesthesia. There is some debate about the necessity of removing the entire cuff along with the catheter. Manual compression for 5–10 min at the venotomy site and catheter exit site is sufficient to achieve hemostasis in nearly all cases.

Complications

Immediate procedural complications associated with dialysis access catheter placement include bleeding, pneumothorax, arterial puncture, cardiac arrhythmias, air embolus, and catheter malposition or malfunction. Long-term complications include central venous stenosis or thrombosis, fibrin sheath formation, and infection [4].

With sonographic needle placement, the risk of pneumothorax is virtually eliminated [20]. Inadvertent arterial puncture should be an extremely rare event. In one large series comparing ultrasound-assisted versus bony landmark-guided IJ vein catheter placement, 100 % of ultrasound-assisted procedures were technically successful versus 94.4 % in the landmark group [20]. Carotid artery punctures, hematoma formation, and pneumothorax in the ultrasound-assisted group were 1.1 %, 0.4 %, and 0 % versus 10.6 %, 8.4 %, and 2.4 % for the landmark group, respectively.

Bleeding after catheter placement can range from minor oozing or hematoma at the venotomy or exit site to severe bleeding or hematoma formation. Patients with end-stage renal disease suffer from some degree of coagulopathy, including a uremia-related platelet dysfunction, an ane-

mia, or a dysfunctional coagulation cascade [28]. Therefore, initiation of dialysis through the recently placed catheter can itself limit periprocedural bleeding. Minor bleeding at the catheter exit site or within the tunnel tract can be managed by correction of coagulation parameters (when appropriate), local management with a compression dressing, small amounts of gelfoam or thrombin injected into the tract, epinephrine injection around the site, or administration of desmopressin to improve platelet function [28]. Major bleeding (though rare) may require transfusion of packed red blood cells, platelets, fresh frozen plasma, or cryoprecipitate.

Air embolism is a rare event during tunneled dialysis catheter placement, which typically occurs in the quick interval between removal of the dilator from the large peel-away sheath and insertion of the catheter into the sheath. In particular, the negative intrathoracic pressure associated with deep inspiration can allow >100 cc of air to rapidly enter the right atrium. While air emboli are usually small in volume and not clinically significant, fatal embolic events have been reported [29, 30]. These events may be more likely in patients with dehydration and diminished central venous pressure, obstructive sleep apnea, or marked sedation during the procedure [4]. This event should be avoided by removing the dilator with the patient performing Valsalva or arresting respiration. Turning the patient onto the left side to keep air in the right atrium (left lateral decubitus position), although frequently taught, is likely useless; the air will already have entered the pulmonary arteries by this time. Treatment is supportive: frequent monitoring of vital signs and oxygen saturation, supplemental oxygen, and IV fluids as needed [4, 31]. Aspiration of air through a sheath or catheter has been described [32].

Infection is the most common long-term complication following catheter placement. Infections include catheter-related bloodstream infections (CRBSI), skin exit-site infections, and/or tunnel infections. An exit-site infection does not extend above the retention cuff in the tract. These infections typically respond well to a course of oral antibiotics [33]. Tunnel tract infections are more serious. They are strictly defined as culture-positive infection within the tunnel with negative blood cultures. However, they should be strongly suspected with erythema and tenderness over the entire catheter tract. Treatment includes catheter removal and a course of antibiotics [33]. CRBSI require at least one positive blood culture and the absence of another source for infection. The incidence of CRBSI in non-tunneled and tunneled dialysis catheters is estimated to be 3.8–6.6 episodes per 1000 catheter days and 1.6–5.5 episodes per 1000 catheter days, respectively [33]. Depending on the organism identified and the patient's overall medical condition, CRBSI are either treated by 1) catheter exchange about 48 h after beginning appropriate IV antibiotics in clinically stable patients with limited access or 2) IV antibiotics plus catheter removal with at least 48 h delay before new tunneled catheter placement [33]. Endocarditis is well known to be much higher in the dialysis population, up to 18 times more common than in the general population [34]. Furthermore, the incidence of infective endocarditis in patients who dialyze via a tunneled catheter is nearly eight times higher than those that dialyze via an AVF [34].

Catheter thrombosis is a clinical problem occasionally encountered after catheter placement. Locking the catheter with high-dose heparin or trisodium citrate is routinely performed to prevent catheter thrombosis. Systemic prophylaxis with a low-dose warfarin or an antiplatelet agent has not been proven to be effective in the prevention of catheter thrombosis [35, 36]. For cases of acute catheter thrombosis, instilling 2 mg of tissue plasminogen activator (tPA) into each lumen is frequently successful at re-establishing patency [37].

In thrombosed dialysis catheters that do not respond to chemical therapy, obstruction by a resistant fibrin sheath should be considered. The fibrin sheath is composed of fibrin and proteinaceous material that coats the entire catheter from the tip of the device to the vessel entry point [2]. Fibrin sheath formation begins almost immediately after placement and can progress over weeks to months [2]. Treatment of a fibrin sheath remains controversial. The frequency of this problem has markedly diminished with the placement of catheter tips in the mid right atrium. Options for treatment include exchange of the catheter over a wire, stripping the fibrin sheath off the catheter shaft using a snare introduced via the femoral vein, or disruption of the sheath by balloon angioplasty. One retrospective study demonstrated no difference in catheter patency among patients treated by catheter exchange over a wire, catheter exchange after fibrin sheath disruption by balloon angioplasty, and fibrin sheath stripping [38]. However, results from a more recent review showed longer catheter patency after disruption of the fibrin sheath by angioplasty compared with routine exchange [39].

Central venous thrombosis can range from a small amount of thrombus around the catheter tip to complete occlusion of the accessed vein and, occasionally, the central veins [40]. In the case of a symptomatic line-associated deep venous thrombosis, such as a thromboembolic event or upper extremity or neck swelling, catheter removal (if possible) and anticoagulation are recommended [41]. Although there is no direct evidence to support its use, anticoagulation remains the mainstay of treatment for symptomatic upper extremity DVT [41]. In patients who cannot be anticoagulated, line removal is often adequate [41]. Right atrial thrombus formation associated with hemodialysis catheters has also been described, although its true incidence is unknown [42]. In cases of right atrial thrombus, catheter removal and

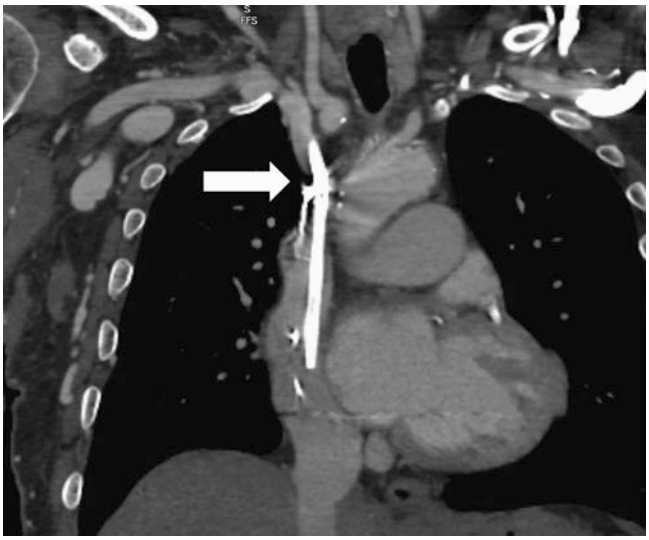

Fig. 13.10 Computed tomography with venous contrast showing high-grade stenosis of the superior vena cava (*arrow*). The patient had marked venous collaterals over the right shoulder

anticoagulation for 6 months are recommended, although reports of thrombolysis and surgical thrombectomy have been reported [42].

Central venous stenosis can occur after either non-tunneled or tunneled dialysis catheter placement (Fig. 13.10) with frequency ranging from 20 to 50 % [4]. Increased risk for central venous stenosis is associated with longer duration of catheter use or a history of multiple sites of catheter placement [2, 43]. As previously discussed, subclavian catheters are associated with higher rates of central venous stenosis, as are left-sided IJ catheters compared to right-sided IJ catheters [11, 12]. Methods of treatment include percutaneous angioplasty, percutaneous stent placement, and surgical correction. Although no study has demonstrated superiority of angioplasty versus stent placement in cases of central venous stenosis, current recommendations suggest angioplasty first, followed by stent placement in cases not responsive to angioplasty alone [2, 5, 43–45]. Stent placement peripheral to the first rib is not recommended due to the risk of crushing a stent in this location.

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The Role of Routine Venography Prior to Fistula Creation

14

Berry Fairchild and Ali Azizzadeh

Introduction

Ideal vascular access for patients requiring dialysis therapy is the arteriovenous fistula (AVF). The majority of patients presenting for permanent dialysis access are suitable candidates, as predicted by the standard principles of vascular surgery, including adequate inflow, adequate outflow, and presence of a suitable conduit. The Dialysis Outcomes and Practice Patterns Study (DOPPS) shows a striking difference in the use of AVF among hemodialysis patients in the United States (24 %) compared with European countries (80 %) [19]. The importance lies in the early identification of individuals suitable for AVF. Creation of an AVF 6 to 12 months prior to anticipated dialysis initiation (when GFR drops below 20–25 ml/min) generally allows for an adequate maturation while avoiding placement of temporary catheters and avoiding associated complications. Whenever possible, autogenous AVFs are preferable to prosthetic arteriovenous grafts (AVG) or central venous catheters (CVC). The Fistula First Breakthrough Initiative has made dramatic progress since its inception, successfully increasing the national AVF rate from 32 % in 2003 to nearly 60 % in 2011. However, the rate of CVC use remains unacceptably high, at nearly 80 % in the first 90 days [20]. In addition to having goals of continued increase in the utilization of AVF, it remains important to minimize the use of CVCs.

Physical examination by an experienced surgeon is the first step in determining optimal fistula location. Additionally, imaging often influences the choice of access location. Clinical guidelines from the NKF-KDOQI [3] states that imaging is only necessary in certain patients and that venography is indicated in special circumstances, including the presence of central venous stenosis and trauma or in patients with multiple previous access attempts. Despite the use of guidelines, up to one third of access procedures fail or mature incompletely [18]. More widespread use of preoperative imaging may reduce the fistula failure rate [18]. Ultrasound is an alternative to venography. However, ultrasound is limited by its inability to assess central venous patency [18]. This chapter will focus on the role of routine venography in vascular access planning.

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Technique

Generally, the nondominant upper extremity is studied at the time of venography for patients who present for the initial access placement. For patients who are not candidates for access creation in the nondominant extremity, a study of the dominant arm is reasonable. Common reasons that preclude AVF creation in the nondominant extremity include a lack of adequate arterial inflow, multiple previous access procedures, history of central venous occlusion, and history of pacemaker placement.

Access to the peripheral veins in the hand is gained, preferably with 20-gauge catheters, although 22-gauge are acceptable. Ultrasound can be used as an adjunct for patients who have difficult access. It is a rare event in which a vein of the hand is unable to be accessed and a vein above the wrist must be used. Factors that can contribute to difficulty in cannulation include an edematous extremity, cold room temperature, and arm position. While edema cannot usually be treated periprocedurally, a cold room resulting in vasoconstriction of the peripheral veins can be counteracted with a warm towel and the hand placed below the level of the heart to encourage venous engorgement. The patient is then positioned supine with the arm in mild abduction. Depending on the operator, the arms may be placed in as much as 90 degrees of abduction.

Contrast (see below) is injected through the catheter in the hand and contrast is followed with fluoroscopy to the central veins. Digital subtracted images of the central veins are acquired to assess for central stenosis or occlusion. If a

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central occlusion is seen, no further imaging of the ipsilateral extremity is needed, and the examination is ended (Fig. 14.1). If no central occlusion is present, additional contrast material is injected and the more distal veins studied with and without a tourniquet applied. Multiple unsubtracted spot images of the distal veins are obtained. The arm may be rotated for additional oblique views as needed for better visualization (Figs. 14.2, 14.3, and 14.4).

Contrast Selection

The choice of contrast is an important consideration, particularly in patients with renal impairment. Iodine-based contrast agents are the mainstay of vascular imaging, but they carry with them the risk of contrast-induced nephropathy (CIN). CIN has been defined as an increase in serum creatinine of greater than 25% or absolute increase of 0.5 mg/dL after contrast administration [10]. While the acute renal failure induced by contrast can lead to the need for renal replacement therapy, the importance of CIN, as demonstrated by several longitudinal studies, is an increase in all-cause mortality [24, 26]. Further, CIN almost exclusively occurs in patients with already depressed renal function, particularly those with advanced renal disease, such as those presenting for venography prior to fistula creation (Heye 2006 *Radiology*). Ideally, patients are evaluated and fistulae created at least 6 months prior to their anticipated need for hemodialysis in order to allow for maturation of AVF. This targeted subset of patients are at greatest risk for CIN.

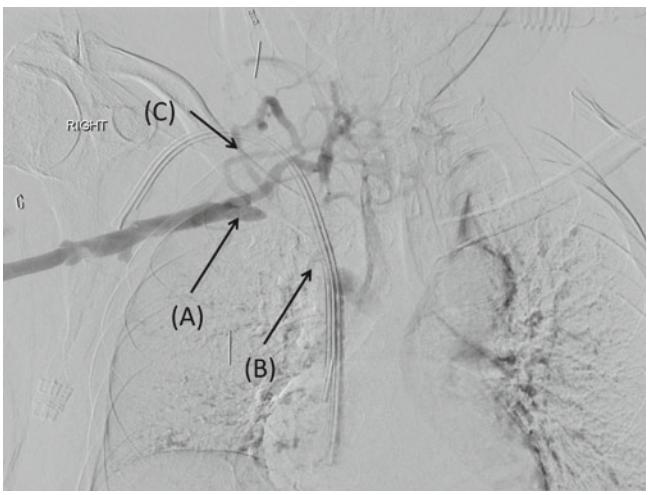


Fig. 14.1 Central occlusion. This right upper extremity venogram shows an occlusion of the right subclavian vein. (*A*) This is likely related to previous placement of a temporary hemodialysis catheter in the right subclavian vein. Contrast is draining into the superior vena cava (*B*) via numerous well-formed collaterals (*C*)

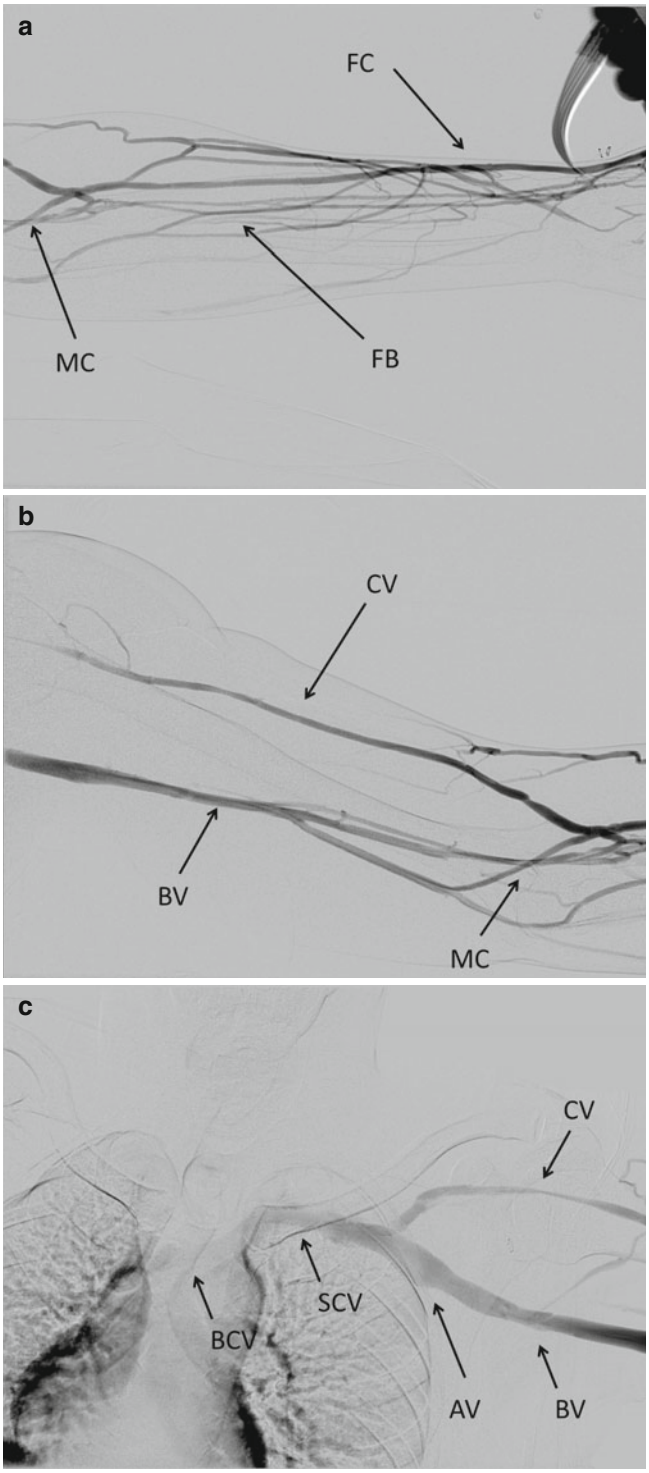


Fig. 14.2 (**a**) A left upper extremity venogram shows the forearm cephalic (*FC*) and forearm brachial (*FB*) veins drain via the median cubital vein (*MC*). The FC vein in this patient is suitable for use in creation of a radiocephalic AV fistula. (**b**) The median cubital vein (*MC*) drains into the basilic (*BV*) and cephalic (*CV*) veins of the upper arm. (**c**) The basilic vein (*BV*), axillary vein (*AV*), cephalic vein (*CV*), and subclavian vein (*SCV*) join the internal jugular vein to form the brachiocephalic vein (*BCV*) which drains into the superior vena cava

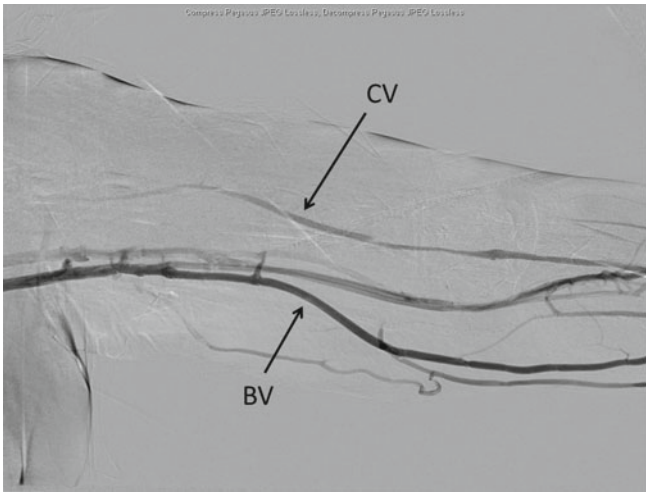


Fig. 14.3 A left upper extremity venogram shows a diminutive upper arm cephalic (UC) and a suitable upper arm basilic (UB) vein. This patient underwent a left upper arm brachiobasilic arteriovenous fistula creation

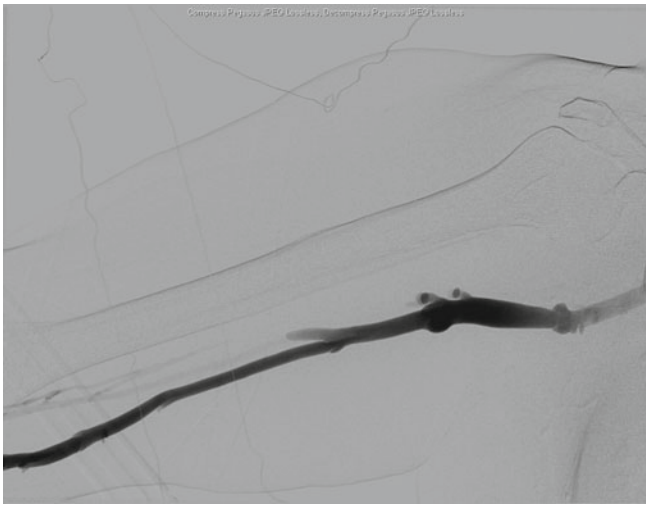


Fig. 14.4 A right upper extremity venogram shows absent superficial basilic and cephalic veins. This patient underwent a right upper arm arteriovenous graft placement

An alternative to conventional contrast-enhanced venography is carbon-dioxide (CO_2) venography, which is 97 % specific and 85 % sensitive in assessing upper limb vein patency and stenosis [22]. Heye et al. reported successful AVF access creation in 77 % of patients without suitable veins on physical examination after preoperative venous mapping with CO_2 venography [23]. Twenty percent of these AVFs were radiocephalic AVFs, which correlated well with similar studies using iodinated contrast and Vasc Surg.

Newer, less nephrotoxic, contrast agents have now replaced the tri-iodinated, high-osmolar contrast that were widely used at the time of the initial CIN studies. Reflective of this, contrast choice in patients with limited renal function varies between institution and surgeon. While CO_2 may be the sole choice of some surgeons, others will use dilute iso-osmolar nonionic contrast, iodixanol (Visipaque, GE Healthcare, Princeton, NJ), dilute low-osmolality contrast agents (LOCA), or a combination of CO_2 and dilute nonionic contrast. Won et al. [1] demonstrated that venography with small doses (10–15 mL) of dilute contrast media is safe in venous mapping in pre-dialysis patients. Further, several studies have shown iodixanol to be slightly less nephrotoxic than LOCA [25, 27] . While the benefit may be marginal, the additional cost of iodixanol over LOCA may be reasonable when large contrast volumes are anticipated.

CO2 contrast may also be considered in those patients with a documented allergy to iodinated contrast agents. The practice of substituting gadolinium contrast agents in these patients has been abandoned due to the risk of nephrogenic systemic fibrosis (NSF), even in patients who have initiated hemodialysis. In patients with a mild or moderate contrast reaction, premedication with steroids and Benadryl prior to iodinated contrast administration is another option. The premedication regimen varies slightly from institution to institution.

Interpretation

Normal Venous Anatomy of the Upper Extremity

Two types of veins are found in the upper extremity, superficial and deep. Superficial veins are located directly beneath the skin, between two layers of superficial fascia, and are used for the creation of AV fistula. Deep veins accompany arteries, creating venae comitantes.

The superficial veins of the upper extremity include digital, metacarpal, cephalic, basilic, and median. The venous network on the dorsal aspect of the hand drains into the main cephalic vein. Near the elbow, at the lateromedial portion of the arm, the main cephalic vein joins the median basilic (cubital) vein medially and the median cephalic vein laterally.

The accessory cephalic vein arises from the main cephalic vein, courses laterally and joins the median cephalic vein in the upper arm. Less commonly, the accessory cephalic vein originates from the dorsal venous network of the wrist and takes a variable course.

The basilic vein arises from the ulnar portion of the dorsal venous plexus. It courses medially until joining the median cubital vein at the lower third of the upper arm forming the upper arm basilic vein. At the elbow, a venous network in the shape of an "M" is formed by the accessory cephalic, the main (median) cephalic, the median cubital, and the forearm basilic veins.

Two brachial veins run parallel to the brachial artery. A perforating vein joins the deep brachial veins with the superficial

veins at the elbow. These perforating veins play an important role in the diversion of blood flow from radiocephalic AVFs through deep veins to central veins when occlusion occurs at the median cephalic or basilic vein near the elbow [11].

The forearm basilic and median cubital veins converge to form the basilic vein, which courses medially in the upper arm. The basilic vein perforates the deep fascia, joins the deep brachial veins, and forms the axillary vein. The axillary vein may be single or duplicated which rejoins to form the subclavian vein at the lower border of the first rib. At the head of the clavicle, the subclavian vein joins the internal jugular vein, forming the brachiocephalic vein.

The main and accessory forearm cephalic veins converge to form the upper arm cephalic vein, which courses anterolaterally. After piercing the clavipectoral fascia, it enters the deltopectoral triangle and finally joins the subclavian vein, just below the clavicle. The cephalic arch is prone to stenosis from cephalic vein vascular access [11].

Selection

Veins considered suitable for fistula creation are those:

1. Suitable in caliber by subjective measurement
2. Uninterrupted over its course
3. Without stenosis

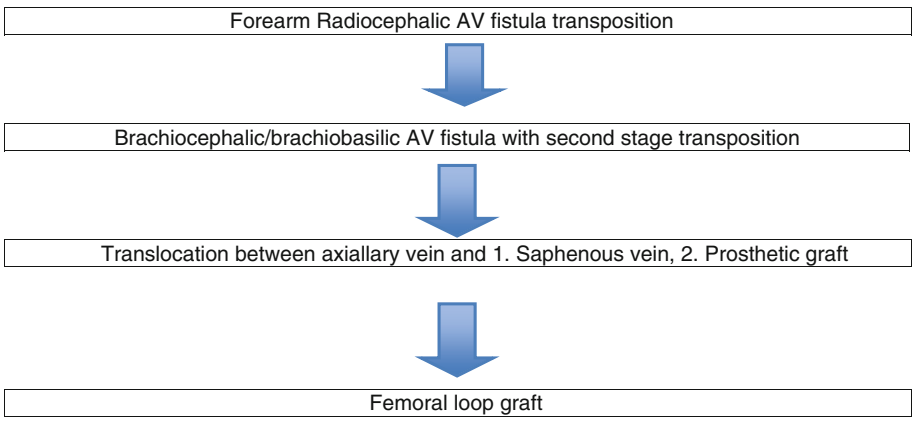
Radiocephalic AV fistula is the procedure of choice for vascular access. Our order of preference is illustrated in the figure below. After forearm radiocephalic (RC) AVF, in order of descending preference, we would elect to perform brachiocephalic (BC) AVF, brachiobasilic (BB) AVF with second-stage transposition, translocation between the brachial artery and axillary vein preferentially using the saphenous vein before prosthetic graft, and, finally, lower limb graft using saphenous or superficial femoral veins and common or superficial femoral arteries with translocation.

Findings Precluding Fistula Formation

Central Venous Stenosis

Central venous stenosis is a significant problem in the creation of long-term access circuit in patients requiring hemodialysis, with incidence reported upward of 40 % [2]. While central venous stenosis can be indirectly assessed on duplex ultrasound [16], the DOQI guidelines state that venography is mandatory in patients with history of ipsilateral central vein catheterization, edema, or differential extremity size as these findings may indicate inadequate venous drainage or central vein obstruction (NRK-DOQI). If not identified prior to AVF creation, the increased blood flow can overwhelm the collateral venous system, resulting in venous hypertension, severe function limiting extremity edema, and possible access abandonment [17]. One of the distinct advantages of routine venography prior to AVF creation is the ability to diagnose and treat central venous stenosis.

The DOQI guidelines reflect the high-incidence central venous stenosis in patients with history of prior central catheterization. In one study, 27 % of patients with central venous stenosis had a history of prior catheter placement [4]. The incidence of central venous stenosis is also contributed to by the central catheter access site and duration of catheter dwell times [4, 5]. Central venous catheters placed via a subclavian access are associated with a 42 % incidence of central venous stenosis, compared to 10 % of catheters placed via an internal jugular approach [6–8]. Additionally, left-side catheters are associated with a higher risk of central venous stenosis as compared to the right [9], perhaps due to its longer and more tortuous course. While evidence suggests that the large caliber of hemodialysis catheters contributes to high incidence of central vein stenosis after their placement [12], smaller caliber catheters, such as PICC lines, are also associated with thrombus formation and central venous stenosis [12, 13].



The mechanism of catheter-related stenosis is not completely understood but is thought to result from endothelial damage, secondary to the presence of the catheter. Microscopic evaluation of the vein in animal models demonstrates development of platelet microthrombi shortly after trauma [14]. Following this initial injury, it is thought that thrombus develops followed by the recruitment of smooth muscle cells, which begin to layer and thicken the venous wall [15]. The result is a less compliant or stenotic central vein.

Distal Variants

Distal variants that preclude fistula formation include length too short for cannulation in hemodialysis, caliber that is too small, and certain anatomic variants. Important anatomic variants include brachial-basilic ladder, early brachial-basilic confluence, and double terminal arch.

Brachial-basilic ladder is the presence of a perforating vein connecting the brachial vein to the basilic vein. Its presence increases the probability of developing stenosis. Early brachial-basilic confluence may make it impossible to create a fistula with enough length for use in hemodialysis. Early confluence additionally increases the probability of stenosis development due to inadequate blood flow. The impact of double terminal arch on the brachiocephalic fistula is unknown but may increase the likelihood of stenosis [21].

Importance lies in the awareness of these upper arm venous anatomic variations. Recognition of certain variants will influence operative planning and outcomes. We advocate for preoperative identification of these variants with the use of routine venography while planning vascular access.

Conclusion

Despite the use of guidelines, up to one third of access procedures fail or mature incompletely [18]. More widespread use of preoperative imaging may reduce the fistula failure rate. Venography is an important tool in the planning of AVF access planning. It is necessary for the exclusion of central vein stenosis and other distal variants.

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Direct Anastomosis: Cephalic Vein Hemodialysis Access

15

Rachel Heneghan and Niten Singh

Introduction

The radiocephalic and brachiocephalic autogenous access approaches are first-line options for dialysis access and listed as "preferred" access by the National Kidney Foundation Dialysis Outcome Quality Initiative (K/DOQI) most recent 2006 guidelines [1]. Both have superior long-term patency to prosthetic grafts in meta-analyses. This chapter focuses on direct anastomosis cephalic vein hemodialysis access, techniques, patency, and outcomes.

Radiocephalic (Cimino) Arteriovenous Fistula

The radiocephalic arteriovenous fistula is the most well-known and current first-choice technique for autogenous access [2]. It was the first surgically created fistula for hemodialysis and connected the radial artery to the cephalic vein in the forearm. It is now commonly known as the Brescia-Cimino fistula and was created in response to the multiple shortcomings and complications of the Quinton-Scribner shunt. In their original paper, 12 of 14 patients achieved maturation and could dialyze without complication [2, 3].

Although multiple variations exist, the original technique joins the end of the cephalic vein to the side of the radial artery just proximal to the wrist (Fig. 15.1). This procedure can be accomplished with one longitudinal incision; however, two can be made if necessary for vein mobilization. The vein is isolated and mobilized near the wrist, the nearby radial artery is identified and adequate length dissected, and the anastomosis is performed with 6–0 polypropylene suture in a running fashion. The details of the surgical technique are described below.

Another variation of the radiocephalic fistula is the "snuffbox" fistula [4]. It is the most distal autogenous fistula and consists of an anastomosis between the end of the cephalic vein and the size of the thenar branch of the radial artery that course through the anatomic snuffbox of the hand. It is performed through a single incision over the area of the snuffbox, and finer suture (7–0) is recommended due to smaller vessel size. The benefits of this approach include an extremely small incision, allowing easy anastomosis due to close proximity of the artery and vein with minimal mobilization, and the potential of increasing the size and arterializing the more proximal veins [4]. Conversely, it has poor maturation and patency in small diameter vessels, although an exact diameter is not quoted in the original descriptive article [5].

Radiocephalic Arteriovenous Fistula: Surgical Technique

A 3-cm longitudinal incision is made in the distal forearm midway between the radial artery and the cephalic vein. Alternatively, the artery and vein can be exposed using an incision in the anatomic snuffbox, although, as noted above, the vessels are smaller at this location. A small skin flap is raised toward the vein side, the cephalic vein is dissected free, and two small spring retractors can be oriented diagonally across the wound to aid exposure. The vein is then dissected until a length of 3 cm or more is mobilized, allowing for transposition onto the radial artery. A skin flap is then raised toward the radial artery side, and approximately 2–3 cm of the artery is exposed by excising the investing soft tissue. It is important to ligate any branches of the artery at this level. Vessel loops should be placed for proximal and distal control. The vein is then transected, distended with saline, and spatulated. Prior to occluding and opening the radial artery, heparin can be given intravenously. The artery is occluded with two

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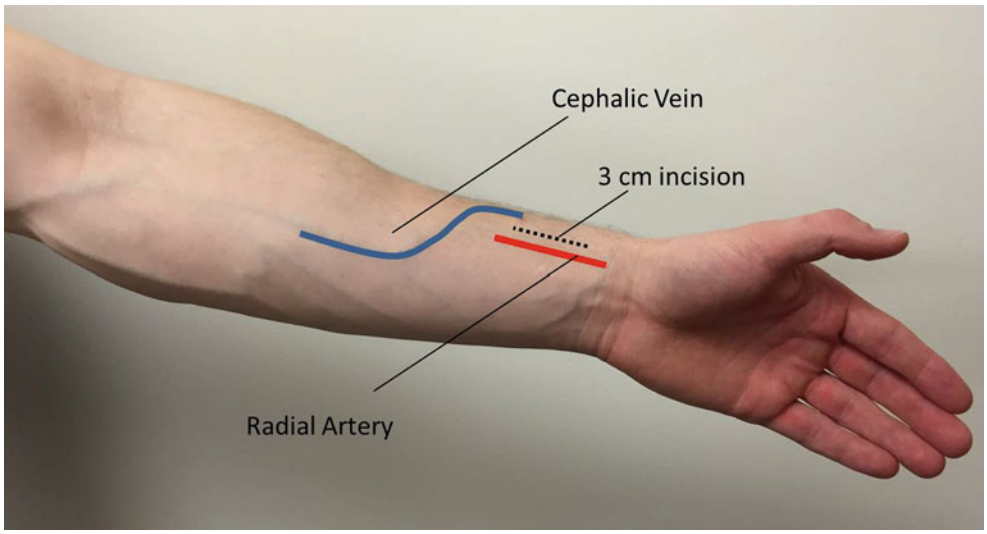

Fig. 15.1 An approximately 3-cm longitudinal incision is made between the cephalic vein and the radial artery proximal to the skin crease at the wrist to create a radiocephalic autogenous access

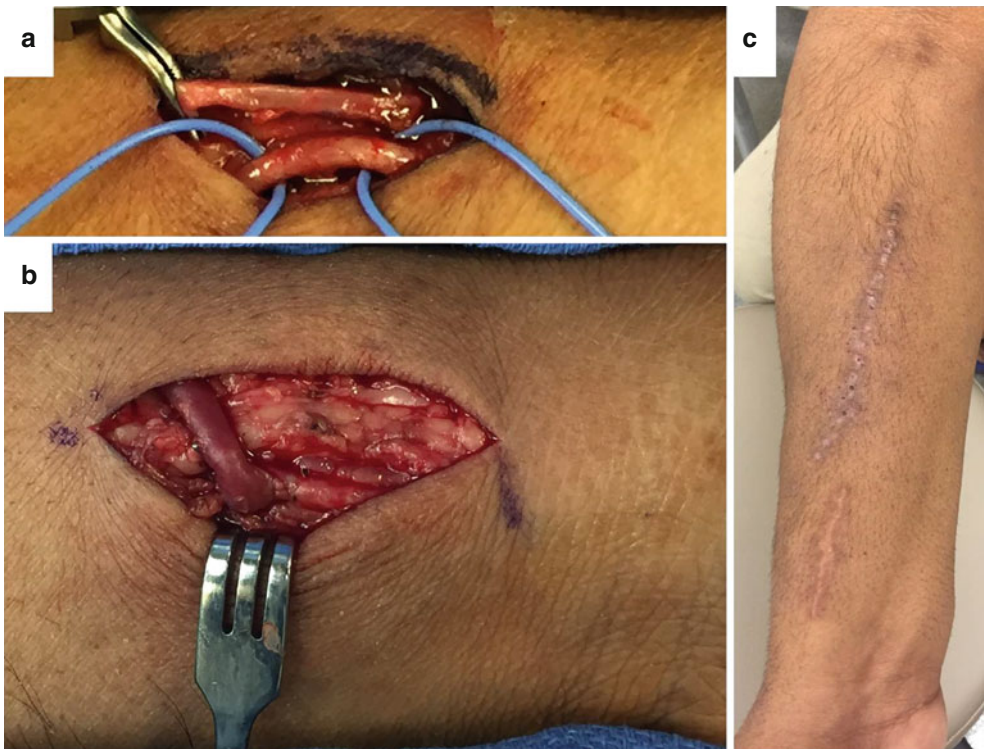

Fig. 15.2 Radiocephalic autogenous access (**a**). Exposure of the cephalic vein (marked by the small clamp) and the radial artery (marked by the vessel loops) (**b**). The cephalic vein is transected and anastomosed in an end of vein side of the radial artery fashion (**c**). A mature radiocephalic arteriovenous fistula in use for 18 months (Images courtesy of Sherene Shalhub, University of Washington)

small microvascular clamps, and a 0.75-cm arteriotomy is created using a #11 scalpel blade and fine arteriotomy scissors (e.g., Pott's scissors). The anastomosis is performed end-to-side using a running 6–0 monofilament polypropylene suture. Other anastomotic configurations have been reported (i.e., side-side, end artery-end vein, end artery-side vein), although it is the general impression that the end vein-side artery is associated with the greatest long-term patency and the lowest incidence of venous hypertension in the hand. After the creation of the anastomosis, the fistula and hand perfusion should be checked with intraoperative Doppler. The fistula should have, at the minimum, continuous signal throughout systole and diastole. Optimally, a thrill should be felt but this can take time to develop. Pulsatile flow in the cephalic vein is not normal and indicates an outflow obstruction. It warrants inspection of the anastomosis with possible revision or further mobilization of the cephalic vein proximally in order to better orient the vein to the artery. The incision is closed in two layers – the deep dermis and subcuticular layer. The deep dermis is closed using an interrupted 3–0 braided, absorbable suture and the skin closed using a running 4–0 monofilament, absorbable suture.

After creation, the radiocephalic fistula is given 6–8 weeks to mature before accessing it for hemodialysis. Prior to the first access for hemodialysis, the fistula should be examined for maturation. In order for a fistula to mature, the vein wall must remodel and thicken in response to higher pressures. This allows it to sustain the repetitive cannulations. A minimum fistula diameter of 0.4 cm combined with a minimum flow volume of 500 mL/min predicts a high level of fistula usability (Fig. 15.1c) [6]. The fistula must also be accessible and within 1 cm of the skin surface with a straight segment that is ideally 6–10 cm in length [6]. More criteria and recommendations for maturation are listed in a following section.

Brachiocephalic Arteriovenous Fistula

The brachial artery to cephalic vein fistula is the next anatomic level autogenous fistula. It consists of an anastomosis between the side of the brachial artery and end of the cephalic vein in the antecubital fossa or upper arm. It has excellent flow and maturation rates but has been associated with higher rates of "steal" phenomenon due to the larger arterial caliber than in the forearm [7]. It also eliminates the forearm for consideration of future access. If the radiocephalic fistula fails, the brachiocephalic fistula is a possibility. In patients with small vessels in the forearm, the brachiocephalic fistula becomes the first-line fistula in most cases when the upper arm vein is of sufficient size.

Brachiocephalic Arteriovenous Fistula: Surgical Technique

The incision for this access varies due to the specific location of the cephalic vein, the more distal median antecubital vein, the brachial artery, and the body habitus of the patient. Three incisions are described: the first is a transverse incision across the antecubital fossa (Fig. 15.3); the second is a sigmoid incision from medial in the upper arm across the antecubital fossa and down along the cephalic vein in the forearm; and the third option is actually two separate incisions – one over the brachial artery and the other over the cephalic vein in the upper arm. There is no superior approach of these three – above all else is adequate exposure to the vessels in the forearm.

We prefer to perform this access in the following way: The brachial artery is palpated in the upper arm just above the antecubital fossa and its course marked on the skin. The cephalic vein is found crossing the antecubital fossa and its course marked as well. Using a sigmoid incision, the skin is incised starting at this point and extended across the antecubital crease and down the forearm, incorporating the marked cephalic vein, and with care not to deeply incise and injure the cephalic vein or its distal continuation, the median antecubital vein. It can be helpful to place marks transversely across the course of the planned incision to aid in skin alignment at closure. Just as in the radiocephalic operation, exposure can be facilitated with two large spring retractors. The cephalic vein is dissected and mobilized for approximately 4 cm with superior and inferior skin flaps. The cephalic vein and its distal continuation as the median antecubital vein typically bifurcates or trifurcates in the antecubital fossa. The proximal trunk of these branches can be preserved and incorporated to create a larger hood for the anastomosis. The large, deep branches of the vein should be suture ligated to prevent uncontrolled bleeding as they can retract into the muscle and soft tissue. After exposure of the cephalic vein, attention is turned to the brachial artery by incising the overlying bicipital aponeurosis. Approximately 2 to 3 cm of the artery is dissected and mobilized. A pair of deep brachial veins flanks the artery and communicates via delicate crossing branches that overlie the artery. These branches must be dissected to allow exposure. The vein is distended with saline and spatulated and any defects repaired. The patient is given 5000 units of heparin systemically, and the brachial artery is occluded proximally and distally with vascular clamps. A 0.75-cm longitudinal arteriotomy is created with a #11 scalpel blade and arteriotomy scissors. The anastomosis is performed in a running fashion using a 6–0 monofilament vascular suture (Fig. 15.4). Upon completion, as in the radiocephalic fistula, the fistula and the arterial signals at the wrist are investigated with the continuous wave Doppler. Unlike the radial artery-based autogenous access, a thrill should be detected immediately at the proximal end of the fistula. As above, the absence of a thrill or a pulsatile Doppler signal mandates further inspection. The solution may be as simple as mobilizing the vein proximally to straighten its course or undoing the anastomosis and redoing it due to technical error. A diminished or monophasic Doppler signal at the wrist suggests that the hand may be ischemic. It is impossible to determine at this point whether this is due to reversible vasospasm or frank hand ischemia. All patients with suspected hand ischemia require close observation throughout the postoperative period with treatment as required, including revision of the anastomosis. The wound edges are re-approximated with an interrupted 3–0 braided, absorbable suture, and the skin is closed with a subcuticular stitch (e.g., 4–0 monofilament, absorbable).

Complications of Direct Anastomosis: Cephalic Vein Hemodialysis Access

Failure of Maturation

In the radiocephalic AVF, failure or slowed maturation can occur because of large tributaries in the forearm that shunt

blood flow away from the cephalic vein. Identification of these tributaries by physical examination, ultrasonography, or fistulagram and ligation is usually sufficient for the fistula to mature (Fig. 15.5) [8]. Ideally, ligation of these large branches should be performed at the time of fistula creation to avoid this complication. Should the radiocephalic access fail to mature without identifiable cause, the fistula will lead to enlargement of the more proximal cephalic vein to allow for new fistula creation in the ipsilateral upper arm (brachiocephalic access).

Access Thrombosis

Although thrombosis is less common in autogenous fistulae than in AV grafts, it nevertheless requires intervention. Unlike AV grafts, AVF can remain patent with minimal flow and should be examined with ultrasound to confirm or exclude the diagnosis [8]. Some indications that the fistula has a venous outflow obstruction and possible thrombosis include high recirculation times, elevated venous pressures, and inability to achieve adequate urea clearance [8].

Endovascular examination is a good first option for addressing anastomotic stenosis, as it can identify and potentially treat unidentified stenosis from the venous outflow to the central veins. Angiography and identification of the stenotic area can be performed using venipuncture in a retrograde fashion, placing a 4–6 F short sheath, and placing a wire past the point of stenosis or occlusion [9, 10]. Tissue plasminogen factor activator (tPA) can be instilled (3 mg) with 3000 units of heparin while occluding the arterial inflow and venous outflow. After 30 min, repeat venogram is performed, and outflow stenosis is balloon angioplastied with a balloon diameter ranging from 4 to 6 mm, 10–12 atm of pressure, for 30 s–2 min [10]. Repeat angiography is performed and if residual stenosis is seen, repeat PTA can be performed with an upsized balloon. At the completion, any arterial thrombosis is cleared with a Fogarty embolectomy catheter [10].

Success with this method is better in stenosis than occlusion, which is not surprising, and within stenosed AVF, poor long-term patency is seen in mature fistulas less than 6 months old and long segment stenosis (greater than 2 cm) compared to older fistulae and short segment stenosis [9, 10]. In one study, overall primary patency after PTA at 12 months

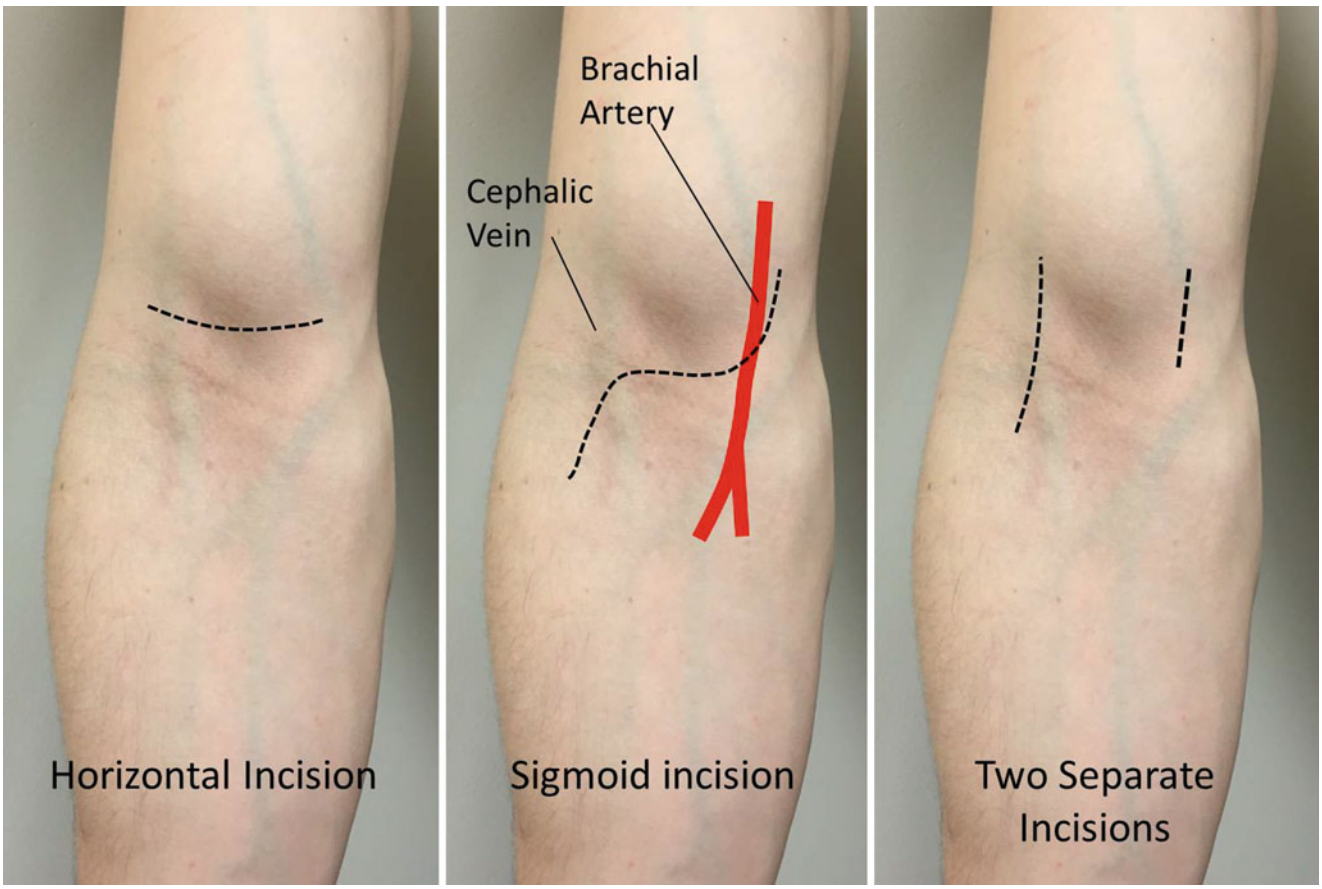

Fig. 15.3 Three incisions for brachiocephalic access, determined by patient body habitus and vessel locations

was 53 % and secondary patency 84 % [10]. Other prognostic factors of restenosis and loss of patency include the presence of at least one comorbid factor – diabetes, coronary artery disease, or peripheral artery disease [9]. More recently, Heye, et al. found that radiocephalic AVF stenosis had a higher technical success rate using PTA than brachiocephalic AVF, and stenosis recurrence was seen in 52.7 % [11]. Recurrence was inversely correlated with AVF age and positively correlated with diabetes, and older AVF had a higher primary and secondary patency rate. Primary patency at 1 year was 48.5 %, assisted primary patency was 77.6 %, and secondary patency was 83.6 % [11].

For patients in whom PTA fails, surgical revision, thrombectomy, or abandonment with creation of a more proximal fistula is the next option.

Venous Hypertension

Venous hypertension causes arm swelling and is quite common after creation of AVF. Severe arm swelling can occur secondary to venous outflow stenosis or central venous stenosis or occlusion [8]. Management of outflow stenosis and central venous stenosis are detailed elsewhere in this textbook. If the patient continues to have uncontrolled arm swelling or develops ulceration of the hand, ligation of the AVF is necessary [8].

Infection

Autogenous access is resistant to infection, as no foreign material is placed at the time of creation. Nevertheless, all dialysis patients have impaired immunity due to their kidney disease and infection can occur. Superficial cellulitis of the skin around the cannulation site can be treated with oral antibiotics with care to appropriate dosing for the renal patient as an outpatient. If a patient presents with signs or symptoms of bacteremia or sepsis, inpatient admission with broad spectrum IV antibiotics is warranted [12]. If a temporary catheter is in place at the time of presentation, an investigation for possible catheter infection is warranted [12].

Aneurysms and Pseudoaneurysms

Repeated cannulation can lead to pseudoaneurysm formation in AVF. Pseudoaneurysms can become infected as well; however, this is not as common in AVF as it is in AV grafts. Dialysis access aneurysms are discussed in chapter xx.

Dialysis Access-Related Steal Syndrome Access-induced upper extremity ischemic steal syndrome is a serious complication that requires close monitoring and possible surgical intervention. It manifests as anything from cool digits to tissue loss, which indicates profound, prolonged ischemia to the hand. This topic is addressed in chapter xx.

Maturation Outcomes

Performing a technically perfect autogenous forearm or upper arm fistula is meaningless if that fistula does not mature. It is interesting to note that in the original radiocephalic description by Brescia and Cimino, their failure to mature (FTM) rate was 11 %, and this is largely due to their cohort which consisted of younger patients with idiopathic glomerulonephritis [2]. Multiple studies cite that approximately 25 % of initial autogenous fistulae require remedial imaging or procedure to aid maturation [13, 14]. In many patients, this causes prolonged dependence on a tunneled or non-tunneled access for dialysis or may cause some patients to require interval placement of a catheter due to worsening of their renal function while awaiting maturation of their fistula. This is not ideal for a variety of reasons – most of all due to the increased risk of infection with catheter placement. Voormolen et al. performed a systematic review of risk factors for nonmaturation and results of early treatment. They concluded that early evaluation of postoperative hemodynamic risk factors, such as poor venous outflow and small venous diameter, is the most effective way to stratify nonmaturation risk [15]. They found across the studies included in the review that with early intervention after identification of postoperative nonmaturation risk factors, there was a high rate of fistula maturation, which averaged 86 %, with 1-year primary patency of 51 % and 1-year secondary patency of 76 % [15].

Long-Term Patency

It is difficult to assess true long-term patency in the dialysis population due to the shortened life expectancy of a majority of these patients and lack of prospective randomized trials comparing autogenous to prosthetic access. Several meta-analyses have been performed regarding long-term patency of autogenous access, as well as comparing long-term patency of autogenous and prosthetic access.

Huber et al., in 2003, performed a meta-analysis of upper extremity AV fistula and graft patency and determined that primary patency of AVF was 72 % at 6 months and 51 % at 18 months, and the secondary patency of AVF was 86 % at 6 months and 77 % at 18 months, which were significantly better than the AV graft's primary and secondary patency rates (Fig. 15.6) [16]. In another meta-analysis of 83 studies performed by Murad et al. as a part of the Society for Vascular Surgery Clinical Practice Guidelines in 2008, primary and secondary patency rates at 12 and 36 months were

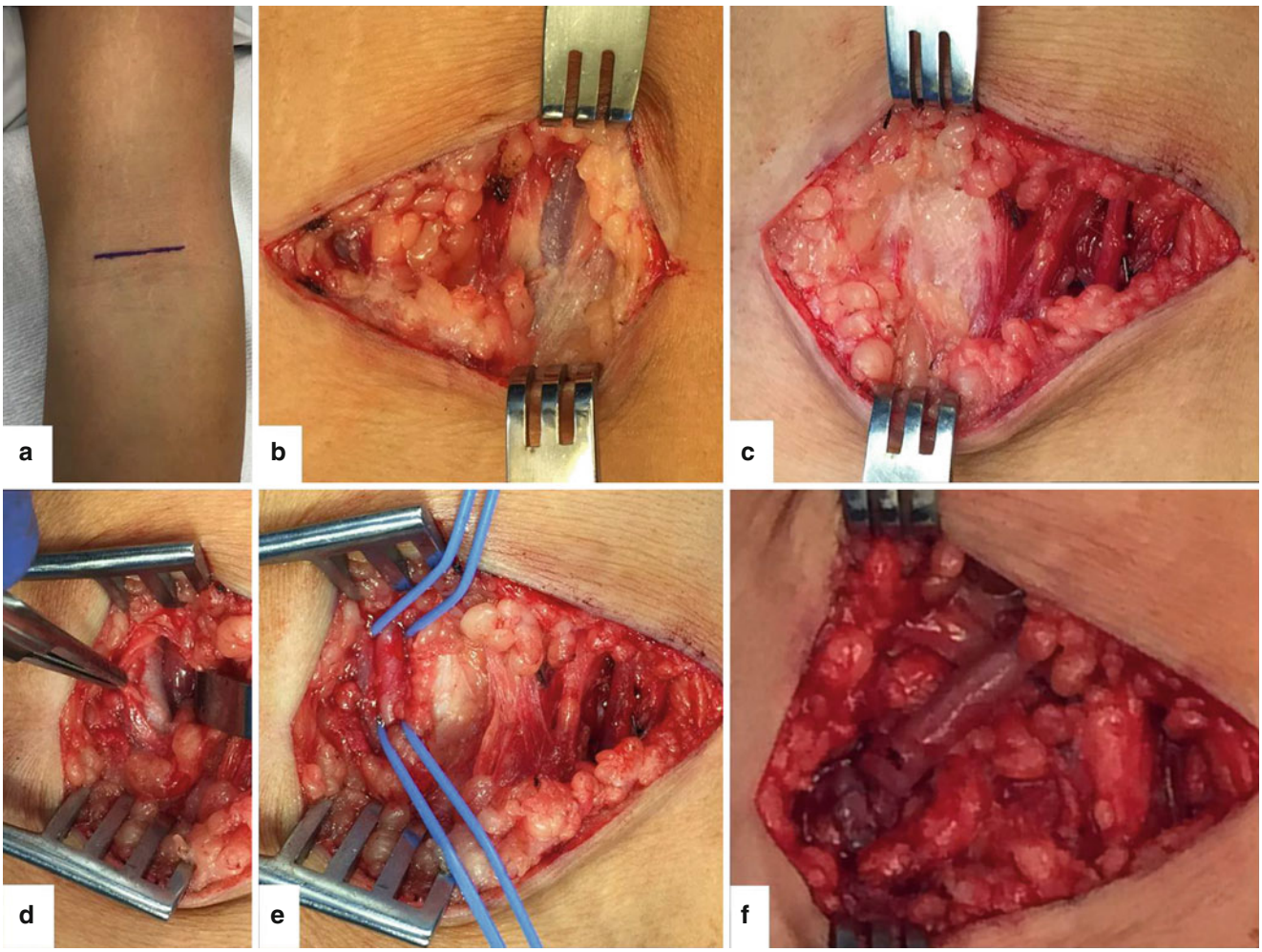

Fig. 15.4 Brachiocephalic autogenous access. A transverse skin incision is created proximal to the antecubital crease (**a**). Subcutaneous flaps are created over the cephalic vein distally to increase the length for mobilization (**b**). The brachial artery dissection begins beneath the bicipital aponeurosis (**c**). The brachial vein is visulualized (d) and the brachial artery dissected and vessel loops are placed proximally and distally (**e**). The end of the cephalic vein is sewn to the side of the brachial artery to complete the anastomosis.

significantly higher in the autogenous access group [17]. They also concluded a decreased risk of infection in AVF, but not other complications, when compared to the prosthetic group [17]. In 2012, Smith et al. performed a systematic review of publications to determine several risk factors for decreased long-term patency of autogenous access. Among the risk factors were increased age, diabetes, smoking, hypotension, BMI >35, arterial diameter <2 mm, atherosclerosis, venous diameter <2 mm, and venous distensibility <0.5 ml/min [18] (Figs. 15.5 and 15.6).

Most recently, in 2014, a meta-analysis of 46 publications totaling 12,383 AVFs found that the pooled primary failure rate was 23 %, and when divided into lower arm it was 28 % and upper arm 20 % [14]. Pooled primary patency was 60 % at 1 year and 51 % at 2 years. There was a significant difference in primary patency between lower and upper arm fistu-

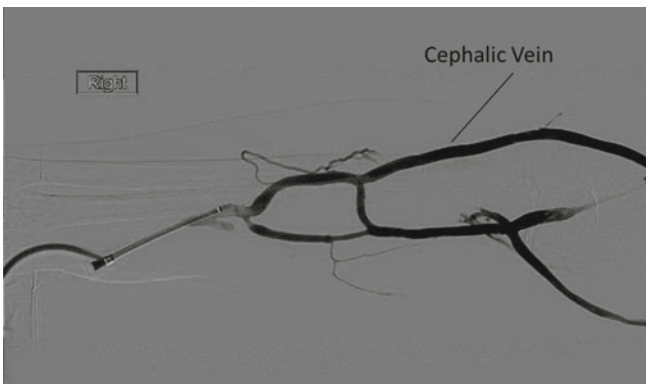

Fig. 15.5 A fistulagram of a radiocephalic arteriovenous fistula that has failed to mature showing the large tributaries in the forearm that are shunting the blood flow away from the cephalic vein (Image courtesy of Sherene Shalhub, University of Washington)

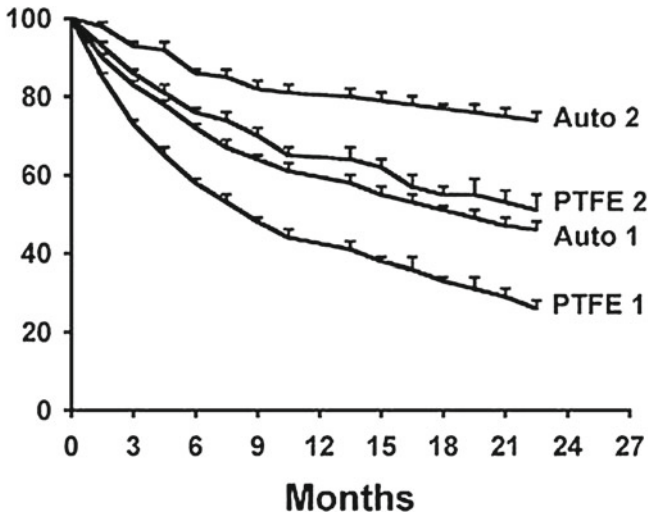

Fig. 15.6 The patency rates (percent patent) for the autogenous (Auto) and PTFE (PTFE) upper extremity hemodialysis access are plotted against time (months) with the positive standard error bars. Both the primary (Auto 1, PTFE 1) and secondary (Auto 2, PTFE 2) patency rates for the two access types are shown. The patency rates for the autogenous access were better than their corresponding PTFE counterparts with the one exception of the initial (1.5 months) time point for the primary patency comparison (From Huber et al. [16])

las at 1 year, but this did not persist at 2 years. Secondary patency was 71 % at 1 year and 64 % at 2 years [14].

Conclusion

The radiocephalic and brachiocephalic autogenous access approaches are first-line options for dialysis access, with superior long-term patency to prosthetic grafts in meta-analyses. With that stated, presented above are criteria the vascular surgeon should follow to ensure selection of the proper access for each patient presenting with ESRD, as all patients are not candidates for native fistulas. A standardized approach to these patients is paramount to attaining higher maturation and patency rates in one's own practice. Familiarity with office-based vascular laboratory studies for fistula surveillance and new endovascular technology for fistula salvage will be crucial as the number of patients requiring dialysis access continues to grow.

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Forearm Vein Transposition

16

Jennifer L. Worsham, Charlie C. Cheng, Zulfiqar F. Cheema, Grant T. Fankhauser, and Michael B. Silva Jr.

Historical Perspective

Brescia and Cimino et al. first described the creation of an arteriovenous fistula for hemodialysis access in 1966 [1]. Fifty years later, the National Kidney Foundation Dialysis Outcomes Quality Initiative (KDOQI) Guidelines continue to support radiocephalic arteriovenous fistula as the preferred initial vascular access [2]. Preference for a radiocephalic fistula is followed by brachiocephalic fistula, transposed brachiobasilic fistula, and lastly arteriovenous synthetic graft [2]. The overarching principal is to begin as distal as feasible and move proximally for future access procedures. The first description of a transposed upper arm brachiobasilic fistula was by Dagher et al. in 1976 [3]. Forearm cephalic or basilic vein transposition has also been described but is less commonly employed. If a forearm basilic or cephalic vein is of adequate size but anatomical constraints preclude a Cimino-type fistula, these distal transposition procedures allow for additional options. While more involved than a Cimino-type fistula, these forearm fistula options preserve upper arm veins for future procedures and may provide reliable dialysis access.

Patient Selection

The use of preoperative duplex ultrasound vein mapping is essential in identifying patients with adequate veins for autogenous arteriovenous fistula creation. Segmental stenoses and deeper suitable veins may be overlooked with visual inspection and physical examination alone. The fact that these suitable veins may not be easily identifiable on visual inspection can impart some protective status from prior venipuncture. Ideally, vascular mapping should be performed using a high-resolution linear ultrasound transducer (7 MHz or higher) with a tourniquet placed around the upper arm. Vein compressibility is assessed along the entire vein as noncompressibility may indicate segmental scarring or thrombosis. As previously reported by Silva et al., the recommended criteria for satisfactory venous conduit is a luminal diameter of at least 2.5 mm [4]. If the vein is marginal in size (2–2.4 m), the surgeon can perform intraoperative vein mapping after the patient has received a regional upper extremity block or general anesthetic. After anesthesia, the marginal vein may dilate and show its true diameter. If a potential cephalic or basilic vein is identified, it should be evaluated for continuity with the upper arm and deep venous systems. The vein should be followed along its entire length to confirm its patency and size until it connects with the upper arm venous system. Central venous stenosis should be suspected if there are differences in extremity diameter, asymmetric edema, prominent collateral veins, history of prior central venous catheter placement, or multiple previous hemodialysis attempts. Consideration should be taken to evaluate these patients with further duplex ultrasound or by venogram if needed.

If there is any doubt of arterial adequacy, such as a weak pulse, arterial duplex can be performed simultaneously. The recommended criteria for satisfactory arterial inflow include absence of a pressure gradient between arms, patent palmar arch, and arterial lumen diameter greater than or equal to 2.0 mm [4]. A recent retrospective single-center study by Masengu et al. explored preoperative ultrasound vessel measurements on wrist radiocephalic arteriovenous fistulae and noted those with arterial volume flow < 50 mL/min were seven times more likely to fail as compared to those with higher flow [5]. Current high-resolution ultrasound technology allows for in-depth assessment of both arterial and venous systems and should always be performed before any fistula creation as they can be used as predictors for successful fistula creation.

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Surgical Technique

Forearm Arteriovenous Fistulae in General

Anesthesia usually consists of a regional upper extremity block or general anesthesia if regional block is infeasible or unsuccessful. If a direct radiocephalic (Brescia-Cimino) fistula is possible, then this should be the first procedure of choice. Various anatomic constraints may make a Cimino-type fistula impractical—a deep forearm cephalic vein, a dorsal oriented forearm cephalic vein, and inadequate radial artery flow at the wrist. The forearm cephalic vein may not be an acceptable conduit while the forearm basilic vein is. When the Cimino-type fistula is not an option, these other fistula options may exist: transposed or superficialized radiocephalic, transposed ulnarcephalic, transposed radiobasilic, superficialized ulnarbasilic, or various loop configurations of the cephalic or basilic veins to the arteries at the antecubital fossa.

During forearm fistula creation, the authors prefer to ligate as many side branches of the venous conduit as possible. This can be performed during initial dissection of the vein or after creation of the fistula. If the entire length of the vein is not dissected, duplex ultrasound can be used to find side branches. Venography can also be used but is seldom necessary with a skilled ultrasound operator. Once side branches are identified, small incisions can be made over the side branches to facilitate their ligation.

At the time of anastomosis creation, care should be taken to prevent any twisting or kinking of the venous conduit. When tunneling or looping is performed, the orientation of the vein should be marked with sterile ink. Clamps should be avoided on the venous conduit since this can injure the fragile venous endothelium. The authors prefer a padded bulldog clamp or single vessel loop to minimize venous trauma. The artery should be handled gently as well since traumatic clamping may lead to dissections that limit inflow or more distal flow. The arteriotomy should be carefully oriented with respect to the orientation of the vein. The arteriotomy may need to be oriented in a more radial or ulnar direction depending on the course of the vein for the most natural positioning of the anastomosis. Arterial inflow and back bleeding should be noted. Deficiency in either should prompt on-table investigation to ensure adequate inflow and prevent distal ischemia.

After completion of the anastomosis and restoration of flow, it is essential that a thrill be felt within the vein. Venospasm is common after manipulation of the vein and initial restoration of flow. Persistence of spasm may be treated with intravascular papaverine or nitroglycerin. Persistent absence of a thrill points to a technical or anatomic defect and requires on-table investigation. Duplex ultrasound or angiography may be performed to evaluate the fistula. Problems identified at the level of the anastomosis may require its revision.

Care should be taken when closing incisions to prevent wound complications. Limb edema is not uncommon after fistula creation and may put stress on incisions. Incisions are closed in layers using absorbable suture. For patients with especially thin skin in the operative field, interrupted nonabsorbable sutures such as nylon may provide better protection against wound breakdown. Care should always be taken to maintain strict atraumatic technique when handling the skin edges.

Radiocephalic Superficialization or Transposition

When the cephalic vein is of adequate size and quality in the forearm but it runs too deeply or too dorsally, transposition or superficialization may be required. This is especially true in patients with obesity. While the cephalic vein is often perceived as a superficial vessel in patients with obesity, it may not course superficially enough to provide a reliable target for hemodialysis access. In other patients the vein is abnormally dorsally oriented, and creation of a fistula there may lead to difficulty during hemodialysis access. Furthermore, dissection of the cephalic vein along its entire course in the forearm allows for complete visualization and ligation of all side branches.

The operative procedure has previously been described by Silva et al. [6]. Once adequate anesthesia has been confirmed, an incision is made directly overlying the vein beginning at its distalmost usable aspect at the wrist and carried toward the antecubital fossa (Fig. 16.1). A single incision or series of skip incisions may be used. The vein is dissected free from all surrounding tissue. Venous branches along the length of the vein are ligated and divided. The vein is transected at the wrist. Heparinized saline is injected through the transected end of the vein with digital compression for occlusion of outflow at the antecubital fossa (Fig. 16.2). This results in substantial dilation of the freed segment of vein. The vein is then wrapped in a saline-soaked sponge, and attention is then turned toward the arterial dissection.

The portion of the radial artery that has been identified as suitable for inflow is then dissected. Although there are typically no arterial branches on the anterior aspect of the artery, there are usually several paired arterial branches leaving the radial artery on each side. These should be controlled or ligated to prevent pesky bleeding during the anastomosis. Vessel loops are placed proximally and distally along the artery for vascular control.

A tunneling instrument is passed to develop the superficial subcutaneous tunnel along the volar surface of the fore-

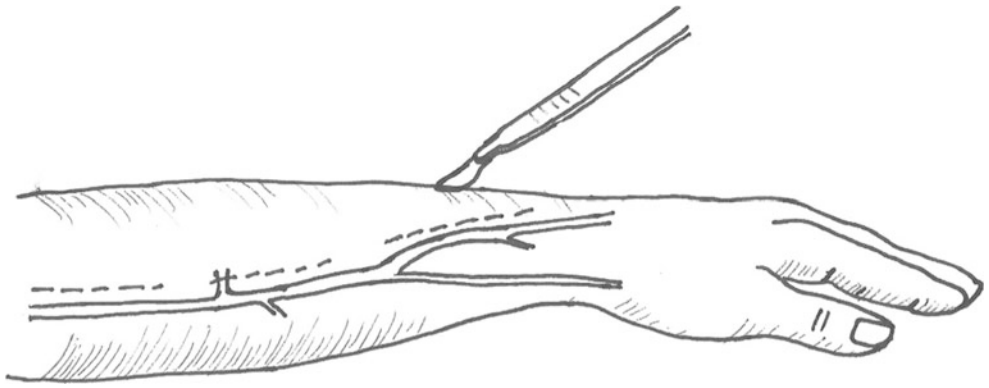


Fig. 16.1 Incision sites overlying forearm cephalic vein for transposition

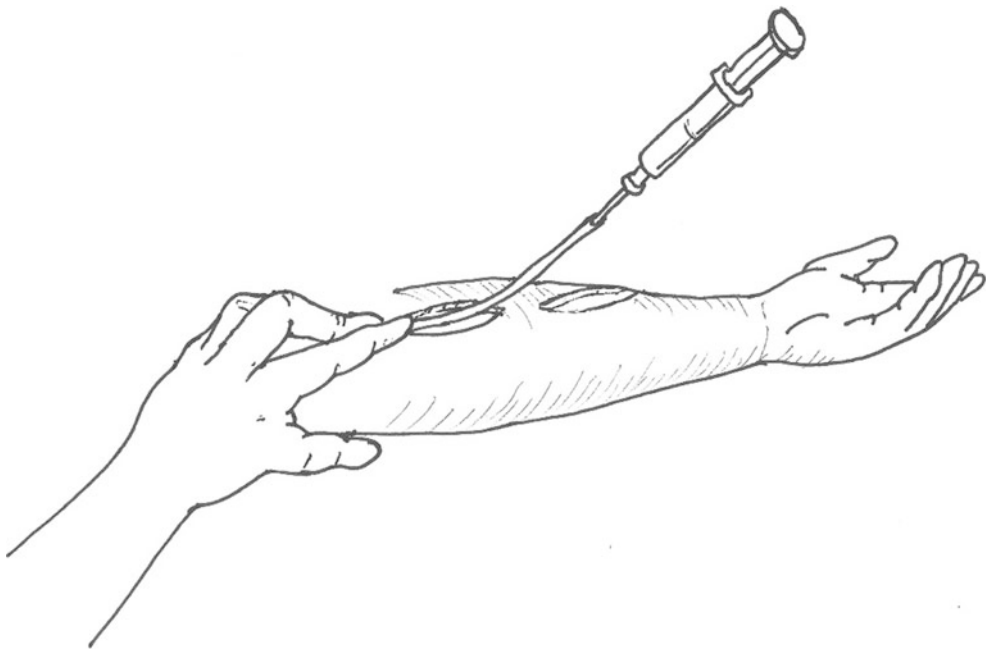


Fig. 16.2 Dilation of dissected forearm cephalic vein with heparinized saline

arm. The vein is marked along its length with a sterile marker. Once the vein has been passed through the tunnel (Figs. 16.3 and 16.4) and hemostasis has been assured, the patient is typically given a bolus of 3,000 units of intravenous heparin. A 15–20 mm arteriotomy is made, and an end-to-side anastomosis is then performed to the radial artery (Fig. 16.5).

Transposed Ulnarcephalic Fistula

The ulnarcephalic fistula is appropriate when the radial artery is not an acceptable site for arterial inflow, but the cephalic vein is of good size and quality. Care must be taken in these situations to ensure adequate perfusion to the hand. An arteriogram is usually necessary to define the arterial anatomy of the forearm and hand. Correctable problems with arterial inflow should be addressed. It is the authors' preference to perform angiographic assessment of the hand perfusion. Perfusion to the hand should be documented with and without ulnar compression since ulnar flow will be diverted through the fistula. Inadequate perfusion of the hand through the ulnar artery or a lack of collateral perfusion is a relative contraindication to creation of an ulnarcephalic fistula.

Similarly to the previously described radiocephalic transposition, the cephalic vein is dissected free from the antecubital fossa to the wrist using a single incision or multiple skip incisions. All venous branches are ligated. The ulnar artery is dissected using a longitudinal incision. The ulnar artery tends to be deeper than the radial artery and is in intimate proximity to the ulnar nerve. A meticulous dissection should be performed taking care to avoid crossing veins and small branches of the artery. The artery is encircled with vessel loops. The cephalic vein is transected, flushed, marked, and tunneled toward the ulnar artery. Heparinization is performed

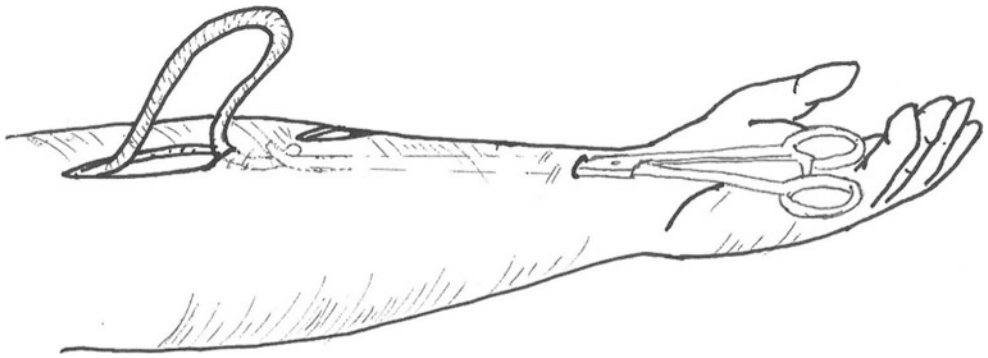


Fig. 16.3 Superficial tunneling for forearm cephalic vein transposition

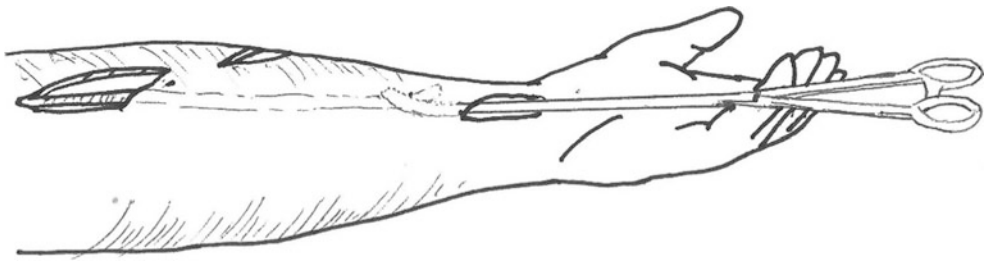
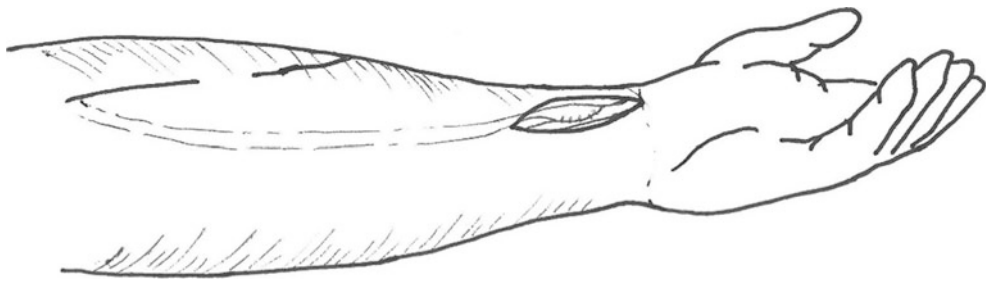


Fig. 16.4 Completion of superficial tunneling for forearm cephalic vein transposition

Fig. 16.5 After completion of radiocephalic anastomosis



after tunneling to prevent excessive bleeding. An arteriotomy is made, and an end-to-side anastomosis is made with the ulnar artery.

Transposed Radiobasilic Fistula

When the cephalic vein is of inadequate size or quality but the basilic vein is adequate, a transposed radiobasilic fistula can be considered. The basilic vein runs deeper than the cephalic vein and runs along the ulnar aspect of the forearm, making its native position inappropriate for dialysis access. The basilic vein in the forearm always must be transposed to a more accessible location. Duplex ultrasound is a useful adjunct for localization of the vein along its course. Side branches can be marked at the same time. Either a single continuous or a series of skip incisions can be made along the course of the vein, dissecting along its entire course in the forearm back toward the antecubital fossa. The radial artery is dissected at the wrist using a longitudinal incision as previously described. The basilic vein is transected, flushed, marked, and tunneled toward the distal radial artery (Figs. 16.6, 16.7, and 16.8). The more radially the vein can be tunneled, the less supination of the wrist will be necessary during dialysis sessions. An arteriotomy is made and an end-to-side anastomosis is made with the radial artery (Fig. 16.9). An example of this fistula after maturation created by the authors is shown in Image 16.1.

Transposed Ulnarbasilic Fistula

The ulnarbasilic fistula is appropriate when neither the radial artery nor cephalic vein is an acceptable conduit in the forearm. The same cautions must be employed when using the ulnar artery for inflow when the radial artery is unacceptable. Care must be taken not to jeopardize perfusion to the hand if the ulnar artery is its dominant or sole perfusion.

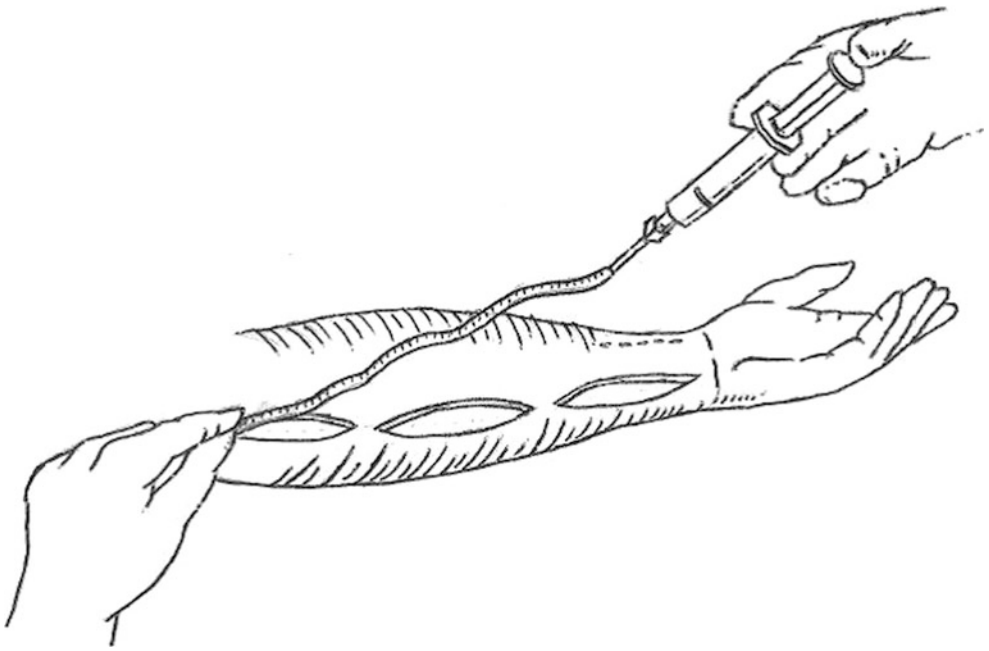


Fig. 16.6 Dilation of dissected forearm basilic vein with heparinized saline

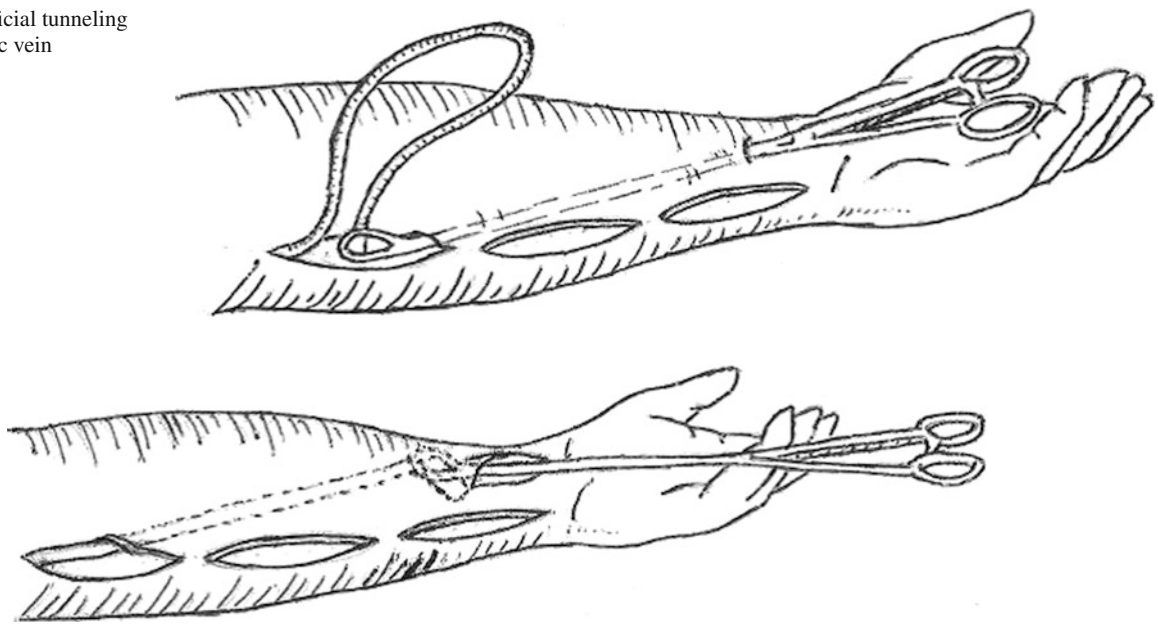


Fig. 16.7 Superficial tunneling for forearm basilic vein transposition

Fig. 16.8 Completion of superficial tunneling for forearm basilic vein transposition

Despite the proximity of the basilic vein to the ulnar artery, the deep and ulnar-oriented position of the vein mandates superficialization and transposition. While the basilic vein could simply be dissected and tunneled in a more superficial position overlying the course of the ulnar artery, it would still be oriented too far to the ulnar side to make dialysis access feasible. Thus, the authors advise a more curved configuration of the basilic vein in the forearm analogous to the transposition of the basilic vein in the upper arm. Unfortunately some of the length of the basilic vein is lost in forming the gentle curve so the anastomosis to the ulnar artery has to be closer to the mid-forearm. The artery can be quite deep at this level and should be localized with duplex ultrasound prior to dissection. Dissection of the vessel at this level should be performed meticulously, taking care to avoid the myriad of neurovascular structures running through the mid-forearm.

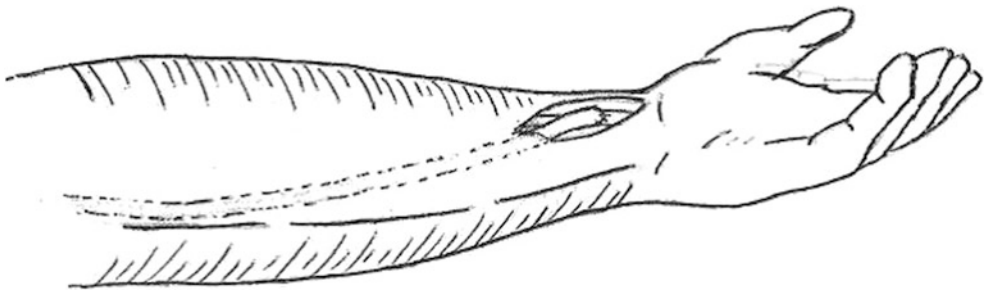


Fig. 16.9 After completion of radiobasilic anastomosis

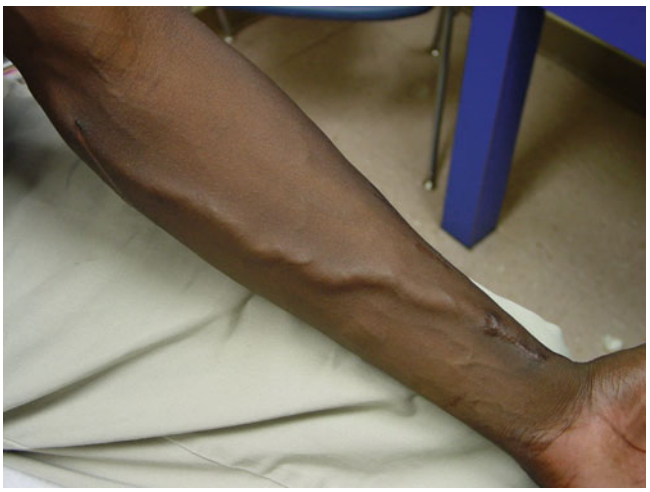


Image 16.1 Forearm radiobasilic fistula after maturation

Forearm Looped Transposition

When the distal radial and ulnar arteries are not appropriate for fistula creation but either the cephalic or basilic vein in the forearm is of appropriate size, a looped forearm vein fistula can be created. Either the basilic or the cephalic vein can be used in this situation. Whichever vein is selected is dissected along its course and its side branches are ligated. Typically an arteriogram has already been performed that demonstrated the arteries at the wrist were unacceptable for fistula creation. The same arteriogram can be used in the planning for arterial inflow at the antecubital fossa. The distal brachial artery and proximal radial artery are the easiest vessels to dissect. The proximal ulnar artery tends to course deeper and more laterally and should only be used if the other vessels are unacceptable. Care must again be exercised if there is single vessel perfusion to the hand. Arteriogram with and without compression of the dominant vessel to the hand can help in planning for fistula creation.

After dissection of the vein and selection of an arterial inflow site, the vein is transected, flushed, marked, and tunneled in a loop on the volar forearm (Image 16.2). The loop configuration is the most susceptible to twisting or kinking of the vein. Venography after tunneling before completing the anastomosis is the surest way to check for twisting or kinking but is not always necessary.

Long-Term Patency

Few studies have directly compared forearm fistulae and grafts. Son et al. compared forearm basilic vein transposition with direct forearm arteriovenous fistulae and forearm straight or looped arteriovenous grafts [7]. The study consisted of 461 accesses of which 389 were direct arteriovenous fistulae (84.4 %), 34 were forearm basilic vein transpositions (7.4 %), and 38 forearm arteriovenous grafts (8.2 %). The direct arteriovenous fistula group consisted of radiocephalic (300 patients) and brachiocephalic (89 patients) fistulae. There was no statistically significant difference in primary, assisted-primary, or secondary patency between these two groups. The 1-year primary patency rates for direct cephalic fistulae, forearm radiobasilic transposition, and forearm grafts were 68 %, 42 %, and 35 %, respectively. The 2-year primary patency rates were 54 %, 30 %, and 10 %, respectively. The primary-assisted patency rates were 89 %, 79 %, and 76 % at 12 months and 83 %, 74 %, and 66 % at 24 months. The secondary patency rates at 12 months were 89 %, 79 %, and 78 %, respectively, and 84 %, 74 %, and 65 % at 24 months. Although the direct cephalic fistulae had better patency rates than either the radiobasilic fistulae or forearm grafts, there were no statistically significant differences between the latter two. Thus the authors recommended the creation of a radiobasilic fistula when radiocephalic fistula is not an option.

Gormus et al. compared forearm basilic vein transpositions with upper arm basilic vein transpositions [8]. The mean follow-up for the ten patients in each group was 10 months. At that time, the patency rate for the forearm group was 80 % as compared to 90 % in the upper arm group. They also concluded that forearm basilic vein transposition was a good secondary choice for access in those patients who have unsuitable forearm cephalic vein.

Silva et al. compared 89 patients with superficial venous transpositions during forearm arteriovenous fistula creations

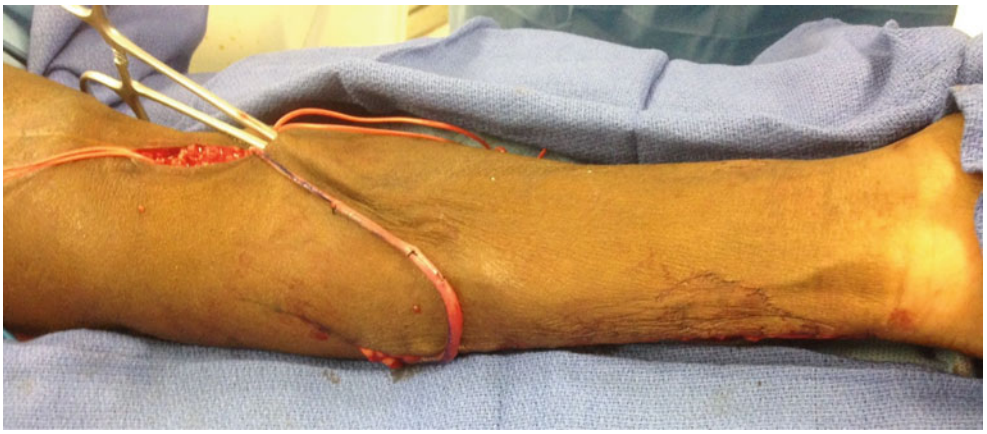


Image 16.2 Tunneling of forearm basilic vein for loop proximal radiobasilic fistula

who underwent either superficial subcutaneous transposition only (15 %), dorsal to volar transposition as well as superficialization (33 %), or volar to mid-forearm volar transposition as well as superficialization (52 %) [9]. Mean follow-up for all patients was 14.3 months. In this series, 18 of the 89 patients had failed fistulae (20.2 %) of which four underwent successful salvage by revision, three were converted to a contralateral forearm fistula, six were converted to ipsilateral bypass grafts, two were converted to contralateral forearm bypass grafts, two received permanent tunneled dialysis catheters, and one died before revision. Primary cumulative patency rates were found to be 84 % at 1 year and 69 % at 2 years.

Maturation Outcomes and Other Complications

Son et al. reported 15 patients with maturation failure at eight weeks postoperatively of which ten patients had direct arteriovenous fistulae (2.5 %) and five patients had forearm basilic vein transpositions (14.7 %) [7]. There were no infectious complications in the basilic vein transposition group, but infection developed in one patient after a direct arteriovenous fistula and in five patients after forearm graft insertion. One patient undergoing basilic vein transposition and one undergoing direct arteriovenous fistula developed wound seromas or hematomas, and both were treated with minor drainage procedures. The higher maturation failure rate in the basilic vein transposition group was statistically significant; however, most fistulae were easily salvageable by percutaneous intervention. Only one transposition patient required a new access operation as compared to three patients in the direct arteriovenous fistula group.

In the study previously mentioned by Silva et al. comparing forearm vein transpositions, successful maturation was achieved in 81 of the 89 patients (91 %) [9]. Two of which had stenoses detected during their initial duplex ultrasound examination and were able to undergo successful revision. None of the patients in this series had complications of fistula infection, pseudoaneuyrsm, or symptomatic steal. Two patients developed postoperative hematomas, but neither required operative intervention.

Conclusion

Creation of a Cimino-type radiocephalic fistula is not practical in all patients, but other forearm fistula options remain. In accordance with the 2008 Clinical Practice Guidelines from the Society of Vascular Surgery, preoperative vein mapping should include the evaluation of forearm basilic veins [10]. The guidelines also advocate radiobasilic fistula creation over an upper arm brachiocephalic fistula when feasible. In the instance that a Cimino-type fistula is not a feasible option, then one of the abovementioned fistula procedures can serve as an alternate choice and provide comparable patency rates with low complication rates.

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Brachiobasilic Arteriovenous Fistula

17

Sherene Shalhub

Introduction

The autogenous brachiobasilic arteriovenous fistula (AVF), also known as the basilic vein transposition fistula, was first reported by Dagher and colleagues in 1976 [1, 2].

Brachiobasilic AVF should be considered in patients with unsuitable cephalic vein or after failed radiocephalic and brachiocephalic AVFs and prior to the use of a synthetic graft [3]. This chapter focuses on the brachiobasilic arteriovenous fistula creation techniques, patency, and outcomes.

Surgical Technique and Patient Selection

The basilic vein is an attractive choice for an autogenous access because it is relatively thick walled, large in diameter (often exceeding 4 mm), and it provides a long length of straight fistula with a high flow rate [4]. The arm basilic vein is naturally deep and located medially on the arm (Fig. 17.1); thus, it is protected from damage caused by previous venipuncture. And while it is an ideal hemodialysis conduit, it requires superficialization to allow access. Thus, the brachiobasilic AVF can be created in a single- or a two-stage procedure. The single stage which was originally described by Dagher [1] involves the anastomosis and transposition as a single procedure. The two-stage procedure is divided into the anastomosis, followed by a period of maturation and then the transposition of the basilic vein with anastomosis. The procedure can be performed under general anesthesia, with a preoperative nerve block and monitored anesthesia care or under local anesthesia as it was originally described by Dagher [1, 2]. The basilic vein mobilization can be performed by using a single large incision, two incisions, or multiple smaller incisions [1, 5–7]. Minimally invasive techniques have been described using video-assisted elevation and transpositions of the basilic vein. These techniques were developed to avoid the long arm incision and may reduce pain though they are not widely used [8, 9].

Given that this is a second or choice AVF in a patient, central venography may warrant consideration in certain circumstances to exclude central venous stenosis prior to proceeding with fistula creation. Indications for central venography include the presence of venous collaterals on the ipsilateral arm; arm edema; ipsilateral dialysis catheter placement; ipsilateral transvenous pacemaker; a prior history of neck, chest, or arm trauma; or previous access surgery.

Single-Stage Procedure

An incision is made over the course of the basilic vein in the proximal upper arm, immediately above the antecubital fossa (Fig. 17.2). The skin incision and the dissection are extended proximally to the axilla and distally to at least the antecubital crease. The incision can be performed as a single, continuous one or a series of shorter "skip" incisions in attempt to reduce postoperative wound complications. The basilic vein courses adjacent to the medial antecubital cutaneous nerve in the upper arm, and thus care should be taken to avoid injuring the nerve. Either the median antecubital or the forearm basilic vein can be used as part of the vein for the access, provided that it is sufficient in terms of caliber and quality. The basilic vein should be dissected throughout its course, with ligation of small branches and over sewing of larger, broad-based branches with silk sutures. The basilic vein was then transected, ligated at the most distal end, and flushed with heparinized saline while noting for any evidence of stenosis or obstruction to the flow. The distended vein is then gently draped over the upper arm in an arc, and the future course of the transposed vein is marked on the skin. The brachial artery is dissected free in the distal upper arm at the site of the planned anastomosis. A tunnel is created along the

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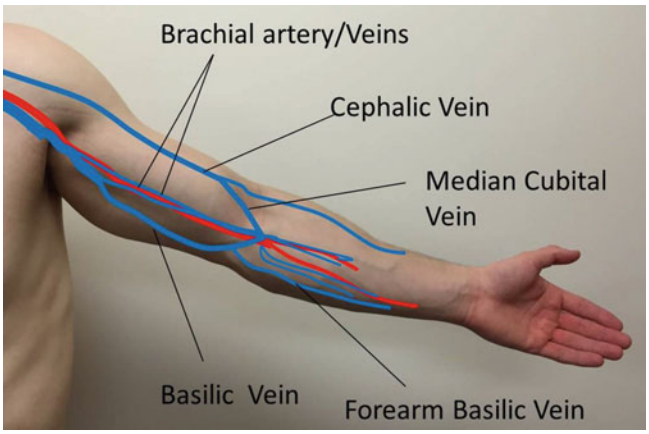

Fig. 17.1 Venous and arterial vasculature of the arm

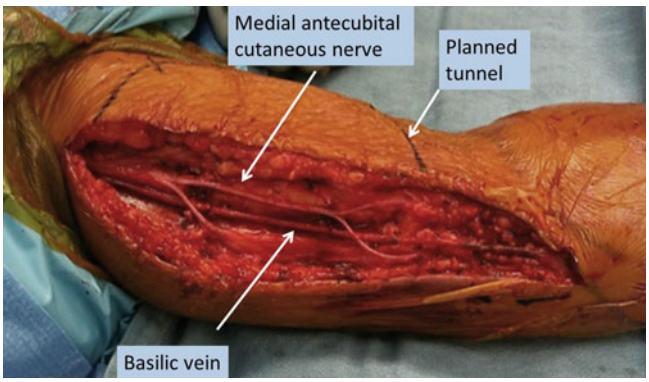

Fig. 17.2 Brachiobasilic autogenous access in a single stage in a patient with a large basilic vein. Skin overlying the basilic vein is incised starting below the antecubital crease and extended longitudinally to the axillary crease

course marked on the anterolateral arm with the use of a semicircular, hollow tunneling device. The tunneler is passed deep to the subcutaneous tissue near the antecubital fossa and the axilla but immediately below the dermis 6 mm below the skin throughout the region that will actually be used for cannulation. It is important to leave a completely straight section of the vein for at least 6–10 cm for ease of cannulation. A pointed-tipped tunneler is particularly helpful because it facilitates passing of the device in the desired plane. Prior to controlling the brachial artery, heparin can be given systemically. In our practice, we routinely use a standard dose of heparin (i.e., 5000 units) that is smaller than the one used for most other open, arterial revascularizations (i.e., 100 units/kg). The artery is occluded with microvascular clamps, and a 6 mm arteriotomy is created using a #11 scalpel blade and fine arteriotomy scissors. The end-to-side basilic vein brachial artery anastomosis is performed using a running 6–0 monofilament polypropylene suture. If a proximal radial artery measures >1.5 mm and is deemed usable, the brachial artery should be preserved for future use per Society of Vascular Surgery (SVS) vascular access guidelines [10]. Depending on the wound status, optional closed-suction drain can be placed in the bed of the basilic vein harvest and brought out through a separate stab wound on the distal upper arm near the antecubital fossa. Care should be exercised during the wound closure to prevent compressing or kinking the basilic vein that constitutes the access.

Two-Stage Procedure

The advantage of the two-stage brachiobasilic procedure is that the transposition is not performed until maturation of the vein occurs, thus avoiding a more complicated procedure with possible wound complications until there is assurance that the access will be successful. Additionally the staged approach allows the vein to arterialize and elongate, thereby increasing the available length that can be elevated or transposed rendering it less likely to thrombose [11].

During the first stage, a limited incision is created in the proximal upper arm, and both the basilic vein and the brachial artery are dissected free. The anastomosis is performed end to side using a running 6–0 monofilament polypropylene suture, and the incisions are closed. The vein is then allowed to mature over the next 4–6 weeks. The second-stage procedure is performed when/if the vein dilates sufficiently for cannulation; in our practice we generally use 6 mm as the threshold vein diameter as defined by the KDOQI "rule of 6s." A continuous incision or a series of skip incisions is made over the course of the vein during the second stage, and the vein is dissected free. The basilic vein is dissected throughout its course, with ligation of small branches and over sewing of larger, broad-based branches. A tunnel is created on the anterolateral surface of the arm in a manner similar to the one described for the single-stage procedure. The anterior surface of the arterialized vein is marked using a marker pen, and the proximal part of the fistula near the anastomosis is controlled with a bulldog clamp followed by fistula transection. The patient is systemically heparinized. The vein is flushed with heparinized saline solution and placed inside the tunnel, with care taken not to twist the vein, using the top marks. The two ends of the fistula are re-anastomosed (venovenous anastomosis) with running 7-0 or 6-0 monofilament polypropylene suture.

Superficialization: Transposition Versus Elevation

While in an ideal setting the vein has sufficient length and the vein can be tunneled in a curvilinear path over the course of the upper arm (Fig. 17.3), ultimately, the management of the basilic vein is dependent on the available length and the body habitus of the patient. If the vein length is somewhat limited

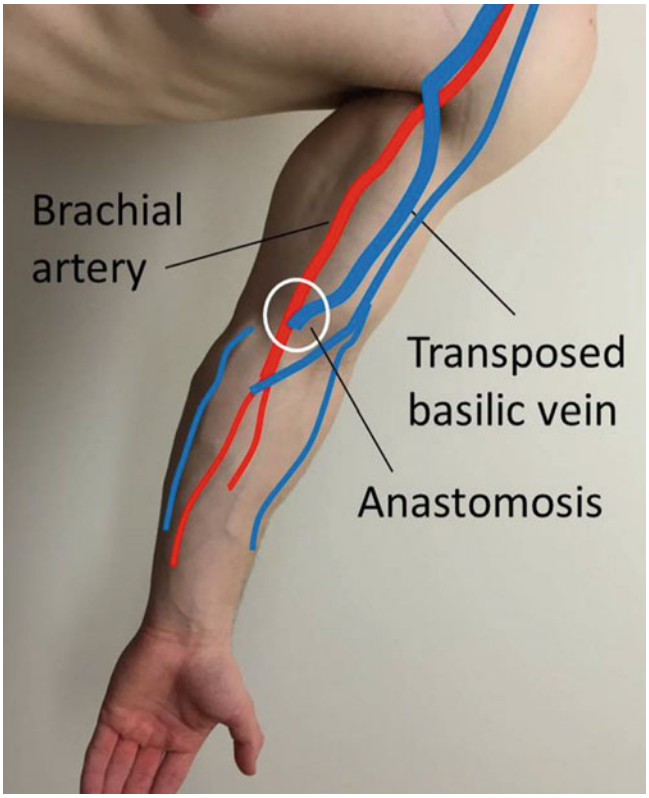

Fig. 17.3 Transposed brachiobasilic arteriovenous fistula. Ideally, the vein has sufficient length to be tunneled in a curvilinear path over the course of the upper arm to allow easy cannulation

and there is a significant amount of subcutaneous tissue, the vein can be simply elevated and the subcutaneous tissue reapproximated deep to the vein, and the vein is simply elevated from its anatomically deep position to lie directly beneath the incision [12]. The medial antecubital cutaneous nerve overlies the basilic vein and must be addressed if the vein will be simply elevated by transecting and re-anastomosing the access (i.e., arteriovenous or venovenous). Simply elevating the basilic vein is somewhat suboptimal for two reasons. First, the mature access courses very medially on the upper arm and can be difficult to cannulate during dialysis. Second, the vein lies immediately below the skin so it would be vulnerable if the wound were to break down (and expose the access). A subcutaneous pocket can be created in this situation by elevation of skin flaps, thereby avoiding having the vein course immediately below the skin, although this option is predicated on there being a sufficient length of vein.

Postoperative Care

The procedure can be performed as an outpatient procedure; however, patients with significant comorbidities can be admitted overnight for observation. The patient's electrolytes are checked and the patient is dialyzed as necessary. The patient's incision and hand function are monitored closely, given the risk of access-related hand ischemia. If closed-suction drains were used, they are usually removed on the first postoperative day if drainage is minimal. Patients are followed in clinic at 2 weeks post procedure, then every 4–6 weeks until maturation of the fistula. For a single-stage brachiobasilic AVF, initial cannulation is usually performed 6–8 weeks after creation. For a two-stage brachiobasilic AVF, the AVF is assessed for maturation and patients scheduled for the transposition procedure after 4–6 weeks. Initial cannulation is usually performed at least 3 weeks following the second procedure.

Complications

The extensive dissection required during the vein mobilization is associated with increased risk of subsequent hematoma (3–7 %) compared to non-transposed AVF [4, 5]. Hematoma has been reported to predispose to fistula thrombosis in most cases and thus may require evacuation to preserve the newly created AVF [13]. This has led some to recommend placement of drains in the incisions, though this is not a standard practice [11]. Additionally, hematoma formation can occur during early attempts at cannulation before the tunneled has healed and the vein fully matured; thus, some recommend a period of at least 6 weeks following a single-stage AVF creation before cannulation.

Wound infection is a consideration in brachiobasilic AVF creation and is reported to occur in 3–5 % of the cases, and less commonly lymphatic leaks occur in 0.5 % of the cases [4, 5].

Obese patients have a higher risk of wound complications, particularly with the extensive incision required for a transposed brachial-basilic autogenous access. Options for obese patients include a forearm prosthetic access, a two-stage brachiobasilic AVF access to avoid the transposition until the access is mature, and the use of subcutaneous lipectomy to remove the overlying fat as an alternative to transposition.

Steal syndrome is a well-recognized access complication and has been reported in 3–5 % of the cases [4, 5]; thus, most authors recommend an anastomosis of only 5–7 mm in length to avoid this complication. In most cases steal syndrome presents in the immediate postoperative period; however, it has been reported late even after 10 years presumably due to expansion of the fistula over time [11]. Occasionally the steal may resolve spontaneously within a few days and in some cases may require ligation of the AVF or a distal revascularization-interval ligation procedure [11].

It is worth mentioning that transient edema of the hand and forearm is common with an incidence ranging between

3.7 and 24 %. In most cases it resolves with arm elevation in a sling without any long-term consequences [11, 13, 14]. In some cases the edema is severe enough to warrant ligation of the fistula [15]. Severe arm edema should raise the possibility of an undiagnosed central venous stenosis.

Maturation Outcomes and Long-Term Patency

Failure to mature has been reported to be as high as 38 % although most other authors have not reported rates as high as this [16]. In a large series of single-stage brachiobasilic AVF, the maturation rate was 87 %. The most common complication prior to maturation is fistula thrombosis (16 %) [4]. Thrombosis has been attributed to the damage caused by extensive dissection of the thin-walled vein [11].

Autogenous brachiobasilic AVF has primary patency rates for the first and second year that range from 80 to 90 % and 74 to 86 %, respectively, with a long-term patency of 70 % at 8 years reported in a large series [17–19]. In terms of choice of a construction as a single-stage vs. two-stage approach to creating a brachiobasilic AVF, multiple studies have demonstrated superior patency rates for the two-stage approach when compared to the single-stage approach [20–22], while others showed no difference in failure and patency rates between the two methods [21, 23, 24].

Interestingly, in a small study of patients with diabetes mellitus, autogenous brachiobasilic AVF had 100 % maturation rates compared to 30 % maturation rates of radiocephalic AVF or 73 % maturation rate of brachiocephalic AVF.

Compared to arteriovenous bypass grafts (AVGs), autogenous brachiobasilic AVFs have been shown to be superior in terms of patency and cost. In a prospective study comparing autogenous brachiobasilic AVF to brachioaxillary AVGs, the AVF had superior primary patency rates (90 % vs. 76 %), 2-year primary-assisted patency rates (74 % vs. 40 %), and secondary patency rates (85 % vs.62 %) [25].

Conclusion

The autogenous brachiobasilic AVF, also known as the basilic vein transposition fistula, is an excellent third if not second choice option for vascular access following radiocephalic and brachiocephalic AVF and obviates the need for graft placement. Transposition is preferable to elevation as it allows easier cannulation during hemodialysis. Current evidence suggests that a two-stage procedure may be associated with better outcomes although more studies are required.

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Hemodialysis Grafts

18

Shawn M. Gage, Ehsan Benrashid, Linda M. Youngwirth, and Jeffrey H. Lawson

Introduction and Historical Perspective

Vascular surgery was forever changed – and the field of dialysis access established – with the advent of the Scribner shunt at the University of Washington in 1960 [1]. This external, Teflon tube is attached to the arterial and venous circulation (in the forearm or ankle) and then joined together in the "U" configuration by connectors and a piece of heparinized Teflon, while the patient is not actively being dialyzed. Later in the same decade, Drs. Brescia, Cimino, and Appell conceptualized the first autogenous, or non-synthetic, dialysis access in the form of the connection of the cephalic vein to the radial artery (radiocephalic arteriovenous fistula) [2].

In 1969, just 2 years after the clinical implementation of the arteriovenous fistula (AVF), the first autologous graft was used for the creation of an arteriovenous access almost simultaneously in both Mexico and Australia [3, 4]. Flores Izquierdo and May described the use of the saphenous vein for the creation of a forearm loop arteriovenous graft (AVG). May et al. observed that there was a group of patients in which both the suitable artery and the vein were lacking for the creation of an AVF, and an interposed conduit was required to provide an area of blood flow and access for hemodialysis.

These seminal events led to much excitement in the field of access creation and hence the further development and use of other materials, such as expanded polytetrafluoroethylene (ePTFE) and Dacron (polyethylene terephthalate) [5, 6] (Fig. 18.1). In the 1970s the use of ePTFE was pioneered as a suitable vascular graft and was rapidly adopted as an alternative material for connecting arteries and veins in an array of configurations around the body [7]. This fundamental advance of using an interposed synthetic tube to provide blood flow superficially beneath the skin for hemodialysis access has been a mainstay of access for millions of patients and can often be a life-sustaining solution for those patients whose, for an array of reasons, creation of a native AVF is not possible.

The conception of prosthetic grafts revolutionized vascular access and gave rise to a number of new access sites that were previously unavailable when creation of an AVF was the sole option. However, this new type of vascular access presented a whole new set of challenges and complications, driving expenditures for dialysis access to another level. Today the health and social realities of ESRD are tremendous, with economic costs in the USA estimated at more than 2.9 billion dollars to maintain malfunction dialysis access [8]. While dialysis grafts have provided reliable access for millions of patients in need of hemodialysis, they are still far from ideal. Currently, regardless of the material used for an artificial AVG, their mean patency remains generally poor averaging between 9 and 15 months, and infection rates are greater than AVFs [9–13]. Further, enduring patency often requires multiple interventions including mechanical thrombectomy, thrombolysis, angioplasty, stent placement, and/or surgical revision. These interventions are fraught with recurrent failure, cost millions of healthcare dollars, and expose the patient to increased morbidity and mortality [8].

In patients lacking suitable vein for conduit, ePTFE is the most commonly used synthetic solution for creation of arteriovenous access. There are multiple modes of failure that plague prosthetic vascular access grafts including neointimal hyperplasia in the outflow vein, thrombosis, infection, graft ultrafiltration (weeping), steal syndrome, and traumatic degeneration of graft material [14]. Further, synthetic conduit has several biologic challenges. Specifically, because the conduit lacks the ability to form a stable endothelium, it appears to be more thrombogenic. Because it is impermeable to white blood cells, synthetic material is more prone to infection,

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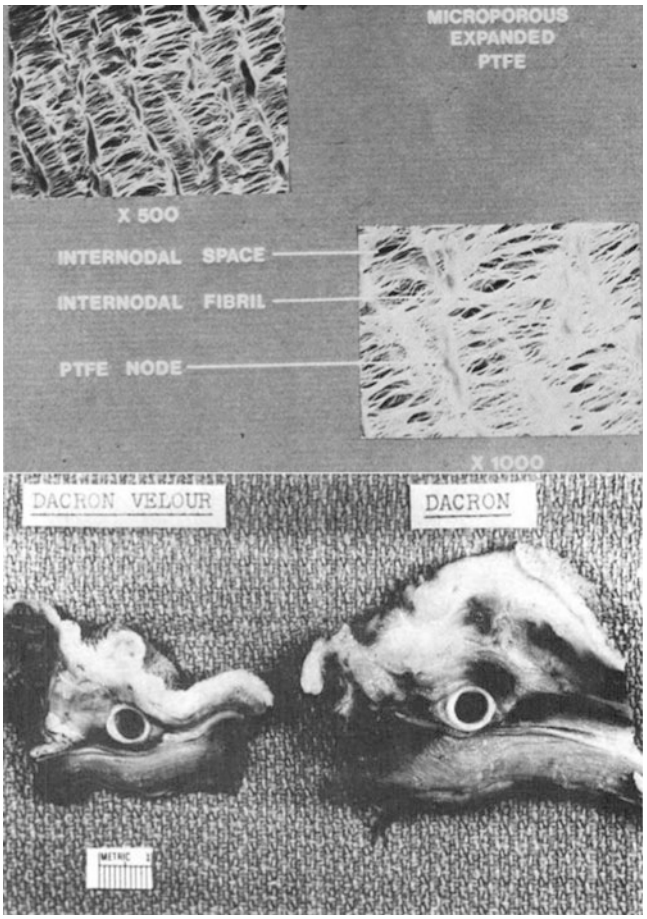

Fig. 18.1 *Top*: ePTFE histology from first conduits used for human arterial replacement circa 1970 (Johnson, Goldfarb, et al). *Bottom:* en bloc explants of Dacron grafts from dogs in an AV access model

which may lead to the need for surgical excision. Additionally, due to mechanisms that are incompletely understood, the body's response to synthetic material can result in venous neointimal hyperplasia leading to venous outflow stenosis. Progressive outflow stenosis increases the pressure in the access and decreases the flow, which can increase the risk of graft cannulation bleeding and ultimately graft thrombosis. There are several proposed mechanisms by which venous outflow stenosis can occur in AV access models. Favored mechanisms cite inflammatory responses to synthetic material, as well as compliance mismatch between native vein and synthetic material resulting in hyperplasia at the transition zone between conduits [15]. Finally, synthetic conduit is prone to degradation over time due to "coring" caused by repeatedly accessing the graft with large bore needles for dialysis, resulting in the formation of pseudoaneurysms.

Although their initial use was met with much excitement, limitations of synthetic AVG such as infection and thrombosis were quickly recognized, leading to the development of biologic or bioengineered conduit, with several examples persisting to this date, including bovine carotid artery (Artegraft®, Artegraft, Inc., North Brunswick, NJ), bovine mesenteric vein (ProCol®, LeMaitre Vascular, Inc., Burlington, MA), and cryopreserved (human) femoral or saphenous vein (CryoVein®, CryoLife, Inc., Kennesaw, GA), among others [16–22]. However, biologic grafts are typically more expensive than standard synthetic ePTFE choices, and early iterations of such grafts were fraught with more troublesome complications such as rapid aneurysmal degradation and did not completely mitigate infectious complications as suspected [23]. Additionally, many patients utilize hemodialysis as a "bridge" to kidney transplantation, subsequently leading to concerns over induction of the immune response and overall antigenic properties of various graft materials.

However, as one can surmise, there have been modifications to previously developed graft materials and the introduction of new synthetic materials, such as polyurethane [24]. Modifications and introduction of new materials have, in theory, provided for earlier cannulation and less graft complications (i.e., ultrafiltration syndrome or "graft weep") than older materials. New graft construction techniques, such as tissue-engineered vessels and three-dimensional (3D) printing, are unveiling an exciting new frontier for further development of easily handled, personalized, injury proof, and readily available HD access grafts, both biologic and synthetic.

Patient Selection

The preoperative evaluation is critical in the planning of vascular access surgery, and a long-term plan should be kept in mind while caring for these patients. Frequently, patients and surgeons opt to begin access on the nondominant extremity, and it seems that this strategy is fair and acceptable to most patients. The decision to implant an upper extremity AVG depends on the algorithm used when planning subsequent vascular access. The NKF/DOQI project guidelines promote fistula formation in the nondominant extremity [25]. The "fistula-first" initiative would suggest creating autogenous access on the dominant upper extremity once native fistula options have been exhausted on the nondominant side. However, a common practice is to remain on the ipsilateral nondominant limb and proceed with forearm looped (FL) or upper arm brachial artery to axillary vein (brach-Ax) AVG implantation.

One must take care not to overlook previous surgical access attempts or endovascular procedures that could have destroyed or obviated venous outflow (i.e., stent deployment which would not allow for sewing or clamping of the vein or previous graft failure with subsequent thrombosis in that segment of the vein). The general approach to AVG surgery seeks to provide the best immediate result while preserving additional options for future access surgery. Once native fistula possibilities in the nondominant extremity have been exhausted, primary FL AVG placement may be considered.

Many surgeons will appropriately proceed to a dominant arm-forearm fistula, in the setting of appropriate venous anatomy, prior to committing to graft implantation. A brach-Ax AVG is a more proximal option usually reserved for failure of forearm access with no compelling options for endovascular or surgical revision. Beyond these locations, axillary artery to axillary vein grafts, chest wall grafts, and the central vein access graft (i.e., Hemodialysis Reliable Outflow [HeRO], Merit Medical Systems, Inc., South Jordan, UT) give the skilled surgeon a variety of options to maintain dialysis access without resorting to a tunneled dialysis catheter.

Determining the degree of target vein patency and the overall quality of venous outflow tends to be our greatest challenge when planning a new vascular access. Typically, one or more means of venous imaging is utilized as an adjunct in planning for new access. Venous duplex mapping of the extremity is simple, convenient, and the most inexpensive method of venous imaging but is limited to the periphery as it cannot evaluate the central veins. Conventional venography, MRV, or CTV are suitable alternatives for evaluation of central venous anatomy [26, 27].

Graft Technology and Graft Materials

In an attempt to provide solutions to the issues, which lead to graft failure, access care providers in collaboration with industry have developed a variety of conduit options and therapies to improve upon the care that we can offer patients in need of long-term vascular access. In that regard, the main focus of access graft advances over the past 10–15 years has been toward improving bleeding, thrombosis, weeping, and infection of access grafts as opposed to addressing the biologic aspects of outflow vein failure and venous proliferative disease. As a result, numerous AVGs with various base scaffolding, wrap or lamination methods, bonding or graft lining, or outflow designs are commercially available for use in our ESRD patients.

Modified ePTFE Luminal Surfaces

Propaten

W.L. Gore & Associates (Flagstaff, AZ) has attempted to make an impact on long-term graft patency by aiming to reduce luminal thrombus by covalently bonding bioactive heparin to the luminal surface of their ePTFE graft known as the Carmeda® BioActive Surface (CBAS®) (Fig. 18.2). Early studies showed encouraging data to support retention of the graft's thromboresistant bioactive properties over time, but more recent studies do not support the notion of improved patency or performance in the hemodialysis access arena [28–30]. Further prospective, randomized trials may be in order to more fully elucidate the graft's long-term performance when compared to standard ePTFE dialysis AVGs.

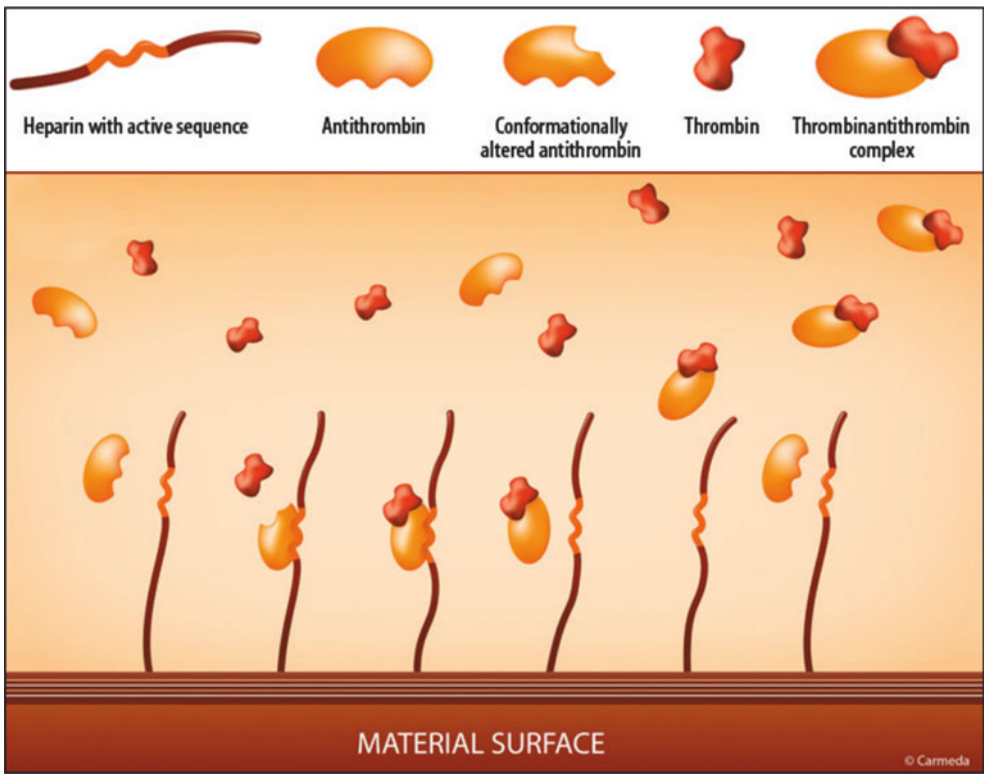

Fig. 18.2 Illustration of CBAS Heparin Surface showing the material surface, base coating, and end-point attached heparin. Also shown are the reactants antithrombin, conformationally altered antithrombin, thrombin, and the inactive thrombin antithrombin complex

Modification of Flow Dynamics

Tapered Grafts

Alteration in the flow pattern of blood through hemodialysis grafts has enabled vascular device companies to attempt to improve pathology related to vascular access, such as steal syndrome, patency, and venous outflow stenosis. Virtually all companies that offer ePTFE for hemodialysis have developed tapered configurations at the arterial end of the graft with the hope of reducing complications such as steal syndromes and high-output heart failure [31]. Most offer a 4 mm–7 mm short taper configuration. Of AV access case litigation, cases related to steal syndrome are the most common. Tapered AVGs can help to reduce the risk of creating a steal situation; however, in general, the potential for steal can be mitigated by alteration of the anastomotic technique on a case-by-case basis.

Venaflo II/Carboflo

In the realm of standard ePTFE material, the choices of graft material are fairly similar and generally come in a 6 mm standard wall configuration which is manufactured by one of five major vendors. As an example of graft modifications, Bard Peripheral Vascular, Inc. (Tempe, AZ) offers the Venaflo II AVG, which aims to optimize hemodynamic venous outflow patterns to reduce outflow vein intimal hyperplasia and thrombosis. Additionally, the Venaflo II as well as Bard's Carboflo graft is lined with carbon which some studies have suggested result in a reduction in platelet aggregation and thrombus formation within the graft when utilizing this technology [32] (Fig. 18.3).

Gore Hybrid

The primary intent of the Gore Hybrid graft is to create a sutureless end-to-end vascular anastomosis and possibly reduce intimal cell proliferation and improve flow hemodynamics in the outflow track of arteriovenous access or arterial bypass circuits. The ePTFE transition to stent-graft (nitinol reinforced section) design creates an end-to-end anastomosis and maintains laminar flow from the graft conduit into the recipient vessel [33] (Fig. 18.4). Fluid and flow dynamics testing suggest that this design may reduce the vessel wall shear stresses conveyed on the outflow track when compared to a conventional end-to-side, sutured anastomosis [34, 35]. Presently, there is no peer-reviewed clinical data which proves that altering the outflow dynamics with this device truly has had an impact on the genesis of neointimal hyperplasia or overall graft patency. However, as in the case of most novel technology, ideas for new and innovative applications are often discovered, and as such, there has been success with expanded application of the Hybrid in various cases and complex situations. The Hybrid graft has been used for complex vascular access, peripheral bypass, carotid reconstruction, and renal and mesenteric artery reimplantation during aortic debranching surgery [36–38].

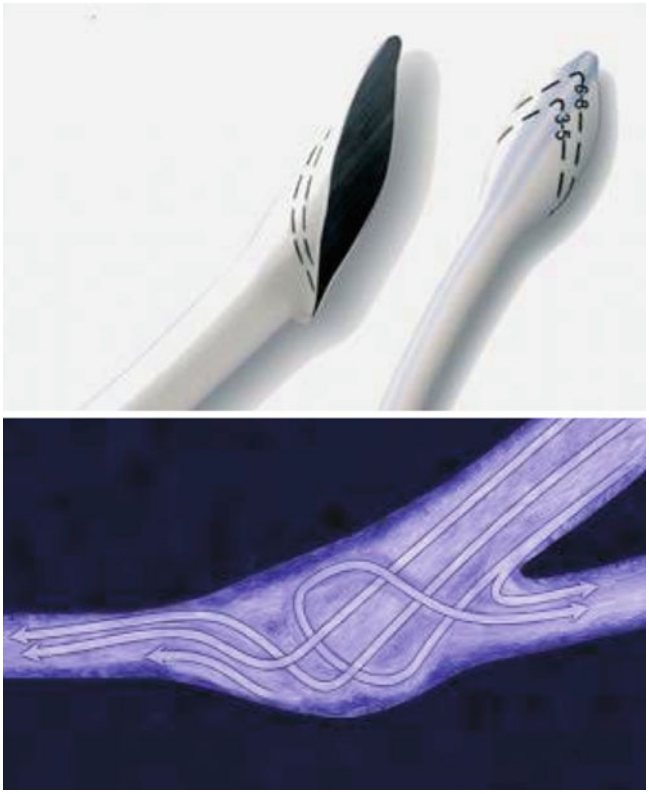

Fig. 18.3 *Top*: Venaflo II showing expanded hood and carbon lining. *Bottom*: Illustration of favorable flow dynamics with expanded Venaflo II hood

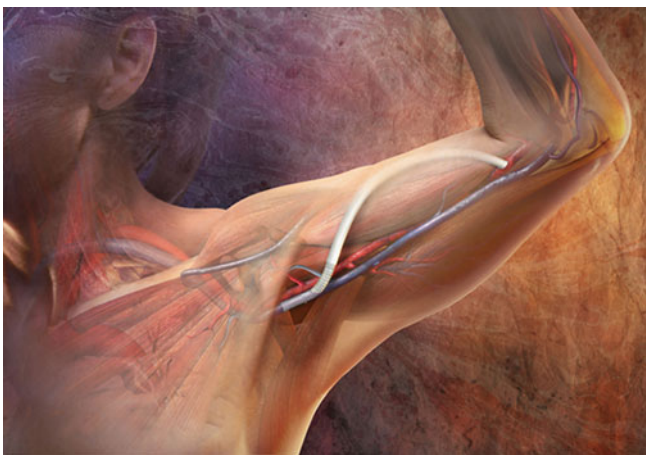

Fig. 18.4 Gore Hybrid Graft

"Low-Bleed" Technology

Flixene

Others have modified PTFE technologies to increase graft wall strength in an attempt to decrease cannulation misadventures, needle hole bleeding, and weeping. The FLIXENE graft manufactured by Atrium Maquet Getinge Group (Hudson, NH) utilizes a Tri-laminate Composite Construction and a hydrostatic protection membrane that dramatically

increases burst and suture strength. Due to its construction, it claims to eliminate graft ultrafiltration syndromes that standard ePTFE grafts can develop. Although not FDA approved for early cannulation, there are several reports that support its use as an "early cannulation" graft [39]. In this setting, patency rates are low and infection rates high [40].

Vectra

The Vectra graft (Bard Peripheral Vascular, Tempe, AZ) is a bridge conduit constructed of a polyurethaneurea as an alternative to ePTFE. This rubbery, elastic-type material handles quite differently than the ePTFE grafts, and studies have suggested that this material seals after cannulation within 1–5 min, nullifying the requirement for tissue incorporation into the graft prior to cannulation for hemodialysis [41, 42]. The company suggests that this graft can be used for hemodialysis 24-h status post-implantation.

Acuseal

W. L. Gore & Associates have developed a multilayer ePTFE AVG with the intent to decrease bleeding and facilitate early cannulation. Acuseal is a tri-layer hemodialysis graft with a thicker outer ePTFE layer, surrounding a middle elastomeric layer, which surrounds a thinner ePTFE layer as the innermost graft layer (Fig. 18.5). This graft also features the CBAS heparin-bound technology. The idea is to reduce hematoma and bleeding after needle cannulation and to also minimize catheter contact time by reducing the time required for tissue incorporation around the graft, prior to needle access. Glickman et al. report on Acuseal's utility as a dialysis graft as well as the graft's utility on early cannulation; however, only half of the patients in the study were cannulated within 72 h [43]. Primary patency was marginal, but cumulative patency was consistent with the historic AVG literature. Tozzi and Aitken had previously reported similar results [44, 45].

Bioprosthetic Technology

Xenogeneic or allogeneic blood vessels, for example, bovine blood vessels or cryopreserved human blood vessels, can be chemically treated leaving collagen, connective tissue proteins, and cells with decreased immunogenicity in order to prepare for their use as conduit for dialysis access. This approach offers the theoretical advantage of matching compliance since the conduit has some of the properties of a blood vessel, though there is evidence of structural alteration by the treatment process resulting in reduced tensile strength and compliance [46]. The first treated xenogeneic conduit was reported in the late 1960s, as a lower extremity arterial bypass conduit made from the collagen matrix of a bovine carotid artery treated by enzymatically removing the musculoelastic portion of the vessel [47]. These grafts are more expensive than standard and most premium grafts but can be a wise option for patients in immunocompromised states, who have small vessels, or those plagued by early thrombosis or chronic infection. There are several xenogeneic or allogeneic grafts currently available as listed below.

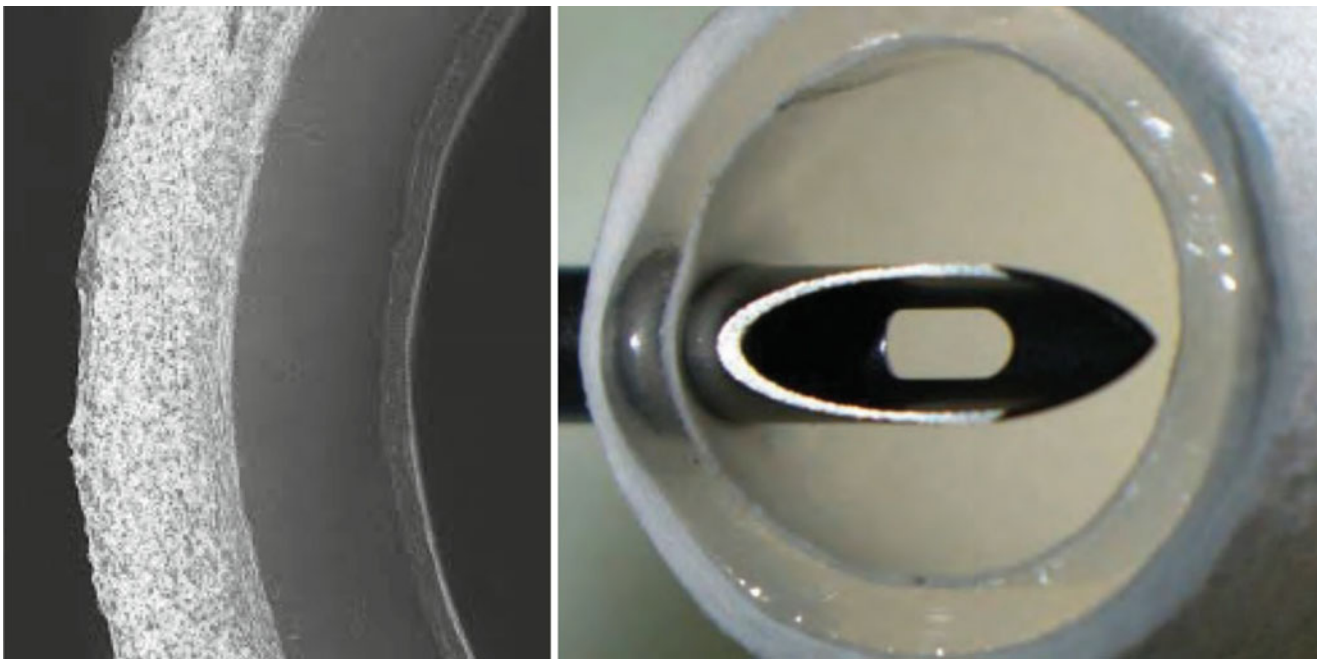

Fig. 18.5 *Left*: Scanning EM of Gore Acuseal demonstrating the three layers of the graft: Outer graft layer of ePTFE, middle elastomeric membrane, and inner ePTFE graft layer. *Right*: needle cannulation through Acuseal

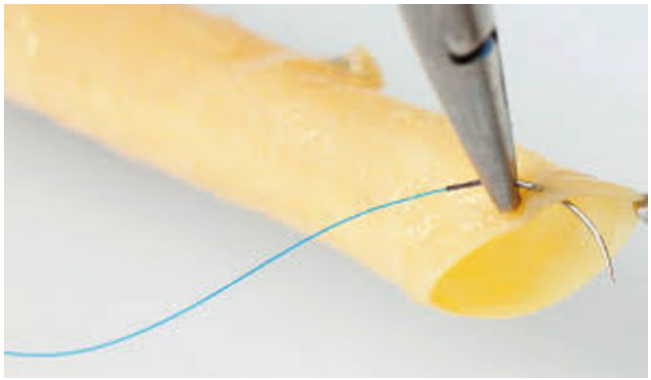

Fig. 18.6 Placement of Needle through CryoVein

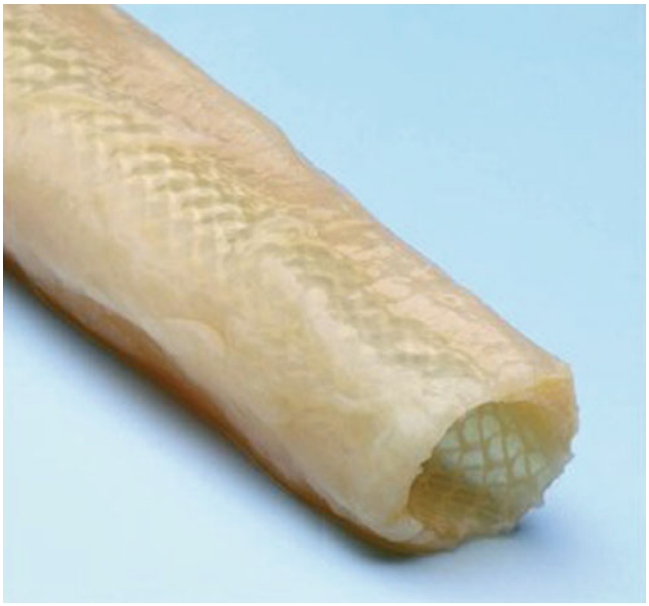

Fig. 18.7 Omniflow II - Dacron mesh template in a sheep bioreactor

Artegraft

In 1970, bovine carotid arteries treated with glutaraldehyde (Artegraft, North Brunswick, NJ) were FDA approved for use among other indications as conduit for dialysis access with similar patency to ePTFE [48, 49]. This product offers a tightly woven and cross-linked, natural collagen matrix conduit derived from bovine carotid artery and has the advantage over ePTFE of behaving more like a human artery and has the theoretical decreased risk of infection because it is made of proteins and cells allowing the host defense to penetrate. However, once implanted in the human host, the media layer of the bovine arteries was susceptible to calcifications in vivo and in some cases resulted in structural degradation and aneurysmal degeneration over time as well as infection [50].

Procol®

Decades later, Hancock Jaffe Laboratories, Inc., Irvine, CA, developed a method to treat bovine mesenteric veins with glutaraldehyde (Procol®, LeMaitre Vascular, Inc., Burlington, MA) (Fig. 18.6). These grafts were developed with the potential advantage of improved vessel compliance and thus theoretic decreased rate of venous stenosis, due to the higher elastin content in the vein when compared to bovine carotid artery. Procol® was FDA approved in 2003 for implantation in patients who have failed at least one prosthetic access graft and was reported to have improved patency over ePTFE, with primary patency at 2 years of 70 % [20, 51]. Despite the positive performance of this product in terms of patency and decreased infection and that it is only modestly more expensive than that of ePTFE, Procol® has not gained widespread adoption.

CryoVein

Cryopreserved treated human greater human saphenous veins, femoral veins, and femoral arteries (CryoVein, CryoLife, Kennesaw, GA) are commercially available for use in dialysis access in the USA. CryoLife is FDA registered as human cells, tissues, and cellular and tissue-based product establishment. As the CryoVein graft is made of allogeneic tissue, it is proposed to be more resistant to infection, and some report using cryopreserved vein for salvaging a localized prosthetic graft infection [52, 53]. However, others report no decrease in infection risk at least when these grafts are used as a thigh graft [54]. Secondary patency for CryoVein used as primary conduit for dialysis access was reported to have similar patency when compared to ePTFE [21]. Some have concern about blood type compatibility for these grafts, though they are treated to remove any blood type proteins. Additionally, CryoVein has been implicated in elevating panel-reactive antibodies (PRA), which may be a concern in the dialysis patient being considered for kidney transplantation. CryoLife developed a method of decellularization of their grafts called SynerGraft which resulted in lower levels of PRA, but their decellularized grafts are not currently commercially available [55].

Omniflow II

Omniflow II (LeMaitre Vascular, Inc., Burlington, MA), a glutaraldehyde-tanned ovine collagen tube grown around a Dacron mesh template in a sheep bioreactor, was originally developed by Bio Nova (North Melbourne, Australia) (Fig. 18.7). These grafts were first approved for use in dialysis access in Australia, Germany, and Canada, but more recently gained approval for use in Europe and the USA [56, 57]. The first version of this product, Omniflow I, had low patency of only 30 % at 4 years with occlusive complications, so changes were made to the culture technique and mesh composition. The newer version of this product, Omniflow II, has much improved primary and secondary patencies in preliminary studies which approach that of arteriovenous fistula, with secondary patency at 2 years of 75 % and a lower infection rate than ePTFE [58].

Central Vein Pathology

HeRO Graft

As a means to provide care for end-stage access patients with central venous stenosis and/or occlusion, Hemosphere, Inc. (Eden Prairie, MN) developed a hybrid "graft-catheter" vascular access device. Officially classified as a graft, this device is FDA approved for use in the upper extremity in patients who would otherwise be catheter dependent, and it was made available for commercial use in 2008. When this graft is properly implanted, arterial blood is shunted from the donor artery into the central venous system without having to create a formal venous anastomosis. The Hemodialysis Reliable Outflow (HeRO) graft (now Merit Medical Systems, South Jordan, UT) is a completely subcutaneous implanted device, which can bypass central venous stenosis and/or occlusion by traversing the lesion endovascularly and terminating in the right atrium or any available large outflow target vein. This device consists of two components: a conventional ePTFE graft component and an endolumenal, large bore, single-lumen, nitinol-reinforced, silicone outflow component. Preliminary studies have shown that this device has primary and secondary patency rates equal or superior to conventional AVGs and superior infection rates when compared to TDCs [59]. The HeRO graft history, implant techniques, and pitfalls are expanded upon in greater detail later in this textbook.

Surgical Technique

Creation of durable hemodialysis access requires careful preoperative planning, execution of intraoperative technical excellence, and proper selection of arterial inflow, venous outflow, and access conduit. There are a number of seemingly minute intraoperative considerations, which require careful attention when placing an AVG. Inflow arteries should have minimal atherosclerotic disease and sufficient pulsatile flow, which should be apparent from the physical exam. Furthermore, arteries must be relatively soft and amenable to clamping (which may not always be apparent of physical exam). Outflow veins should be greater than 3 mm in diameter and free from prior traumatic injury, thrombus, scar, or occlusion.

Manipulation of the neurovascular structures must be done with care. We prefer the use of silicone vessel loops to control the vessels and nerves; however, distraction performed too forcefully can lead to injury. Arterial dissection can occur as a result of aggressive manipulation as can neuropraxia or frank neurologic damage if the nerve is handled too vigorously.

Application of proper technique when tunneling conduit is also important. Tunneling the graft too deep can lead to a variety of potential complications. Furthermore, difficulties when attempting to access the graft may result in the dialysis unit avoiding its use. Care must be taken to prevent conduit twisting or kinking. A subtle twist or kink creates an immediate stenosis that poses a risk of acute graft failure. When placing in a looped configuration, tunneling too tight of loop can lead to kinking at the apex of the graft.

Geometry and creation of the anastomosis is also of utmost importance. One must assure construction of an appropriate angle and bevel when fashioning the conduit hood. Improper craftsmanship can lead to kinking of the hood and subsequent impingement of inflow or outflow. Too much tension on the artery after the anastomosis has been sewn can lead to tenting of the back wall of the artery and can impede the inflow of the AVG. An arteriotomy that is too large can promote an overabundance of flow within the dialysis circuit and ultimately lead to steal syndrome.

AVGs placed in a loop configuration require one incision for vessel exposure (e.g., infraclavicular, for chest wall; axilla, for axillary tear drop; antecubital fossa, for forearm loop; or inguinal region, for femoral loop) and another smaller, counter incision opposite the vessel exposure to aid in the tunneling process. AVGs placed in a "straight" configuration (soft "C") require two vascular exposure sites, typically, arterial exposure distally and venous exposure more proximally on the extremity (e.g., upper arm brachial artery to axillary vein, forearm radial artery to brachial vein, or femoral distal superficial femoral artery to common femoral vein).

A tunneling device is then used to deliver the graft in the subdermal space in order to facilitate cannulation. The Kelley-Wick tunneler is used for ePTFE grafts and a sheath tunneler is necessary for autologous and biologic grafts. It is of the utmost importance to position the graft as superficial as possible to facilitate access identification and safer cannulation practice. Furthermore, tunneling the graft deeper at the counter incision and anastomosis sites will reduce the likelihood of graft exposure in the event of wound separation or infection. It is our preference to perform the venous anastomosis first in an attempt to reduce needle hole bleeding while performing the second anastomosis, but in the case of biologic grafts, conduit distension under pressure is necessary to allow standard elongation of these particular grafts (i.e., Procol, Artegraft, CryoVein). It is for this reason that when using biologic conduit for vascular access, it is important to sew the arterial anastomosis first.

Future Directions

Tissue-Engineered Vascular Grafts (TEVG)

The first efforts of tissue-engineered vascular tubes via endothelial cells lining biodegradable scaffolds were led by Weinberg and Bell [60]. However, these pioneers had difficulty achieving the structural integrity necessary for the pressures

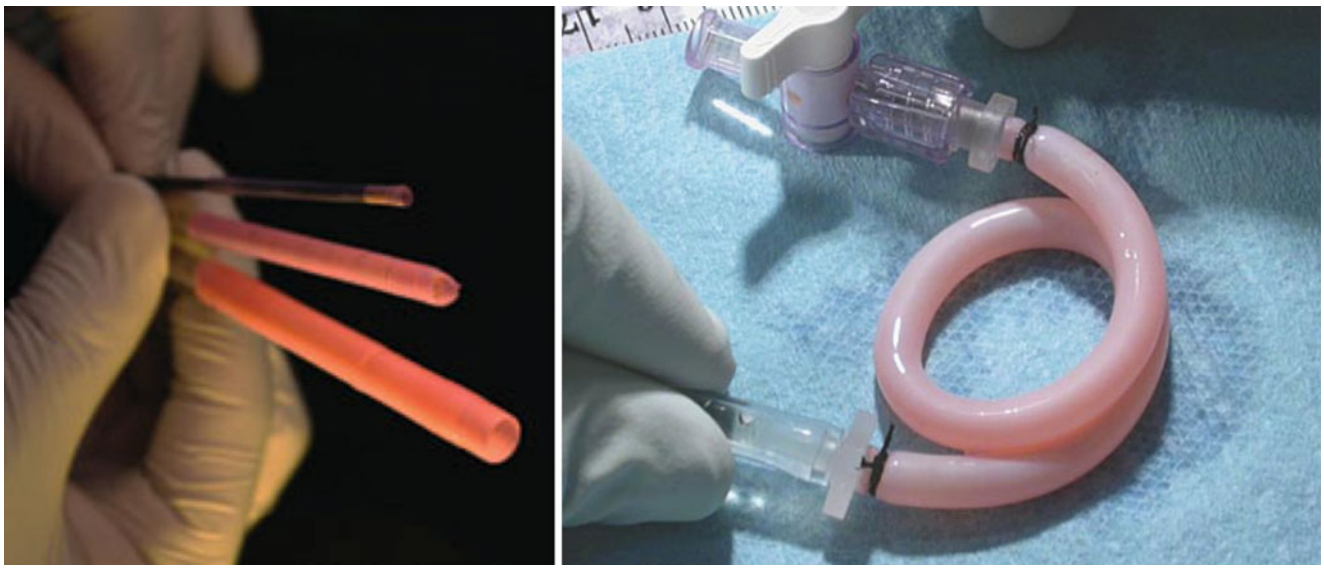

Fig. 18.8 *Left*: Cytograft sheet-based tissue engineered cells wrapped around mandrel. *Right*: Cytograft lifeline graft under pressure noting good kink radius

necessary for supporting human dialysis, and the conduits were subject to degradation. As techniques improved, clinical success was seen in 2001, when Shin'oka et al. reported development of a TEVG produced in vitro by creating scaffold composed of L-lactide and E-caprolactone reinforced with a polyglycolic acid (PGA) woven fabric [61]. There are now several teams embarking on the challenge to develop off-the-shelf blood vessels, but the two current leaders in the field, US biotechnology companies, Humacyte and Cytograft, are conducting clinical trials to test the safety and efficacy of the Human Acellular Vessel (HAV) and the Lifeline™ graft, respectively.

Cytograft

In 2007, L'Heureux et al. reported a novel method of creating a TEVG based solely on autologous tissue called sheet-based tissue engineering [62]. This TEVG, currently in early clinical trials, is a sheet-based graft, created through tissue culture by growing the recipient's own fibroblast cells taken from biopsy into a sheet which is then wrapped around a mandrel multiple times and allowed to incubate (Fig. 18.8). The tube is then seeded with autologous endothelial cells prior to implantation. The Lifeline™ graft (Cytograft, Novato, CA) is a completely autologous conduit; however, the time required to culture the recipient's own cells into a graft spans approximately 6–9 months. Lifeline™ has shown some early success in human clinical trials but with varied results [63]. As such, this early technology is not available as an off-the-shelf blood vessel replacement. Cytograft has addressed this criticism by creating an allogeneic version of this sheet-based technology. The process requires freezing and devitalizing the conduit by air-drying the fibroblast layer and storing at −80 °C and then rehydrating and warming the conduit 5 days prior to implant [64]. This process is sufficient to mitigate antigenicity of the graft while still maintaining the structural integrity. This approach has broadened the applicability of the technology but still has not quite reached the status of a readily available, off-the-shelf blood vessel.

Humacyte

Humacyte's HAV (Research Triangle Park, NC) is a tissue-engineered vascular conduit and offers off-the-shelf capability in an allogeneic biodegradable scaffold model. The HAV is a sterile, non-pyrogenic acellular tubular conduit composed of human collagen types I and III and other extracellular matrix proteins, including fibronectin and vitronectin [65]. The Humacyte platform technology uses qualified, banked, human vascular cells that, when cultured on a tubular mesh under controlled bioreactor conditions, generate a complex array of extracellular matrix proteins that over time yields an integrated, biological structure (Fig. 18.9). A decellularization process occurs rendering the vessels acellular, leaving behind a robust, bioengineered, non-immunogenic, human vessel suitable for vascular access, bypass, or reconstruction, and does not have branching vascular structures that require ligation. Humacyte developed its acellular human collagen-based vascular implant to overcome the limitations associated with synthetic materials and autologous vessels. Because the extracellular matrix material mimics native vascular tissue but is nonliving, it possesses all of the advantages of an autologous conduit and also has the off-the-shelf availability of synthetic grafts. The Humacyte vessel has the potential to be stored for at least 6 months on site in the hospital, allowing product to be available on demand in the operating room.

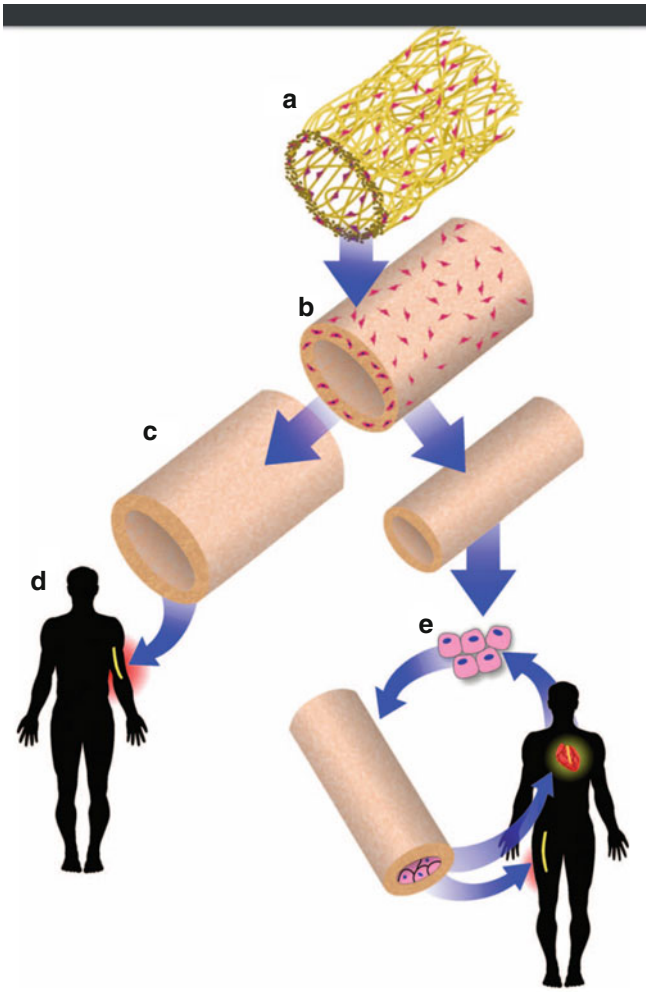

Fig. 18.9 Production of readily available HAVs. Each vessel is generated in the laboratory by (**a**) culturing human cells on a polymer scaffold that degrades as the cells produce extracellular matrix proteins to form (**b**) a tissue. Vessels are then decellularized, leaving (**c**) an extracellular matrix tube (the TEVG), which may be refrigerated until the time of patient need. (**d**) HAVs are then used in an AV access application (6 mm ID) or (**e**) smaller caliber vessels may be used for coronary applications

Upon implantation, it is anticipated (based on preclinical studies and a limited number of explanted HAV from human subjects) that the collagen matrix comprising the vessel will be infiltrated and remodeled with host cells, resulting in a living vascular tissue more similar to the histological composition of native vessels (Fig. 18.10). This may improve the longevity of the vascular access implant and decrease the likelihood of infection. The Phase II AV access clinical trial recently completed 2 years of follow-up for all patients in the trial. Midterm results show no signs of immunologic rejection and a low rate of infection [66]. A Phase III AV access, randomized, open-label, clinical trial will commence in the second quarter of 2016 to evaluate the patency of the HAV when compared to the standard ePTFE AVG.

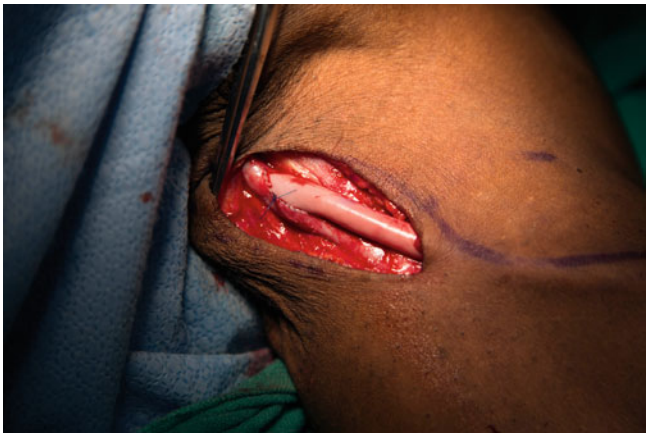

Fig. 18.10 Venous anastomosis of HAV from first US implant during the Phase II clinical trial

Injury Protection/Reliable Access

Bullet Proof

Despite success and popularity, prosthetic AVGs have significant disadvantages and are plagued by multiple modes of graft failure. Specific issues that afflict AVGs include thrombosis, infection, weeping of serous fluid, aneurysm formation, and traumatic degradation of the graft material [67–70]. These complications often result from improper needle cannulation and graft handling (Fig. 18.1) but can also be attributed to the inferior material and construction of current AVGs. For example, graft degradation can be significantly accelerated by inadvertent puncture of the posterior or sidewall of the graft. These unintentional punctures can result in perigraft hematoma or pseudoaneurysm (PA) formation, which can lead to graft bleeding, thrombosis, and failure [71–73] (Fig. 18.11). Overly aggressive graft compression, in an attempt to provide hemostasis following needle withdrawal, can also result in graft thrombosis and failure. Finally, the most problematic complication of these grafts is the degradation that occurs as a result of repetitive needle cannulation and coring of the AVG material. This unavoidable complication commonly leads to PA formation. As the graft material degrades, a weak pseudo-conduit develops that allows for continued blood flow, but it has little integrity. Over time these pseudoaneurysms can develop mural thrombus, which can lead to complete thrombosis of the graft. Conversely, the PAs can continue to grow and the overlying skin can become thin and excoriated. This poses a serious risk of rupture, hemorrhage, exsanguination, and death. The impact of these complications on ESRD patients is significant, resulting in pain, disability, and surgical intervention to treat an expanding hematoma or PA. Management of these complications leads to millions of dollars in healthcare expenditures annually [74].

Currently, no available grafts offer protection from needle access injury, and no FDA-approved HD grafts offer imme-

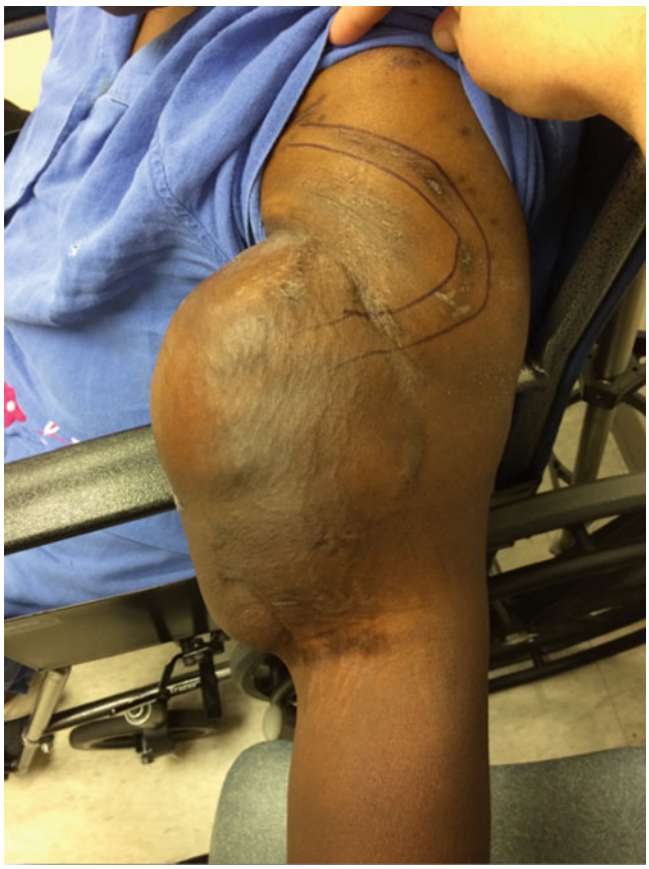

Fig. 18.11 Extremely large hematoma on the upper extremity of a patient following a back wall injury of ePTFE AVG with a dialysis needle during a dialysis session

diate cannulation. Only 2 grafts are FDA approved for early access (24–72-h post-implant [Vectra, CR Bard, and Acuseal, W.L. Gore]), but outcome data for these devices is lacking. To mitigate dialysis access graft cannulation complications, InnAVasc Medical, Inc. (Research Triangle Park, NC) has developed an AVG modification that incorporates two multilayer cannulation chambers with low-bleed technology that are resistant to posterior and sidewall needle penetration/injury, the *Bullet Proof* vascular graft (BPG) (Fig. 18.12). This device may eliminate many of the current complications and costs associated with AVG failure and infection.

InnAVasc's graft modification technology is designed to create one contiguous flow lumen without transition points.

This device may eliminate complications associated with AVG cannulation by preventing posterior and sidewall needle injury. The self-sealing technology allows for immediate graft cannulation following implantation and may reduce the need for temporary dialysis catheters, which are prone to complications and associated with increased mortality [75].

Conclusions

The limiting factors that affect all foreign bodies continue to plague dialysis access grafts. Since these patients are often immunocompromised and represent a cohort with multiple comorbidities, they are often less tolerant to infectious or technical insults. In the 40 years leading up to the turn of the century, technology in this area had not particularly excelled, and as such, the most common prosthetic graft in use today remains ePTFE. Ease of handling, cost, and reasonable technical results make it the most commonly placed AVG in dialysis patients. It is often available as stock in most facilities and comes in a varied size and shape profile. More recent advances in science and medicine are tapping cellular and genetic therapies to address a core issue of vascular disease. In the last decade, there have been great strides toward a realization of a true off-the-shelf blood vessel, and current clinical trials will start to reveal the evidence as to whether this tissue-engineered vessel technology is truly a step toward liberation from synthetic grafts for vascular access, bypass, and reconstruction. If so, we will witness the first disruptive technology in this space in over 50 years. As science and technology continue to advance, our patients will one day enjoy an ideal vascular access that is self-sealing, thromboresistant, compliant, biocompatible, injury proof, durable, easy to sew, easy to sterilize, easy to access, resistant to infection, readily available, and cost-effective.

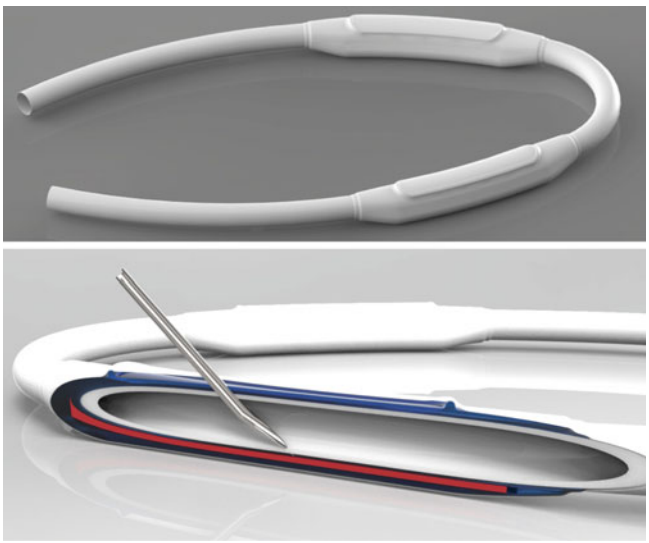

Fig. 18.12 *Top*: Illustration of the bullet proof vascular graft showing two distinct cannulation chambers with raised cannulation zone indicators. *Bottom*: Longitudinal cross section of a bullet proof cannulation chamber showing the inability of the needle to penetrate the back wall (*red* plate)

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Part IV

Hemodialysis Access Use and Assessment

Current Hemodialysis Techniques

19

Lynda K. Ball

Introduction

Cannulation of vascular access is both an art and a science. While a person can be taught the basics of inserting needles into a vein, the art of cannulation is all in the details – the nuances of each individual access. Cannulation is more about what is felt rather than seen as palpation is by far the single most useful tool to prevent complications associated with needle insertion. Palpation allows the identification of areas to avoid and determine how deep the access is below the skin surface and to ascertain the appropriate angle of insertion and the feeling of pressure release as a fistula is entered so that an the needle angle is dropped as it is advanced into the arteriovenous fistula (AVF) or arteriovenous graft (AVG).

From a surgeon's perspective, a successful AVF is one with sufficient flow to dilate the vein and thicken the walls – this enables insertion of needles ranging in size from 17 gauge to 14 gauge for the dialysis treatment (Fig. 19.1). But in order for the vascular access to be used successfully, surgeons also need to consider additional criteria to allow for safe, successful cannulation. The National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI) defines fistula maturation as "the process by which a fistula becomes suitable for cannulation" and focuses on the Rules of Sixes: blood flow greater than 600 mL/min, a diameter greater than 0.6 cm, and a depth of approximately 0.6 cm [1]. Thus, additional considerations include sufficient length of the vascular access – at least 6 in. for the cannulation zone to prevent damage to the vessel wall (i.e., aneurysms) from long-term cannulation. The vascular access depth is also important, ideally close to the surface of the skin and no more than 6 mm deep with discernable margins. Current needles used in the USA are available in three lengths – 5/8 in., 1 in., and 1.25 in. – and are made of stainless steel. When an AVF or AVG is deep, the cannulation angle needed is a steep one, which significantly decreases the amount of the needle within the vessel. Any sudden movement by the patient can cause needle dislodgement and infiltration. Assessment of an infiltration in deeper tissue is difficult and can range anywhere from slight discomfort from bruising and swelling to compartment syndrome. Deep vascular accesses may be labeled as uncannulatable if staff cannot perform the dialysis treatment, so they may be abandoned without intervention.

In recent years, techniques have been developed by surgeons and interventionalists to salvage such vascular accesses. One technique is superficialization of the vascular access [2]. A second technique is lipectomy (liposuction), which involves removing the excess tissue between the surface of the skin and the fistula [3]. These techniques have preserved future vascular access sites and made cannulation and dialysis treatments safer for patients. It is important that the surgeon takes into account the anatomic location of the vascular access. The vascular access needs to be in a location such that the patient can sit in a comfortable position for approximately 3–4 h. Vascular access placed near the axilla (Fig. 19.2), for instance, makes it difficult to position the arm that is comfortable for the patient, and leads to joint stiffness from remaining motionless during treatment. Also, compression of the dialysis tubing as it exits the arm can set off machine alarms, interrupting dialysis. Additionally, this creates a challenge for the cannulation process as it is difficult for the staff to position themselves for the cannulation process without feeling like they are sitting in the patient's lap. While this may not seem like a serious problem, this inconvenience can lead to shortened dialysis treatments. Shortening dialysis treatments by even 10 min a session due to discomfort equals 2 weeks of missed treatments in a year, which impacts morbidity and mortality.

While location and depth are major issues, utilizing the correct cannulation technique can also impact the number of

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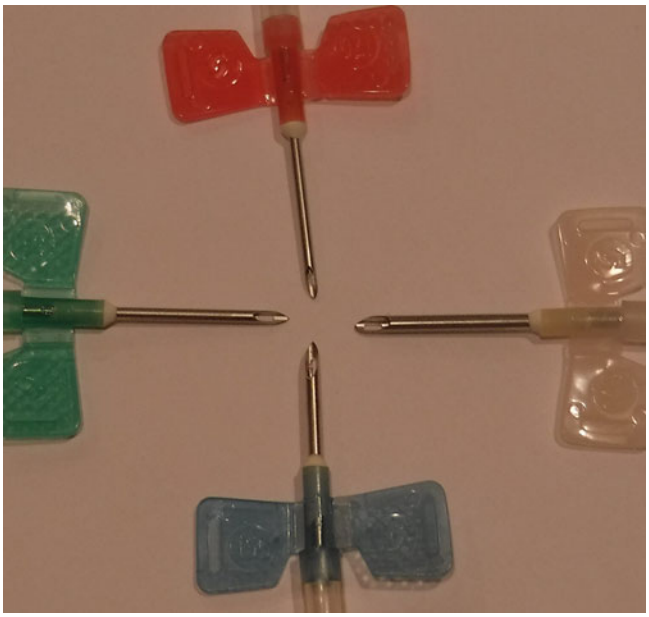

Fig. 19.1 Needle gauge size for a hemodialysis treatment range from 17-gauge needles for slower blood flow rates (250 mL/min) and initiating dialysis with a new arteriovenous fistula, up to 14-gauge needles for blood flow rates in excess of 450 mL/min. Dialysis adequacy will dictate needle gauge size and blood flow rates. (Counterclockwise from the top) 17 gauge, 16 gauge, 15 gauge, and 14 gauge

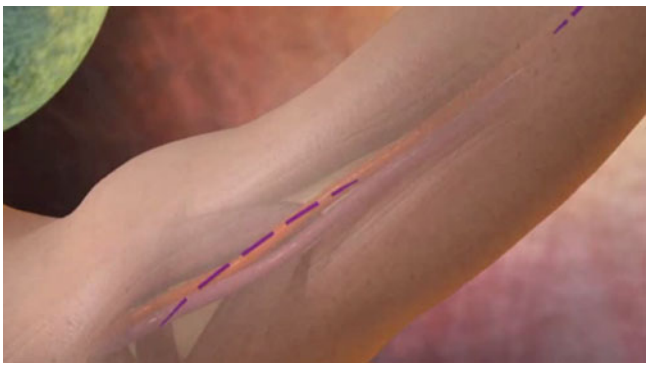

Fig. 19.2 Vascular access placement close to the axilla area is not only difficult for staff to cannulate but is uncomfortable for the patient as the arm would be kept in this position for a 4-h dialysis treatment (Courtesy of B. Inman)

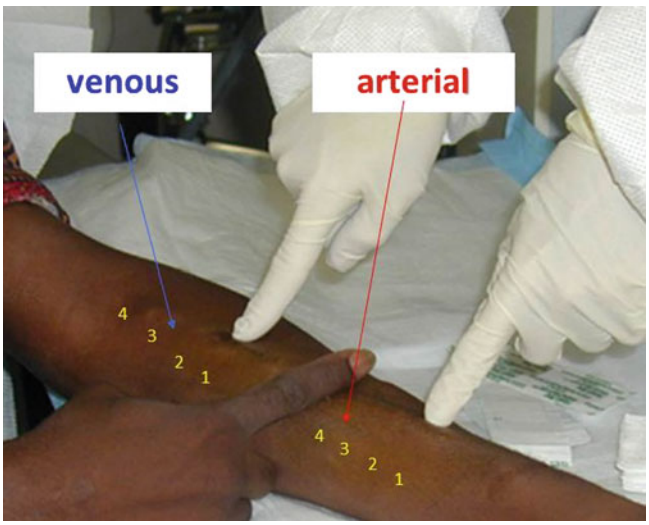

Fig. 19.3 Site rotation "rope ladder" cannulation involves finding a new site for each treatment for both the arterial and venous needle. Spacing out the needle sites over time will allow the arteriovenous fistula to evenly dilate and at the same time continue to thicken the wall to prevent infiltrations (Courtesy of B. Inman)

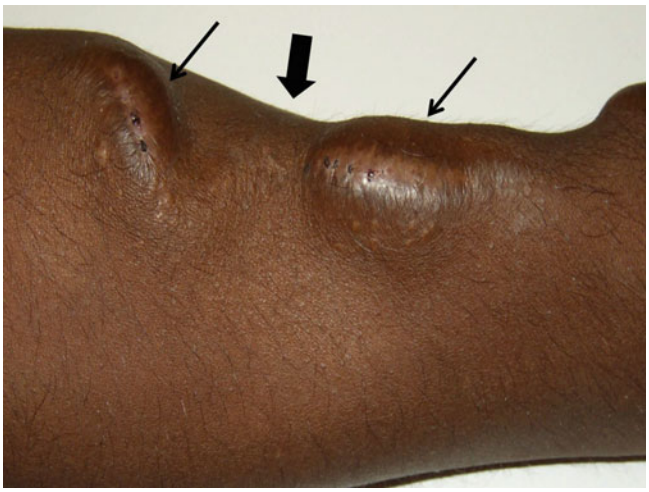

Fig. 19.4 Aneurysm formation as a result of repeated cannulations in the same small areas. Notice the two mountains (*thin black arrows*) and a valley (*block arrow*). It is very difficult to utilize the portion of the arteriovenous fistula in the valley because the wings of the access needle hit the mountain. This aneurysmal degeneration leads to a decreased cannulation zone for further needle insertions

interventions required for an access, as well as the overall life of the access.

Cannulation Techniques

Three cannulation techniques have been described: site rotation called "rope ladder," area puncture, and constant site also known as "buttonhole" [4, 5].

Site Rotation Cannulation "Rope Ladder" This technique utilizes the entire length of the AVF leading to even dilation of the vessel and giving cannulators the most surface area available for needle insertion (Fig. 19.3). For each dialysis treatment, cannulators select two new sites for needle insertion, staying at least ¼ inch from the previous cannulation site and not returning to that area for approximately 2 weeks to allow healing of previous cannulation sites. Impediments to site rotation cannulation are areas that are associated with

high infiltration risk: areas with curves, flat spots (stenotic areas), or a segment that is too deep to reach. Also, short-segment AV fistulas (≤3 in.) will be subjected to more damage and potential shorter use-life due to more frequent aneurysmal degeneration.

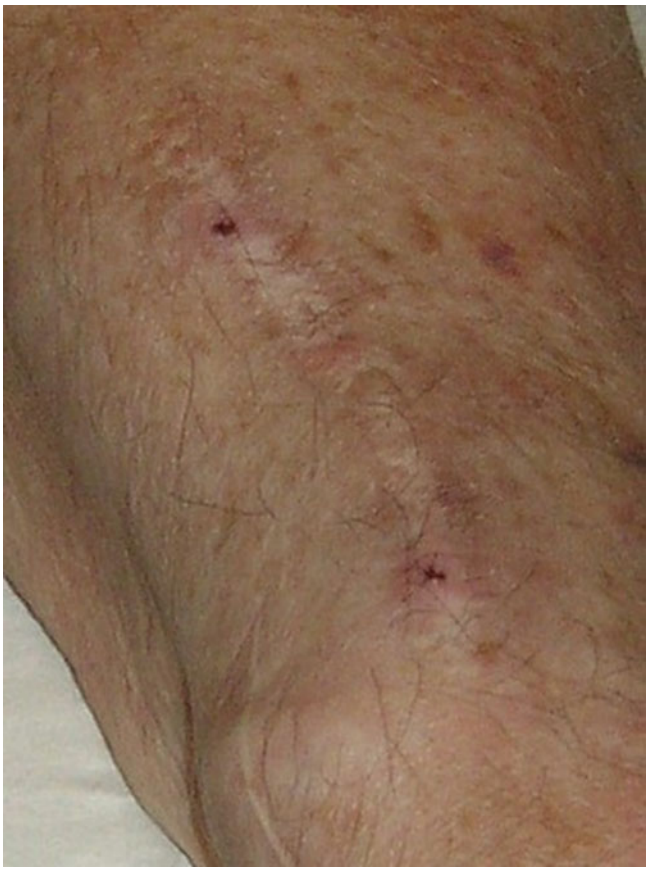

Fig. 19.5 Buttonhole cannulation technique in an arteriovenous fistula. Notice there are only two cannulation sites, with adequate space in between to eliminate the risk of recirculation. These sites had been in use for 3 years at the time of the photograph

Area Puncture Cannulation Needle insertion occurs in the same small area of the access with each cannulation. This technique is also known as "one-site-itis." This technique leads to multiple puncture sites as shown in Fig. 19.4 resulting in the creation of "two mountains and a valley." Surprisingly, while we do not teach this technique, it is evident that it is a major cannulation technique utilized across the USA.

Constant Site or Buttonhole™ Cannulation This technique involves creating a tunnel from the surface of the skin to the blood vessel wall and then making one entrance site into the AVF wall (Fig. 19.5). The vessel wall tissue reorganizes into a stoma-like configuration, and when the needle touches the tissue, it opens up and allows the needle to enter the AVF. When removing the needle, the tissue closes back up and a small thrombus plug forms at the vessel wall and a scab forms on the surface of the skin. The creation of the tunnel and entranceway into the AVF is done utilizing sharp needles, and once the needle slides right down the tunnel, a transition to blunt needles occurs (Fig. 19.6). This technique became very popular in the USA around 1999 when a buttonhole tunnel was needed to access the LifeSite™ device. As popularity for this technique has grown in the USA, there are now some significant complications (i.e., infection, endocarditis) that have become apparent. The buttonhole technique has two permanent exit sites, compared to no permanent sites with site rotation cannulation. This technique incorporates concepts that are not a factor with site rotation cannulation such as colonization of bacteria and scab removal. It is known that bacterial count around exit sites is higher than surrounding skin (lessons learned from peritoneal dialysis

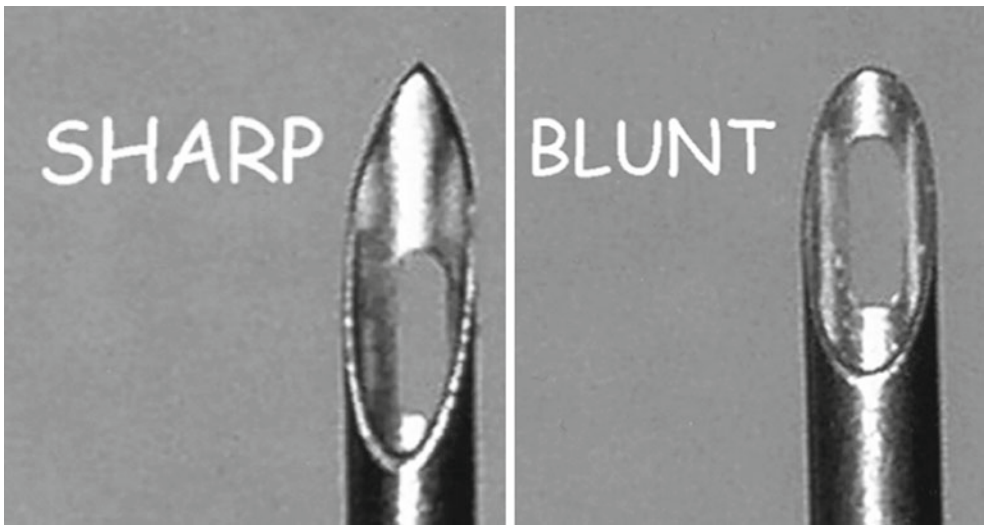

Fig. 19.6 Sharp versus blunt needles. Sharp needles are utilized for site rotation cannulation and for the creation of the buttonhole tunnels and entranceway to the fistula wall. Once the buttonhole tunnel and entranceway are created, there is a transition to blunt or dull needles for cannulation (Reprinted with permission of L. Ball and the American Nephrology Nurses' Association, publisher, *Nephrology Nursing Journal*, June 2006, Volume 33/Number 3)

and central venous catheter sites regarding colonization of bacteria surrounding exit sites in the skin). Improper cleaning or damage to the tissue could lead to an exit site infection. Dialysis patients carry staph on their skin and their noses at higher rate than the general population [7], making cleaning sites before needle insertion one of the most important aspects of infection prevention. Over the last decade, best practices have been identified to reduce the infection rate and its associated complications [6]. Patients are instructed to wash their access just prior to sitting down, and then staff preps the skin twice, once before scab removal and again after scab removal to ensure the bacterial count is as low as possible before inserting needles. Performing this two-step cleaning protocol can decrease the amount of bacteria surrounding the exit sites [8, 9]. As a result, this is the gold standard for constant site access cleaning.

The other compounding issue is scab removal. By inserting the needle repeatedly in the same spot at the same angle over a 3- to 4-week period, the result is the creation of a tunnel from the surface of the skin to the outside of the blood vessel wall of the AVF. The scab serves to protect the tunnel from bacteria and potential tunnel infection. So before every cannulation, scabs need to be completely removed. While the patient is having their dialysis treatment, the staph from other parts of the arm migrate back to the exit sites, so that when the needles are removed, staph can become incorporated into the scab. That is why it is imperative that scabs be completely removed and why cleaning must occur after scab removal. All makers of blunt cannulation needles have scab-lifting devices, but care must be exercised to prevent digging (Fig. 19.7). Digging can cause three potential issues: making the exit site bigger, which can allow staff to utilize in incorrect angle of insertion allowing for multiple tunnel creation; breaking the tissue surrounding the exit site that could cause an exit site infection; and breaking off pieces of the scab and pushing it down into the tunnel causing a tunnel or blood stream infection. The appropriate way to utilize a scab-lifting device is to lift a corner of the scab with the tip, then turn it on its side and scrap across the scab. Soaking scabs with saline and gauze for 3–5 min makes scabs much easier to remove [6].

Fig. 19.7 Scab-lifting devices. With the buttonhole technique, a major concern to prevent infection is to completely remove the scabs from the exit sites. There are three manufacturers of blunt buttonhole needles in the USA: (*left*) JMS Harmony, (*center*) Medisystems Steri Pick, and (*right*) Nipro BioHole. On the end of each of these needles is the scab-lifting device

The buttonhole technique requires much diligence, and any break in the process could result in infection. It is critical that staff be observed for competency, at least annually, to ensure that they are performing the technique correctly utilizing the evidence-based practices that have been identified. Careful selection of patients is important in reducing the risk of infection. The buttonhole technique literature has identified distant infection including endocarditis, heart valve growth and replacement, and spinal abscesses. As a result of a repeated pattern of these distant infections, patients with a history of endocarditis, heart valve disease, or artificial implants could be at higher risk for infection based on research outcomes, and their nephrologist should speak about the infection risk prior to initiating the buttonhole technique (Kelly Sutherland & Linda Mills, Vascular Access Coordinators at St. Joseph's Healthcare, Hamilton, Ontario, Canada). Patients who pick at their scabs are also at increased risk for infections and are not considered appropriate for this cannulation technique.

Assessment and Cannulation of a New Vascular Access

It is of the utmost importance to have good communication between the surgeon, nephrologist, and expert cannulator when determining if a fistula is sufficiently mature to cannulate. While surgeons can check the diameter and flow rates of a new access, they do not have experience with cannulation, in particular, cannulation with the pressure exerted within the fistula from the blood pump of the dialysis machine. A fistula may appear and feel ready to cannulate, but the vessel wall may still be fragile and unable to tolerate the needle puncture. It takes a lot of cannulation experience to identify if there might be problems with needle insertion (i.e., infiltration), and if there is any doubt, then leave the needles out. There is good evidence to support identifying expert cannulators for assessment and needle insertion on all new AVFs – someone who will tell a nephrologist or surgeon that the access is not ready to cannulate and that it should be reevaluated by the physician before anyone inserts a needle. Robbin and colleagues (2002) evaluated experienced dialysis nurses and found an 80 % success rate of accurately predicting eventual fistula maturity [10].

While evidence-based research surrounding cannulation is limited, there are evidence-based practice guidelines. The KDOQI Clinical Practice Guidelines and Recommendations (www.kidney.org/professionals/guidelines) and the Fistula

Fig. 19.8 The do's and don'ts for cannulating new AV fistulas

Do's	Don'ts
Insert needles bevel up	Flip needles
Tape securely	Tape tightly
Insert needle evenly into the center of the vessel using the correct angle for the depth of the vessel	Push, pull, and/or redirect
Sit down	Stand up
Hold one site at a time with two fingers for 10 minutes – no peeking	Use clamps post treatment
Always use a tourniquet or manual compression every treatment for assessment and cannulation	Assess or insert needles without plumping up the AV fistula
Stretch the skin taut – either side-to-side or below the AVF	Pinch the AVF when inserting needles or blocking flow above the AVF

First Breakthrough Initiative (FFBI), now known as Fistula First Catheter Last (www.esrdncc.org/ffcl/), are both excellent resources with regard to cannulation of AVFs. For the initial cannulation, it is strongly recommended to utilize a smaller-gauge needle (17-gauge needle) to decrease injury to the vessel and prevent a large infiltration, hematoma, compression of the vessel, and possible clotting of the AVF [11]. Patients should be prepared for the potential for infiltration prior to any cannulation attempt. First-time cannulation has one of the highest risks of infiltration mainly because it is the first time that the vessel will have increased blood flow with additional pressure exerted on the walls from the use of the blood pump. A list of best practices "Do's and Don'ts" for cannulation of new AVFs (Fig. 19.8) should aid in decreasing infiltrations related to needle positioning and manipulation or increasing pressure within the cannulation zone [12].

Complications

Surgically connecting a high-pressure, high-flow artery to a low-pressure, low-flow vein causes two of the most common insults to the venous system – stenosis and aneurysm formation, both of which are seen in majority of the time in the arterial system. Staff must be able to recognize and respond to these two major complications because these complications impact the longevity of a vascular access.

Hemodialysis Access Stenosis The frequency and location of stenosis is dependent on the patient's cardiac status (i.e., ejection fraction, blood pressure), shear stress within the vessel [13], location of the access (i.e., forearm, upper arm) [14], and the type of access (i.e., AVG, AVF). Improper cannulation technique could potentially cause a stenosis within the cannulation zone, but is not the prevalent cause of stenosis. Too shallow angle of insertion can cause the needle to lacerate the endothelial lining on the top of the fistula wall. Exerting excessive pressure when inserting needles could cause adhesions within the cannulation zone or cutting of the endothelial lining. And not cannulating directly over the center of the fistula could cause damage to the side wall of the AVF. All of this damage could potentiate stenosis formation within the cannulation zone.

The "arm raise" technique is one way to evaluate if there is a stenosis present, and patients with AV fistulas should be taught how to evaluate their access as part of their care [11, 12]. First, the patient holds his or her the arm with the access in a dependent position and pumps the fist – this will engorge the AVF. Next, with fist still clenched, the patient raises the arm above the head and observes what happens to the fistula: a complete collapse of the fistula indicates that the venous drainage system is open and there is no blockage; a partial collapse at the proximal end and engorgement of the distal end indicate a stenosis within the cannulation zone; and distention of the entire fistula would indicate a stenosis outside of the cannulation zone, either outflow or central arch stenosis. If there is partial or no collapse, patients need to be referred for evaluation of stenosis. If a central stenosis is suspected, the fistulogram should be completed all the way back to the heart to identify the location of the lesion.

Hemodialysis Access-Related Aneurysms Aneurysm formation in AVFs occurs from a combination of two factors: cannulation technique and pressure within the vessel. As was discussed earlier in this chapter, the area puncture technique is responsible for the damage to the vessel wall. The microvascular network in this small area of the fistula wall is literally destroyed; there is a loss of the muscle layer (media) and is replaced with collagen, which causes the area to become fibrous with loss of elasticity [15, 16]. As a result, the vessel wall begins to thin and any increase in pressure within the vessel (i.e., increased blood pressure, stenosis) will cause the thinned wall to bulge creating the aneurysm (Fig. 19.9).

Several retrospective studies of the CMS-2746 (ESRD death forms) and the medical records of patients who experienced fatal vascular access hemorrhage described risk factors associated with aneurysm formation [17, 18] and went as far to say that these are preventable deaths. It

is, therefore, critical that staff know when to refer damaged accesses before they become dangerous and have the potential for rupture [19]. KDOQI, in the 2000 Update, made recommendations for when to refer aneurysms for evaluation [20]:

(1) Skin over the AVF is compromised – any skin breakdown, blebs, blisters, skin sloughing, and/or large unhealed scabs
(2) Risk of fistula rupture – shiny, tight, firm to palpation, leaking
(3) Available puncture sites are limited – aneurysms take up the entire cannulation zone

In addition, KDOQI strongly advises against cannulating an aneurysm, citing hemorrhage, exsanguination, and death as the ultimate outcomes.

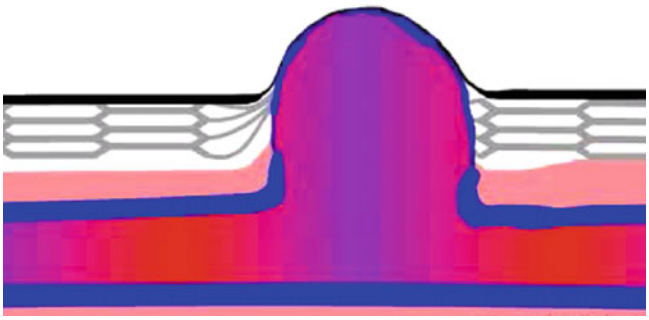

Fig. 19.9 Damage to the endothelium lining of an AV fistula caused by cannulation in the same small area (i.e., the area puncture technique). Repeated cannulation weakens the wall of the AV fistula, and when there is an increase in pressure in the venous system (i.e., stenosis, increased blood pressure), a bulge of the weakened area occurs. As you can see, the vessel lining thins and as it pushes against the surface of the skin, it will also thin the surface of the skin. This can potentiate a potential for rupture of the fistula (Courtesy of B. Inman)

Hemodialysis Access Infiltrations Infiltration can range from a small hematoma to compartment syndrome with potential loss of the access from the swelling and pressure (Fig. 19.10). There are many reasons that an infiltration can occur; most are related to the cannulator's skill set [21]. The most common reason for infiltration is a too steep an angle of dialysis needle insertion. If the access is created within 6 mm of the surface of the skin, then

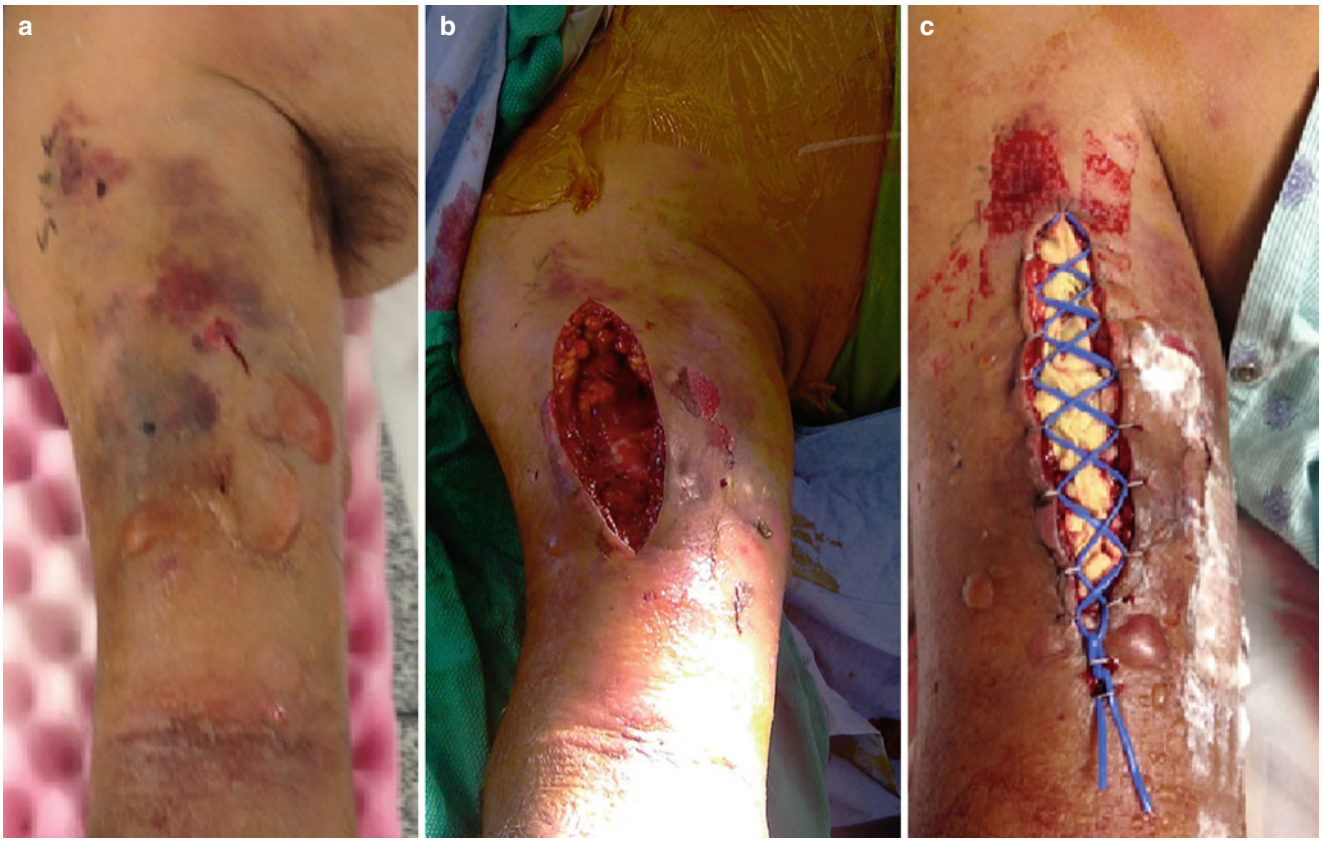

Fig. 19.10 A case of infiltration of a brachiocephalic arteriovenous fistula leading to hematoma formation with compression of the outflow vein and compartment syndrome of the right upper extremity. (**a**) The patient presented with massive arm swelling with blister formation, pain, and hand numbness. (**b**) Posthematoma evacuation. (**c**) Temporary closure. The wound was closed a few days later and the fistula salvaged (Courtesy of S. Shalhub, MD)

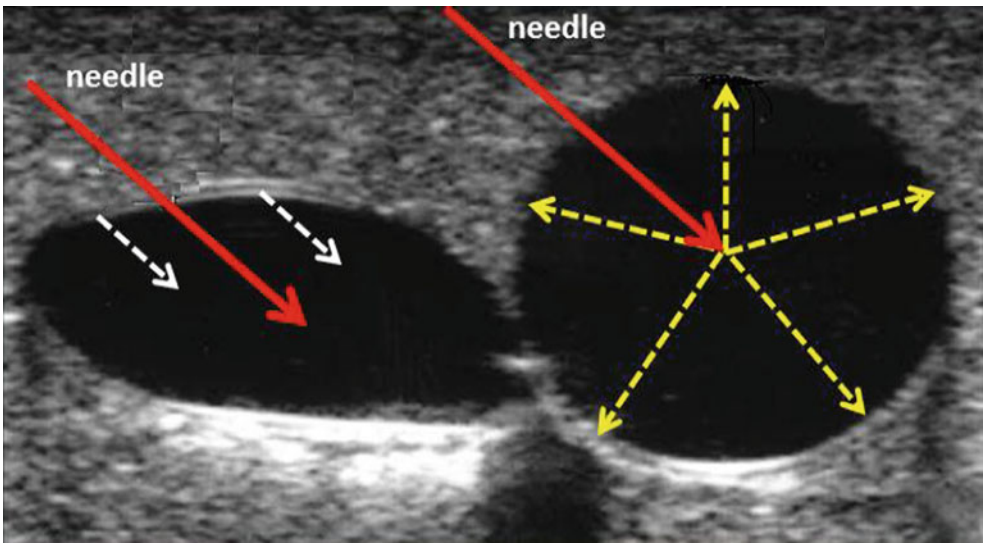

Fig. 19.11 Tourniquet versus non-tourniquet use for AV fistulas. When you apply a light tourniquet, it causes the vessel to plump up like the vessel on the right. As the fistula plumps, it causes the vessel wall to distend and tense, and it allows the needle to pass through without pushing hard. A tense wall also decreases the pain associated with cannulation. In addition, you can be slightly off in your angle of insertion and still not damage the vessel lining or infiltrating the access. Without a tourniquet, the vessel wall is not tense and requires more pressure when inserting the needle. It also compresses the vessel, and it decreases the room for error increasing the risk for infiltration

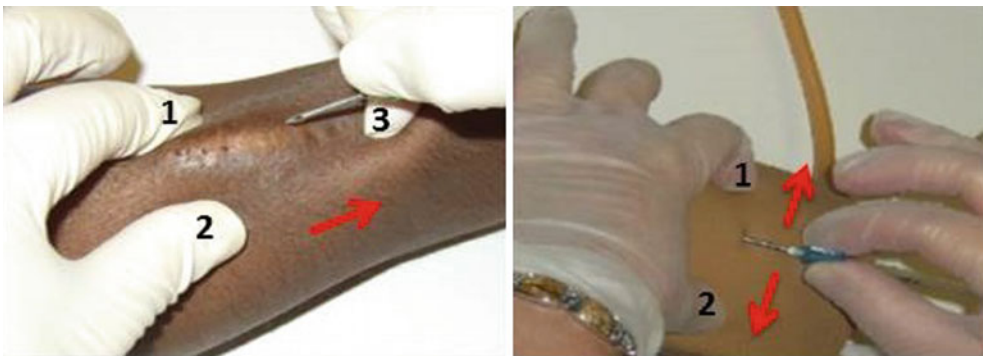

Fig. 19.12 The 3-point technique for site rotation versus the 2-point technique for the buttonhole technique. In the *left picture*, you can see the three different points: Number *1* and *2* help to identify the width of the AV fistula, while number *3* is the finger that stretches the skin taut to help to decrease pain associated with needle insertion. In the *right picture* is the 2-point technique that is used for the buttonhole technique. The skin would be stretched from side to side maintaining the integrity of the tunnel and keeping the tunnel in a stable position to prevent damage to the tunnel wall as needles are inserted

the angles of entry would range from 20 to 35° utilizing a 1-in. needle. If the access is deeper, then there is an increase in angle of insertion and/or change from a 1-in. needle to a 1-1/4-in. needle. This means that a very small portion of the needle is actually within the vessel. Any sudden movement by the patient can then cause the needle to pop out of the access causing an infiltration. Standing up to cannulate also causes an increased angle of insertion, particularly with the venous needle. Staff should be trained to sit down and be close to the access and keep the wings of the needles perpendicular to the access to ensure there is no side-wall infiltrate when advancing needles into the vessel.

Lack of tourniquet use is the second major reason for infiltrations. Tourniquets perform several functions, but the most important reason is to increase the vessel diameter allowing for more cannulation area should the angle of insertion be too steep. In addition to the added space for needle insertion, it makes the wall of the vessel tense, allowing needles to be inserted with less pushing pressure, resulting in less cannulation pain. The combination of no tourniquet and a thickened non-tense fistula wall means pushing harder to insert the needles which cause the vessel to flatten slightly, bringing the back of the blood vessel closer, allowing for a potential back-wall infiltration (Fig. 19.11).

Stretching the skin tight or taut prevents native vessels from rolling that could cause a side-wall or back-wall infiltrate. The three-point technique for site rotation and two-point technique for constant site cannulation (Fig. 19.12) are best practice techniques that not only help to prevent infiltration but also decrease pain associated with needle insertion as a result of compression of the nerve endings and blocking of the "pain-to-brain" response [6].

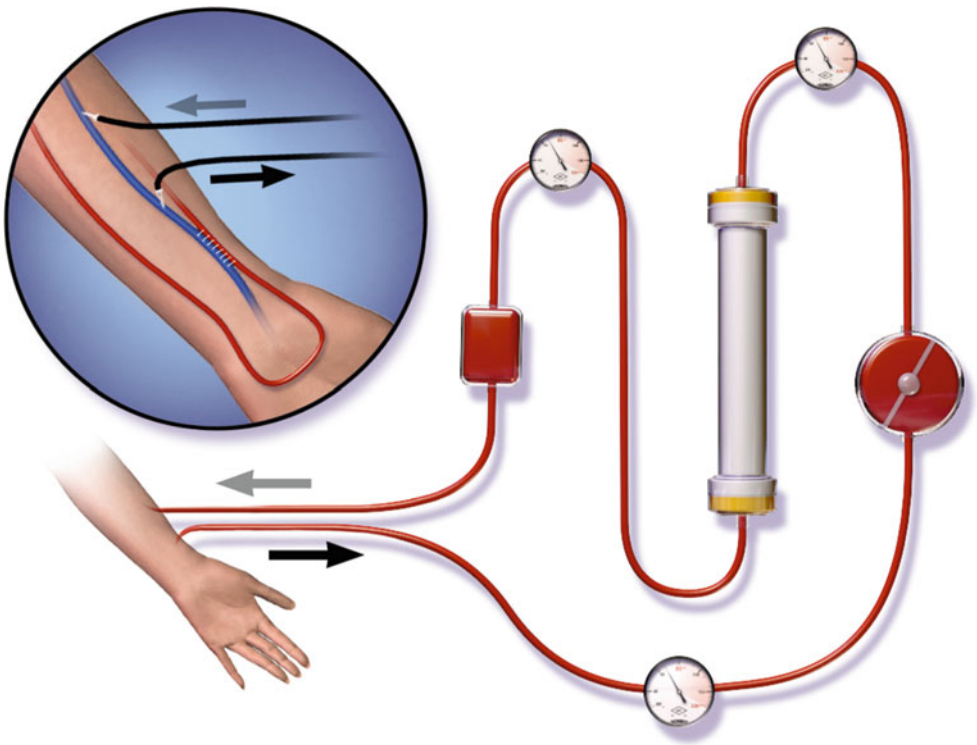

Fig. 19.13 The dialysis circuit begins at the arterial needle. The blood pump pulls the blood out into the extracorporeal circuit, through the artificial kidney, then to the venous drip chamber and returns to the patient via the venous needle (Blausen.com staff. "Blausen gallery 2014". *Wikiversity*)

Hemodialysis Access-Related Steal Syndrome This can happen any time during the life of a vascular access. Patients may complain of an extremely cold access hand and severe pain as a result of hypoxia due to decreased blood supply to the hand, affecting both the tissue and nerves. In addition, patients may lose motor function to their hand, which could lead to "claw hand," when the fingers curl up and freeze in the shape of a claw. At the dialysis center, clinical assessment for steal can be completed in as little as 10 s [11]. A comparison of the access hand to the non-access hand is the key to identifying the impact to the access hand. The nurse should grasp both hands in front of her to begin the assessment as follows:

- Evaluate for a difference in the temperature of the hands
- Assess the nail beds for paleness or blue tinge
- Assess the finger tips to see if any ulcers or necrotic spots have developed
- Have the patient squeeze hands to check for grip firmness/motor movement

Next, on a scale of one to ten, ten being severe pain, the patient is asked to rate the pain level in the access hand and is asked if the pain worsens as the blood pump speed is increased. If the patient usually experiences more than one of the signs and symptoms, the nephrologist is notified so that he/she may evaluate for referral to the surgeon or interventionalist.

The Hemodialysis Machine

Once the needles have been inserted, syringes are utilized to check that there is good flow in and out of the access. Once good flow is verified, the needles are secured and then connected to the extracorporeal circuit of the dialysis machine for the hemodialysis treatment. In order to complete the dialysis process, there needs to be a way to pull the blood out of the body, clean it, and return it to the body. This process is performed by the use of a blood pump that creates a vacuum, which pulls blood from the bloodstream via the arterial needle (closest to the arterial anastomosis) into the extracorporeal circuit (Fig. 19.13). This pressure is always a negative pressure measured from the arterial needle to the blood pump and called *pre-pump arterial pressure* (AP) (Fig. 19.7). AP should be monitored throughout the dialysis treatment and never be allowed to become more negative than –250 mmHg, as this seems to be the tipping point where increased hemolysis occurs due to sheer stresses.

Dialysis nurses perform assessment of the needle tubing to verify there are no kinks, clots, or clamps causing the increased pressure. They also assess for any internal problems anywhere from the arterial needle site back to the artery – a juxta-anastomotic stenosis would be the first thing to consider when there is an increased negative pressure resulting from insufficient flow. For instance, if the blood pump is set for 400 mL/min blood flow rate (BFR), the artery should be able to deliver the 400 mL/min blood flow to sustain the dialysis treatment. However, if there is an inflow ste-

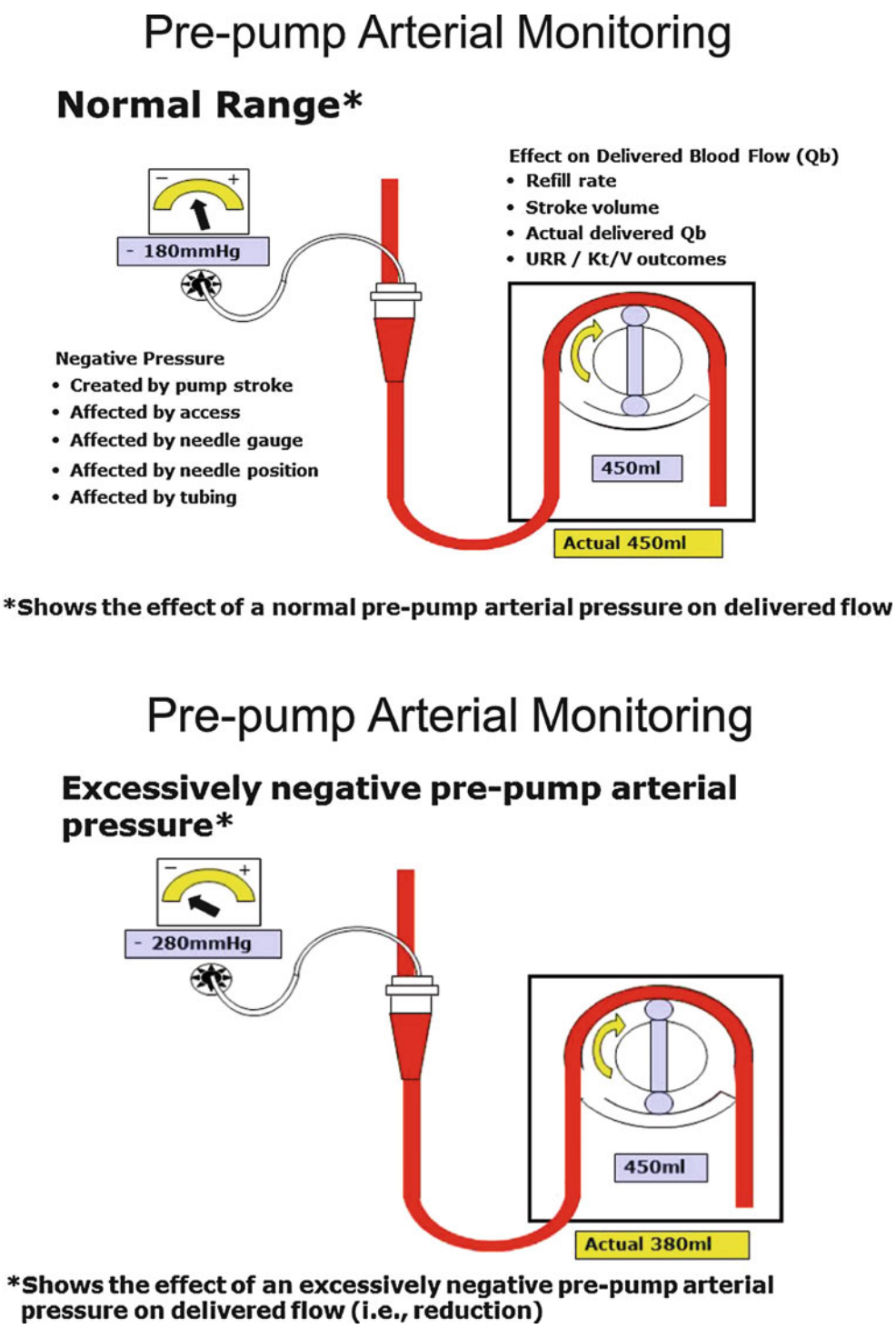

Fig. 19.14 Effect of increased negative pre-pump arterial pressure on delivered blood flow (Used with permission of the Fistula First Breakthrough Initiative)

nosis, the artery will not be able to provide the 400 mL/min BFR; therefore, the blood pump will pull blood from the venous end of the fistula, which means pulling in the opposite direction of flow that requires much more suction, making the arterial pressure become more negative. Palpation of the 3-inch segment near the anastomosis, known as the juxta-anastomotic region, could reveal a flat spot and the exact point of narrowing that would need intervention. Regardless of the needle gauge size, the arterial pressure should never exceed -250 mmHg.

If the physician orders an increased blood pump speed to achieve adequate dialysis, the AP will tell a nurse when to change to a larger-bore needle – as the pressure becomes more negative toward the -250 mmHg, that would be the time to increase needle gauge size. This would lessen the resistance and decrease the pressure, allowing an increased blood flow rate with the new larger-gauge needle. If dialysis is continued with more negative arterial pressure, then the blood pump speed that the machine is set to will not be achieved (Fig. 19.14), and this leads to less than optimal

Fig. 19.15 The 2-finger hold after needle removal. Holding one needle site at a time would reduce the double compression of the fistula, which could potentially cause reduction or stop the blood flow through the fistula

cleaning of waste. These are the standard needle gauge size and the BFRs associated with them [11]:

- 17-gauge needle = 200–250 BFR
- 16-gauge needle = 250–350 BFR
- 15-gauge needle = 350–450 BFR
- 14-gauge needle = > 450 BFR

Blood is returned to the body through venous needle (needle furthest from the anastomosis) via the blood pump and is always a positive pressure. Measurement of the *venous pressure* (VP) is performed by setting the blood pump to 200 mL/min BFR at the initiation of dialysis. If the VP is greater than 140 mmHg for three consecutive treatments, there is a potential for an outflow or central stenosis that needs to be evaluated. The most important point of venous pressure monitoring is to watch for a trend of increasing pressures, which indicates blood backing up into the fistula and preventing the blood in the extracorporeal circuit from returning to the patient. Clinical indicators of increased venous pressure would include blood squirting out around the needles during cannulation, increased bleeding times at the end of treatment (i.e., someone who required 3 min to achieve needle site hemostasis and now is requiring 30-min to achieve the same result), increase in the size of current aneurysms, or the formation of new aneurysms in the cannulation zone.

Once the dialysis treatment is complete and the blood returned to the patient, needles must be carefully removed to allow hemostasis to occur. To prevent excess compression on the AVF, which could cause thrombosis, the needles should be removed one at a time utilizing the two-finger technique (Fig. 19.15). With every needle insertion, two punctures occur – one through the surface of the skin and the other through the blood vessel wall that are slightly staggered. Two fingers side by side are roughly 1 in. wide, which is the standard length of the dialysis needles; therefore, one finger would be placed on the skin puncture, and the next finger would be placed in the direction of the needle insertion and would cover the vessel puncture. This would allow for a solid clot to form within the vessel. Mechanical clamps, especially spring-loaded one, should be avoided due to the inability to control the amount of pressure on the AVF. It is also vital that patients learn to hold their own sites in order for them to know what to do should they have a spontaneous bleed away from the dialysis center. While much emphasis is placed on using monitoring devices, having patient care staff that can perform correct assessments and having an understanding of vessel physiology, the skill set to successfully cannulate, and knowledge of the dialysis machine and alarms are the most valuable asset a dialysis facility can possess. There needs to be an excellent cannulation training program, competency evaluation often, and good communication between the interdisciplinary team – these are the elements that are needed to make vascular access last as long as patients need them.

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Outpatient Surveillance at the Dialysis Center

20

Suhail Ahmad

Introduction

Vascular access is the most important component for hemodialysis (HD), without which, dialysis cannot be provided. Further, the quality of the vascular access determines the patient outcome in terms of morbidity and mortality. A poorly functioning access increases the risk of hospitalization and shortens the survival expectancy and is associated with increased cost; conversely a well-functioning access ensures good outcome and lowers the cost of care [1].

Unfortunately failure rates for both Arterio-venous fistula (AVF) and Arterio-venous graft (AVG) are high, often leading to adverse outcomes and increased financial burden. When AVF fails to function, the patient faces exposure to Central-venous catheter (CVC) with problems associated with this form of access. The lost AVF means the loss of a major vein as a future location of permanent access; these veins are precious as these are "lifeline" for the patient. Timely intervention to correct emerging problem may prevent the access failure. For timely intervention, however, recognition of developing problem is essential; that is only possible if the access is monitored regularly. Developing a monitoring and surveillance program that can diagnose a potential problem before the access fails is critically important and has been recommended by quality guidelines, such as KDOQI and Society for Vascular Surgery [2, 3]. Access failure can be divided into early or primary and late or secondary failures.

The Primary (Early) Failure Primary failure is defined as an AVF that is not usable up to 3 months post-surgery. This could be a result of poor initial surgical outcome or failure of the vein to arterialize enough to be used as an access, commonly referred as failure to mature. Proper assessment before and after surgery has been shown to reduce early failure rates. Both surgeon and nephrologist must be versed in proper evaluation techniques and interpretations of findings to increase the AVF use. Beathard et al. [4] reported early failures in 100 patients; Table 20.1 describes the causes of the failure [4]. Proper evaluation protocols using appropriate techniques must be adopted to ensure success:

A. *Pre-surgery evaluation*: Major evaluation points are discussed in Tables 20.2 and 20.3. Selection of artery that has good flow, is not the only source of blood to distal parts, and is free of significant disease must be determined before the surgery (Table 20.2). Similarly, the vein should be free of clots and stenosis and be of sufficient size (Table 20.3). A careful vascular mapping and physical examination usually ensure this.
B. *Post-surgery evaluation*:
   (a) Basic information: The nephrologist needs to know the date the access (particularly AVF) was created, exact anatomical location and names of the vessels used, direction of blood flow, and any significant pre-surgery or intra-surgery problems that were noted.

Table 20.1 Types of lesions identified causing early failure in 100 cases

Identified lesions	Number
Anastomosis stenosis, arterial (ASA)	38
Anastomosis stenosis, venous (ASV)	15
Stenosis, venous (SV)	20
Accessory tributary (AT)	12
Central venous stenosis (CVS)	9
Arterial stenosis (AS)	4
Diffuse small veins	3
AT with ASV	24
AT with SV	6
AT with ASV and SV	4
ASV with SV	6

From Ref. [4], with permission

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Table 20.2 Elements of preoperative assessment

History:
Gender, age, comorbid conditions, such as peripheral vascular disease
Diabetes mellitus, heart failure, infections, etc.
Past history such as failed access, PICCs, cardiovascular surgery
Defibrillators, pacemakers, injury, etc.
Examination:
Local area, cardiovascular, neuromuscular, etc.
Arterial: flow evaluation, pulse, Allen test, etc.
Venous: clots, stenosis, occlusion, tributaries, distensibility size evaluation
With and without tourniquet
Diagnostic tests:
Ultrasonic, Doppler examination:
Vein mapping, potential location of good fistula
Lumen diameter: minimum arterial lumen 1.5 or 2 mm
Minimum venous diameter 2–4 mm
Other tests:
Doppler transducer pressure, oximetry, digital pressure, changes in arterial wave form with fist clenching, flow estimation, etc.
Arteriography only if necessary, avoiding the use of contrast

Table 20.3 Predictors of successful AV access

Vein diameter (mm)	Blood flow (ml/min)	Success (%)
>4	>500	95
<4	<500	33
>4	<500	60
<4	>500	60

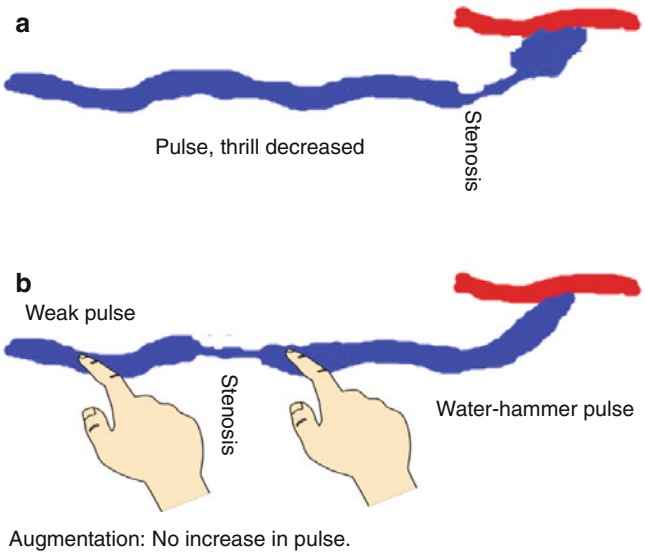

Fig. 20.1 (**a**) Showing Artery, anastomosis and body of the fistula. Juxta-anastomosis stenosis is a narrowing immediately after anastomosis. (**b**) Showing stenosis in the body of fistula

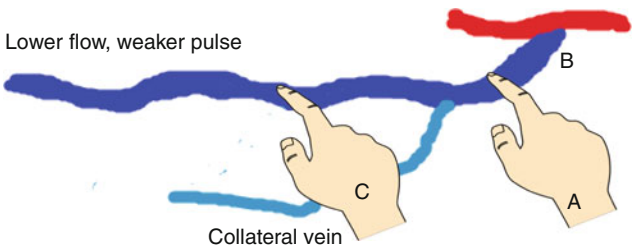

Fig. 20.2 Venous tributary draining blood away from the main fistula. Digital occlusion at point A, the thrill will disappear at point B. Pressure at point C, the thrill will appear at point B, suggesting Large flow in the collateral vein. Tying off collateral vein should Improve the fistula flow

(b) Inflow problems: The most common cause is juxta-anastomosis stenosis (Fig. 20.1a), although stenosis in the body of fistula can also be present (Fig. 20.1b). As discussed below in detail, a good examination including palpation, auscultation, and augmentation by digital occlusion helps in delineating these common problems. If an inflow problem is detected early, appropriate intervention can be taken, leading to a functional AVF.

(c) Outflow problems: Presence of a prominent tributary diverting blood from the main fistula will prevent maturation of the AVF. Figure 20.2 and the discussion below further describes the problem and technique to diagnose it.

The Secondary (Late) Failure Secondary failure is defined as failure of a permanent access after it has been successfully used for dialysis, according to some investigators, for six or more dialysis treatments. Secondary failure of access contributes to under-dialysis, increased morbidity, and even mortality. In addition, the cost of care is also quite high, estimated to be in billions of dollars annually. Diagnosing an access problem and taking corrective measures in a timely fashion appear to be effective in reducing the above problems. Routine monitoring and surveillance are necessary in order to predict impending failure so that problems can be corrected in a timely fashion in order to (a) prevent under-dialysis, (b) prevent other complications such as infection, and (c) preserve the access vein. Thus, the importance of monitoring and surveillance cannot be emphasized enough. In the United States, the Centers for Medicare and Medicaid Services (CMMS) mandates that all dialysis providers must have a well-defined protocol of successful surveillance and monitoring of access with "…strategies including device-based methods such as access flow measurements, direct or derived static venous pressure ratios, duplex ultrasound, etc." [5]. While both monitoring and surveillance have the same goal of evaluation of an access and detection of impending problem and are complimentary, monitoring usually refers to evaluation of vascular access by

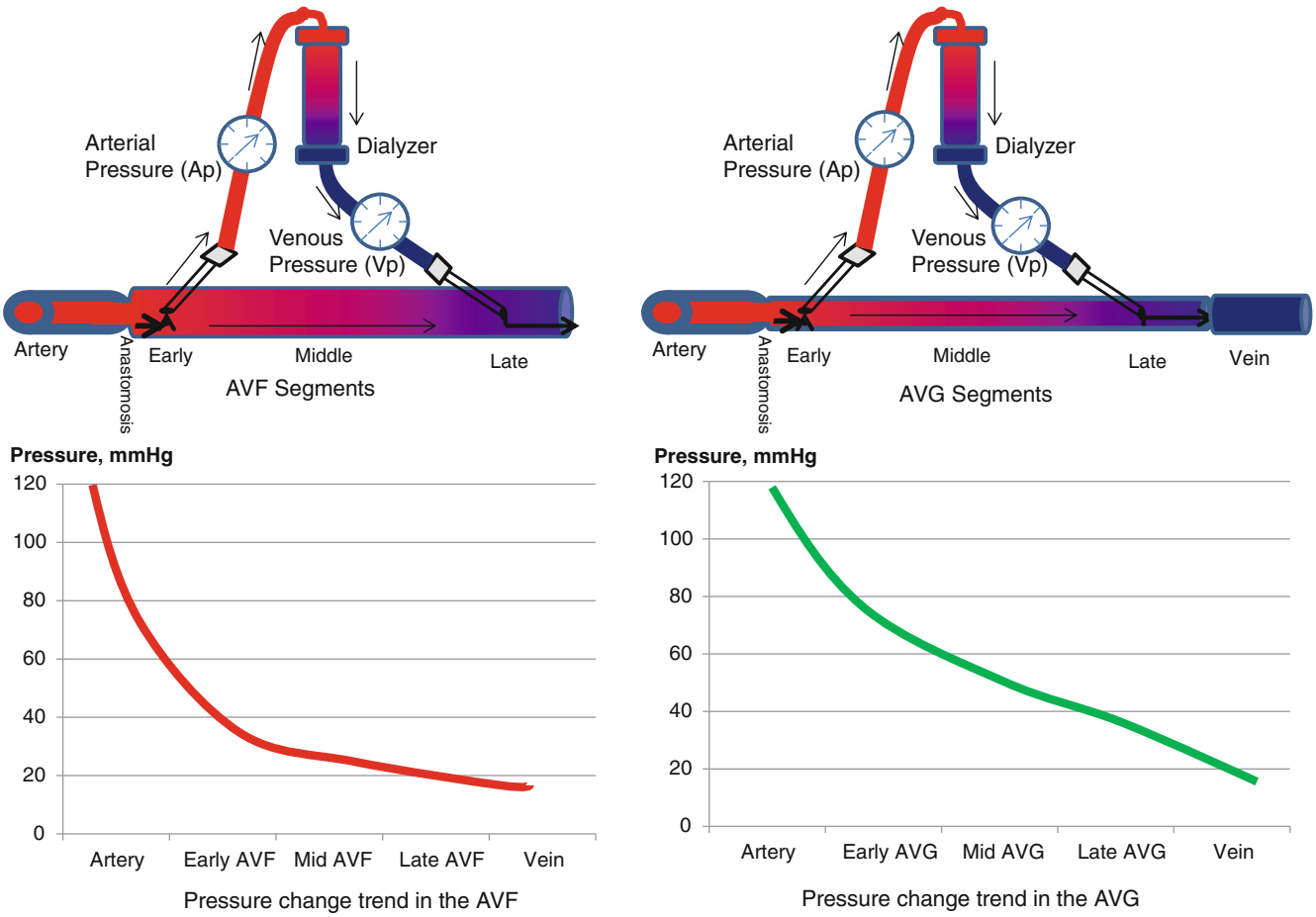

Fig. 20.3 AVF and AVG connected to dialysis machine (*top figures*). Pressure profile in AVF & AVG (*bottom figures*)

physical examination, and surveillance is an ongoing access assessment by special tests and diagnostic procedures.

The most common complications that threaten AVF and AVG are thrombosis and stenosis; one potentially can lead to the other. A stenosed access is likely to develop clots; however, it is unclear whether repeated clot formation is the major contributor to stenosis. Most of monitoring and surveillance is focused on the early detection of compromised blood flow caused by stenosis or thrombosis. The major part of discussion is thus focused on the problem of stenosis and thrombosis with brief discussion about other complications in the following sections.

Basic Physics of Vascular Access Basic understanding of blood flow and pressure dynamics in the permanent access is necessary for a physician to perform an appropriate examination, properly analyze the data, and establish the correct diagnosis. The flow and pressures are different in AVF from that encountered in AVG. Hemodialysis access is created by connecting a high-flow and high-pressure arterial conduit to a low-flow and low-pressure venous conduit either directly, the AVF, or through a tube of synthetic or biological material, the AVG. In an AVF, blood flows rapidly and under high pressure into the vein, pressure being very high adjacent to the anastomosis. Veins are capable of expanding, unlike grafts, and the dilatation leads to reduced resistance and the rapid dissipation of pressure further downstream (Fig. 20.3). However, the synthetic tube for AVG is not distensible, and resistance inside remains high, declining very slowly to the venous pressure at the venous anastomosis. AVG require higher blood flow rates, such as 1 L or so per minute, in order to remain patent. In contrast, AVF are functional even at lower blood flow rates of 500 ml/min or lower (even down to 200 ml/min). The connection of a high-pressure system to a low-pressure system causes turbulent flow and eddy currents, felt as a thrill and auscultated as bruit. In well-functioning access, the thrill/bruit is present through the entire AVF and AVG and felt both during systole and diastole. The location, intensity, and timing of the thrill and bruit are affected by the flow rates and development of stenosis and/or thrombosis, and this information is used in the diagnosis of any developing problems.

Monitoring of Vascular Access

Physical Examination A proper physical examination (PE) is an invaluable tool in discovering emerging problems in a timely fashion, thus preventing serious complications, potential loss, and poor outcomes. Though subjective in nature, with experience this can be performed quickly and accurately and is considered a critical part of patient care. Studies have shown that the sensitivity of a good PE in diagnosing AVF stenosis ranges from 70 to 100 % and specificity 68–93 % (Table 20.4). Unfortunately, experience has shown that majority of nephrologists (as many as over >80 %) miss abnormal physical findings, particularly in AVF. Like any PE, the three elements include inspection, palpation, and auscultation. Basic knowledge of blood flow dynamics as discussed above is helpful in understanding the steps of PE and evaluation of findings. Most of the discussion will focus on AVF, but similar principles apply for AVG. Elements of physical examination and findings are summarized in Table 20.5.

Inspection Quick examination of an access and surrounding areas will reveal many clues of underlying problems. Inspection of the body of access should look for signs of infection such as redness, pus, bleeding, dermatitis, or aneurysmal dilatation. As discussed below, observation of collapse of a dilated fistula upon raising the arm, the arm-raising test, is normally present, and a lack of collapse may suggest clotting or downstream stenosis.

(a) The arm, chest, neck, and face should be examined for presence of edema or dilated collateral veins, which may suggest downstream stenosis of a central vein, a larger vein draining the fistula, or in the AVF itself.
(b) Examination of the distal arm, particularly of the hands (for access that are located in upper and forearms), for presence or absence of skin changes, swelling, and abnormal coloration, is important to confirm good distal perfusion.

Palpation and Auscultation These are used to find new diagnostic findings as well as to confirm findings of inspection. Examples include palpation of a hard nodule, expression of pus from infected access, temperature of skin, palpation of pulses in the distal arm, and evaluation of edema.

Thrill, *Bruit*, *and Pulse*: Palpable buzz (thrill) and auscultated sound (bruit) are a result of turbulent blood flow with eddy currents through the vascular access and can be used to diagnose problems, its locations, and severity. Nature of the pulse at various sites is also very helpful in delineating problems with the access. In general terms, a thrill is more related to inflow of blood into the access than outflow, and pulse reflects the outflow of the blood. However with complete thrombosis or stenosis as blood flow stops, both thrill and pulse disappear. These examinations are performed both unaugmented, that is, without any digital pressures on the access, and augmented, after application of digital pressure on various sites of the access:

(a) *Thrill and bruit*: Good flow through the access is associated with strong thrill/bruit throughout the access and is present during both the systole and diastole.

Table 20.4 Accuracy of physical examination in detection of AVF stenosis in five prospective studies

Authors	Number	Location of lesion	Sensitivity	Specificity (%)
Asif et al. [8]	142	Inflow	85	71
		Outflow	92	86
Leon et al. [9]	45	Inflow	100	78
		Outflow	76	68
Campos et al. [10]	84	Overall	96	76
Tessitore et al. [11]	119	Inflow	70	76
		Outflow	75	93
Coentrao et al. [12]	177	Inflow	98	88
		Outflow	97	92

The diagnosis confirmed by angiography in four and by Duplex Doppler in one study (from Campos et al. [10])

Table 20.5 Diagnostic elements of the physical examination used in the assessment of autogenous arteriovenous fistula dysfunction

	Thrill	Pulse	Arm elevation test	Pulse augmentation test
Inflow stenosis	Weak, systolic	Weak	Excessive collapse	Weak
Outflow stenosis				
Body of fistula	Systolic	Strong	No partial vein collapse	n.a.
Cephalic arch stenosis	Systolic	Very strong	No partial vein collapse	n.a.
Central vein stenosis	Systolic or normal	Strong or normal	No or modest partial vein collapsea	n.a.
Coexisting inflow-outflow stenoses	Weak, systolic	Normal	No or modest partial vein collapse	Weak

n.a. not applicable
[a]Edema of the arm and shoulder; breast, supraclavicular, neck, and face swelling may be present as well in brachial-cephalic fistulae only

As blood flow decreases, either due to stenosis or thrombus, the thrill/bruit becomes weaker, and with further decreased flow (significant obstruction), the thrill/bruit is felt/heard only during systole, becoming weaker or disappearing as flow becomes even slower. Change in the nature of thrill/bruit will reflect flow into the fistula and will change with augmentation as discussed below.

(b) *Pulse*: Palpation of pulse on the access is commonly utilized. Palpation could be unaugmented or augmented:
   (i) Unaugmented: When blood flow is good, palpation should reveal strong pulse throughout the AVF. With obstruction, the pulse downstream of stenosis becomes weaker; however, upstream from obstruction, it becomes quite pronounced – often described as "the water-hammer pulse" (Figs. 20.1 and 20.4).
   (ii) Augmented: Without any obstruction (stenosis), digital pressure will increase the force of pulse upstream of pressure. The presence of significant stenosis will result in a weak pulse downstream from stenosis, and digital pressure may further weaken it. The pulse upstream from stenosis, however, will already be a strong water hammer in quality, and digital pressure will not further augment it (Figs. 20.1 and 20.4).

In summary, a thrill at anastomosis indicates blood flow into the AVF. A strong thrill indicates good flow, while a weak thrill is a sign of poor flow. A thrill that is present throughout the cardiac cycle indicates good flow and if felt only during systole indicates poor flow. Pulse indicates resistance to blood flow downstream from palpitation point, with soft indicating no stenosis and hyperpulsatile hard pulse indicating increased resistance such as presence of stenosis downstream from the point of palpation.

Thus, the combination of inspection, palpation, and auscultation yields invaluable information about the status of vascular access. Figures 20.1, 20.2, and 20.4 summarize common problems with access PE findings. With practice, the healthcare provider can develop these skills accomplishing the PE that does not take a long time. Table 20.4 summarizes common problems and elements of PE with findings [6].

Other Complications Hand ischemia (or of other distal parts) may develop after the creation of an access. Often preexisting arterial insufficiency causes this complication that may require urgent intervention. Excessive diversion of blood through the fistula may also contribute to hypoperfusion, and surgical reduction in access flow might help the situation (steal syndrome and venous hypertension, Fig. 20.5a, b). On physical examination, the affected parts may be cold, pale, or cyanotic. Pain or paresthesia may be present, and in severe cases, necrosis of the skin may develop. The development of weakness and pain immediately after surgery in the presence of good perfusion may suggest ischemic neuropathy and requires urgent fistula ligation.

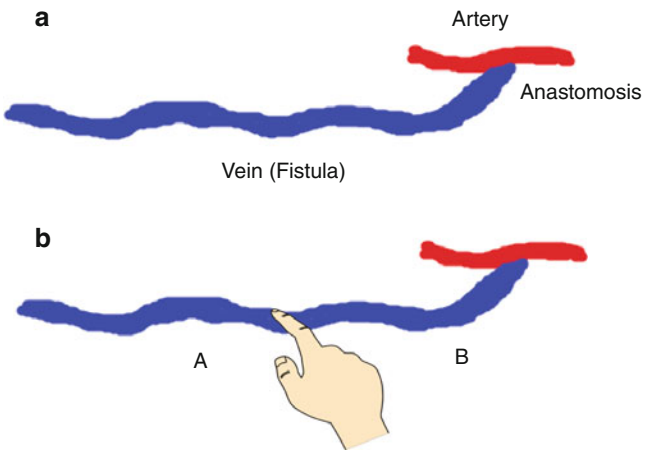

Fig. 20.4 (**a**) Showing un-augmented examination. Well developed AVF, strong thrill throughout systole & diastole Good strong pulse throughout the AVF. (**b**) Showing augmented examination. Thrill decreases throughout, pulse at point B increases (water-hammer), at point A decreases

Access Surveillance

The blood flow through an access is the most direct method to measure the quality of access; a change (reduction) in the flow rate may also predict presence of a problem (stenosis or thrombosis). As discussed above, AVF generally have lower flow rates of 500–800 ml/min and usually do not have problems with clotting even with blood flow as low as 200–300 ml/min. In contrast, AVG require higher flow rates of 1000–2000 ml/min to prevent clotting; once the flow drops to below 600 ml/min, the risk of thrombosis increases. KDOQI Guideline [2] recommends further diagnostic work if AVF flow rates drop below 400–500 ml/min and below 600 ml/min in AVG. This is particularly important if there is a downward trend in blood flow rates or a 25 % or more decrease in flow rates with or without other indirect measurements of access flow rates (see below).

Direct Methods to Measure Access Flow

(a) Dilution Methods: These methods are based on Fick's principle. During dialysis, saline is injected in the dialysis tubing, and either an ultrasound (US) or heat or light sensor is employed to measure the dilution of blood through

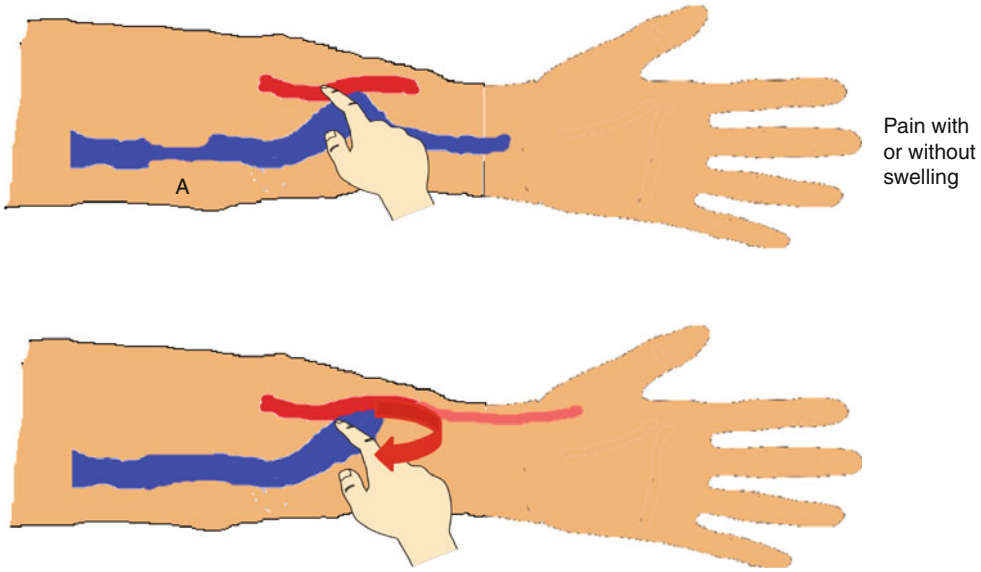

Fig. 20.5 (**a**) Venous hypertension: Increased pressure in the vein reduces the venous return from hand causing pain in thumb or entire hand. (Sometimes confused with 'steal syndrome' see below.) If it is caused by a stenosis (point A), dilating it would improve symptoms. If it is due to side-to-side anastomosis, fixing this may be required. (**b**) Steal Syndrome: Increased arterial flow into the vein reduces distal flow to hands causing symptoms. Pressure on anastomosis occluding venous flow improves symptoms. Surgically reducing fistula flow helps

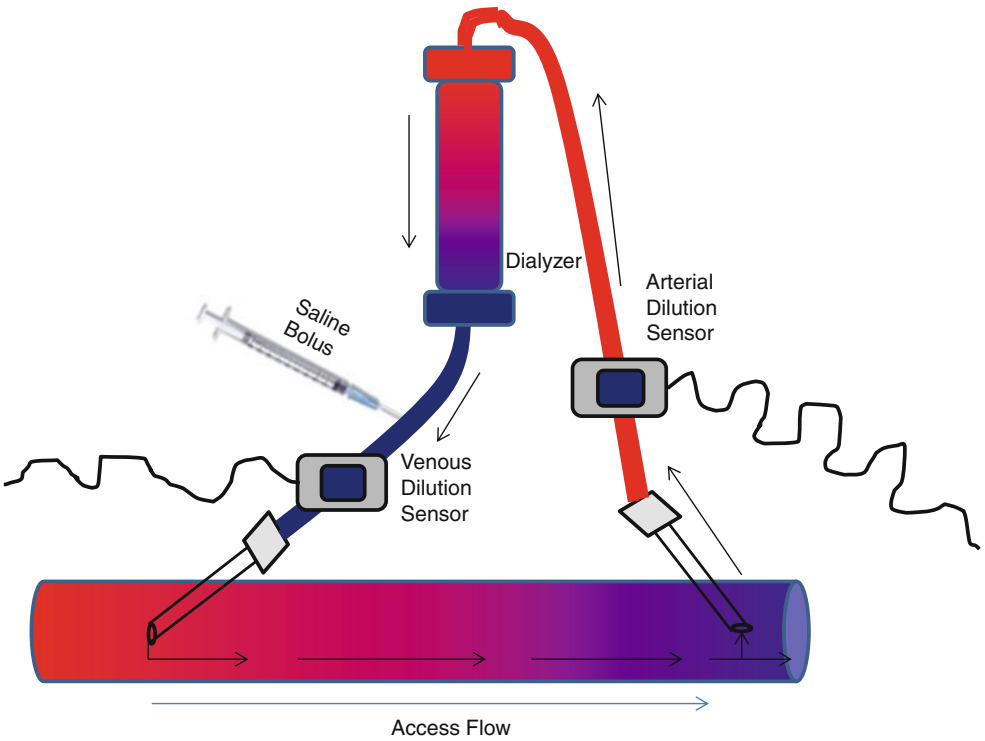

Fig. 20.6 Showing saline dilution method to measure recirculation and access flow. Note lines are switched, access flow is from left to right, venous needle is upstream and arterial needle downstream. Venous & arterial dilution sensors are clamped on the arterial & venous lines and connected to US

the dialysis lines, and the data are used to calculate access flow rates. The exact method involves switching of arterial and venous segments of lines so that the arterial line is downstream from the venous return line (Fig. 20.6), and, therefore, the dialyzed blood being returned into the access is picked up (recirculated) by the arterial line feeding the blood into the dialyzer. Flow dilution sensors are clamped on the arterial and venous segments, a saline bolus is injected into the venous line, and dilution sensor measures the amount of dilution. This diluted blood goes through the access, and a part of this diluted blood gets aspirated into the arterial segment by the blood pump. The

volume of dialyzed blood being returned to the dialysis system represents recirculation (*R*), and is caused by reversal of the lines. The dilution sensor in the arterial line measures the extent of dilution (*R*). Comparison of the two values (dilution in venous and arterial segments) gives the access flow rates by the following relationship:

Recirculation (*R*) α blood flow through dialysis machine (Qb)/access blood flow (Qa)

Values for *R* and Qb (controlled by the blood pump) are known; Qa can be calculated.

(b) Doppler Ultrasonography: Several ultrasonic Doppler machines are available and can be used for the detection of stenosis by velocity measurement; the access diameter is determined by the transducer, and Qa is calculated by the velocity and access diameter values. These methods have several limitations, since the accuracy of values depends on placement of transducer and its angles (operator-dependent factors); the confounding effect of turbulent flow on measurement and access diameter being variable at different levels are other factors that impair the reliability of these methods.

Indirect Methods to Monitor Access Flow

(a) Dialysis Line Pressure Methods: The pressure in the extracorporeal blood lines is dependent on intra-access pressures and resistance in the extracorporeal blood lines. The access pressure is dependent on mean arterial pressure and intra-access resistance to the blood flow. When the artery is connected to what will be the permanent access (vein for AVF and graft for AVG), the arterial pressure drops in the post-anastomosis segment. However, the pattern of this pressure decrease is different between AVF and AVG (Fig. 20.3); in the AVF, the arterial pressure markedly drops immediately after anastomosis, and further decline in pressure is very slow after that. In contrast in AVG, the decline in intra-access pressure is less marked in the early segment but continues its decline throughout the access. Thus a change in extracorporeal pressure profile is a more sensitive measure for AVG blood flow relative to the AVF flow.

(i) *Venous Pressure* (*Vp*): The post-dialyzer segment of dialysis tubing (Fig. 20.7), returns blood to the

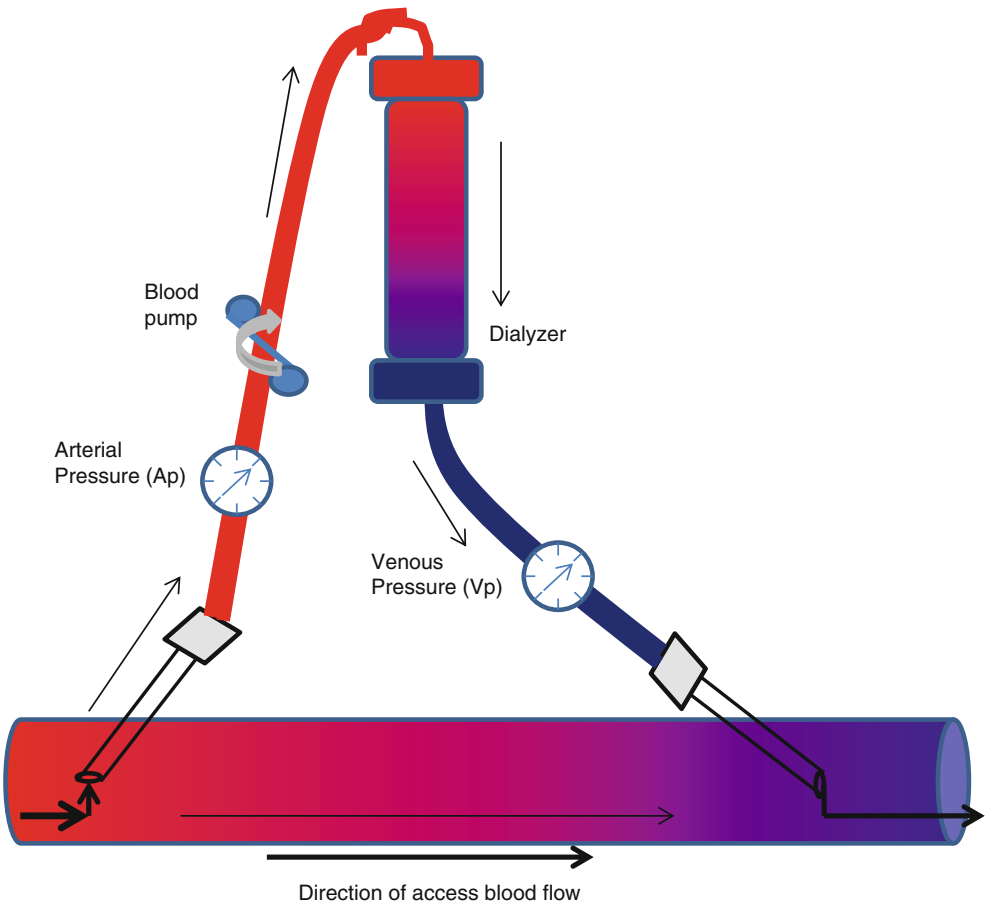

Fig. 20.7 Showing the arterial and venous tubings in relation to the dialyzer and access. The location of pressure sensors are also shown. Note the arterial sensor is pre-pump thus normally gives a negative pressure reading when pump is operating

access, and the pressure in this tube is positive, reflecting the resistance to blood being returned to the access. A trending increase in this pressure may suggest development of access stenosis (or thrombosis) downstream from the venous needle. In contrast, a significant decrease in this pressure may suggest stenosis upstream from the needle. During dialysis, the Vp can be measured with blood pump active (Dynamic Vp) or with blood pump stopped (Static Vp).

(a) *Dynamic Vp*: When the blood pump is active, the Vp depends on access flow (Qa, and systemic blood pressure); Qb (dialysis pump rate); resistance before the pressure sensor (with increase resistance, such as a clot or kink in line, the Vp will be lower); resistance downstream from sensor, primarily at the needle site (increase resistance, will increase Vp); diameter of needle; and viscosity of blood (hematocrit).

(b) *Static Vp*: When the blood pump is stopped (no flow through the extracorporeal circuit), the Vp depends on access pressure (flow and systemic pressure) and vertical height difference between pressure sensor and access. The Static Vp is not affected by many of the factors that influence dynamic pressure discussed above and is therefore more reliable and recommended by most of the guidelines as the preferred method of surveillance. The ratio between Static Vp and MAP gives important information regarding a possibility of obstruction in the access (stenosis or thrombus). The steps for measuring Static Vp and calculation of the ratio are discussed below with example.

Following the trend in Static Vp over time: For each dialysis treatment, the blood pump is stopped, and the blood line between dialyzer and venous drip chamber is clamped; Vp is recorded, for example, 70 mmHg. Increasing trend, over time, in the Vp may be indicative of developing stenosis.

Following the ratio between Vp and MAP: A more sensitive measure is the ratio between corrected Vp and MAP; steps are discussed below:

(a) Systemic BP is measured and recorded; from this, MAP is calculated. MAP = pulse pressure/3 + diastolic pressure. Example: BP 150/90, MAP = ((150–90)/3) + 90) = 110 mmHg.

(b) Vp = 50 mmHg.

(c) If Vp is measured at the level of the access (venous drip chamber is at the level of venous needle), the ratio can be directly calculated: Ratio = 50 (Vp)/110 (MAP) or 0.45, which is less than 0.5 and is acceptable.

(a) If the Vp is measured at a level higher than access (drip chamber is higher). The vertical height between center of venous drip chamber and vascular access is measured (dialysis units can fix this height difference, eliminating the need to measure it each dialysis). Let us assume it is 30 cm.

(b) Corrected Vp = Measured Vp + (height in cm * 0.76, converting to mm Hg) + 3.4.

For example, corrected Vp = 50 + (30 cm * 0.76) + 3.4 = 76.2 mmHg.

(c) Ratio between corrected Vp and MAP is calculated, 76.2 (corrected Vp)/110 (MAP) = 0.69.

A ratio >0.5 is indicative of presence of stenosis. In this example, the ratio of 0.69 is higher than 0.5, and stenosis should be ruled out. Similarly, a ratio between Static Ap (pre-pump) and MAP of >0.75 is suggestive of stenosis [2]. As seen in Figure 20.3, the pressure (ratio) drops immediately after the anastomosis in AVF, whereas this decline is gradual in AVG, and therefore the ratio is more useful in AVG than AVF.

(ii) *Arterial Pressure* (*Ap*): Pressure measured in the arterial segment before pump is a useful indicator of amount of suction generated at the arterial needle. Compared to Vp, the Ap has not been found to be as useful in predicting stenosis, often being ignored or not measured. With the use of very high-flow, high-efficiency dialysis, however, in this author's opinion, this is an important measure and should be included in monitoring and surveillance. A dynamic Ap which is more negative than −150 mmHg increases the risk of recirculation, under-dialysis, and hemolysis [6] and also suggests upstream stenosis. This pressure also may be useful in prediction AVF complications [7]. As discussed above, similar to Vp, KDOQI recommends the use of the ratio between Ap and MAP.

(iii) *Other Measures*: There are other indirect measures that may sometimes suggest a problem with vascular access.

- Recirculation: Access recirculation in which dialyzed venous blood gets recirculated to the arterial segment of dialysis apparatus may be indicative of access malfunction and can be used as an additional surveillance tool.
- Dose of dialysis: Access inefficiency may be one factor in the development of otherwise unexplained reduction in dialysis dose. The newer online urea monitoring devices that

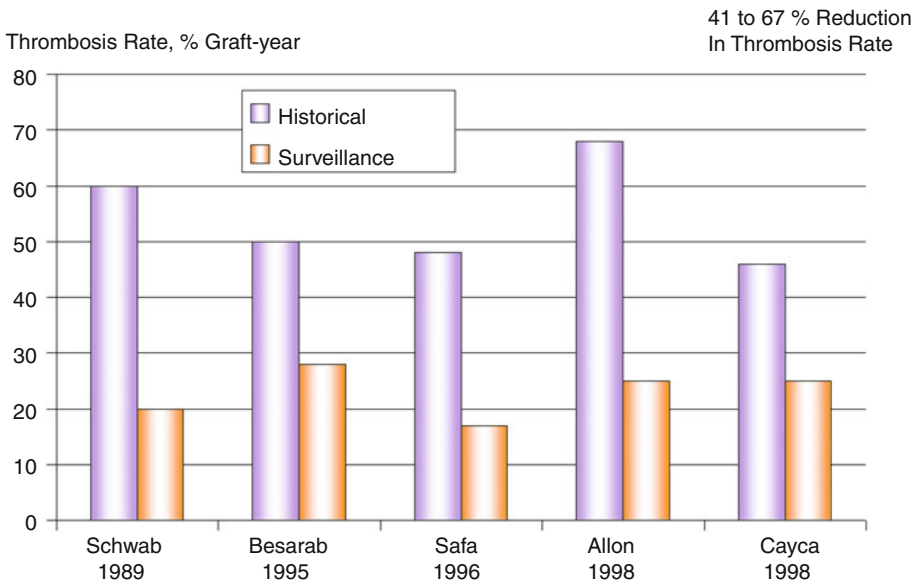

Fig. 20.8 Prospective surveillance & prompt rx of graft stenosis reduces thrombosis

Table 20.6 A suggested scheme to help in developing an outpatient program to monitor access

Procedures	Who is responsible	Frequency	Remark
Complete PE	Physicians	Monthly or when diagnosing a problem	Important and valuable
Inspection, thrill, and bruit	Dialysis staff	Each dialysis	Important and valuable
Static Vp and MAP ratio	Develop algorithm	Each dialysis	Important and helpful
Static Ap and MAP ratio	Develop algorithm	Each dialysis	Helful in AVF and to avoid problems
Recirculation, Kt/*V*, post-dialysis bleeding	Dialysis staff and physicians	When there is indication, discuss trend	Provides additional data
Blood flow studies	dedicated staff	Monthly, if tool available	Value has not been proven, limitations

measure rate of urea decline during dialysis and extrapolate the dose of dialysis from this information may also give useful information about access on an ongoing basis. For example, a significant change in the intradialytic urea decay curve, if mechanical problems are ruled out, may point to access problems or occurrence of recirculation.

- Post-dialysis bleeding after removal of needles: Dialysis access problems sometimes may lead to prolonged bleeding (in excess of 15–20 min) after the removal of needle after dialysis is completed.

The benefits of an elaborate surveillance programs have been questioned by some investigators. A review of literature shows a lack of well-designed prospective studies, analyzing the benefit or lack of benefit of access surveillance leading to questions raised about the value of these programs. On the other hand, majority of the published studies, however, have shown that PE has a specificity of 76–98 % and sensitivity of 71–93 % in detecting stenosis of fistula (Table 20.4). Several studies have also shown a reduction in thrombosis of access after the institution of surveillance program compared to historical data before the institution of such programs (Fig. 20.8). These studies have reported that surveillance and monitoring programs are associated with preservation of access and a reduction in access-related cost and hospitalizations [13, 14].

Properly performed PE is invaluable in detecting access problems, can be easily learned and quickly completed with minimal cost and without utilization of invasive or expensive tools, and has a very high rate of successful detection of problems (Table 20.4). Simple monitoring and surveillance program coupled with prompt intervention can prevent access thrombosis and increase life of the access. Some authors have questioned the value of surveillance program [15]. NKF-KDOQI recommends the use of monitoring and surveillance to reduce access failure rates [2]. NKF-DOQI Guideline 1 succinctly states, "…the basic skills have been largely abandoned in favor of technology and need to be taught to all individuals who perform hemodialysis procedures." Outpatient

assessment of dialysis access must be learned by each physician involved with dialysis patient care (nephrologists, surgeons, and interventionists). The basics must be taught to dialysis providers such as technicians and nurses. Simple surveillance programs can be easily developed and adopted by the dialysis facilities, and as guidelines suggest, these efforts will be successful in improving overall care of dialysis patients and reduce cost. One such program is suggested in Table 20.6.

Even after more than five decades of the use of dialysis, vascular access remains the Achilles heel of hemodialysis treatment, adversely affecting patient quality of life and outcome in terms of hospitalization, missed treatments, inadequate delivery of dialysis dose, clinical complications such as infection, and survival. The cost in the United States related to access is estimated to be about three billion dollars annually. Both early and late failures of access place significant burden on healthcare cost and patient outcomes. After the creation of access, one-third (in some instances much higher fractions) of access fail to function, causing delay in treatment or more often use of CVC for dialysis which in turn leads to increased cost and complications (cost of complications related to access through central venous catheter is about $90,000 per patient).

Close monitoring, evaluation, assessment, and timely intervention can reduce this high rate of primary failure. Patient should be seen by healthcare team once every 2 weeks or so after the surgery, both to assess the progress of maturation process and any complications caused by the creation of access such as tissue ischemia or venous hypertension. Lack of maturation process should direct the focus on determining the cause such as channeling of blood to accessory veins, the presence of stenotic area on the target vein, etc. Further diagnostic work such as sonography followed by appropriate intervention usually leads to success.

After access is used for dialysis, ongoing physical examination and surveillance reduces complications and hospitalization and increases the life of the access. A quick albeit careful examination usually discovers developing problem that can be corrected, preventing sudden failure with all of associated adverse consequences. Simple inspection, palpation, and auscultation looking for changes in character, duration, and intensity of thrill/bruit are often sufficient. If problems are suspected further examination with augmentation and location of changes in the bruit is helpful in identifying the problem. Surveillance is helpful, if conducted properly and focused on the trend of any change. Static Vp and Vp/MAP ratio as well as Ap/MAP ratio is recommended since this can be done every dialysis and does not require any special device. Serial blood flow directly or indirectly may be helpful but requires special device and staff training, and its value is controversial. Pre-pump Ap and Ap/MAP ratio appear to be more sensitive for AVF and Vp more sensitive for AVG problems. Good access monitoring and surveillance program at the dialysis units and by nephrologist are invaluable in maintaining well-functioning access.

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Detecting Pending Hemodialysis Access Failure: The Physical Exam

21

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Introduction

A proper physical examination is an invaluable tool in discovering emerging problems of a vascular access in a timely fashion, thus preventing serious complications, potential loss, and poor outcomes. Though subjective in nature, with experience this can be performed quickly and accurately and is considered a critical part of patient care. The 2006 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) and the 2008 Society for Vascular Surgery practice guidelines recommend that physical examination be performed on all mature arteriovenous fistulas (AVFs) on a weekly basis [1, 2].Studies have shown that the sensitivity of a good physical exam in diagnosing AVF stenosis ranges from 70 to 100 % and specificity 68–93 % (Table 21.1) [3–6]. Like any physical examination the three elements include inspection, palpation, and auscultation. Basic knowledge of blood flow dynamics as discussed in the previous chapter is helpful in understanding the steps of physical examination and evaluation of findings. This chapter focuses on the physical examination of the newly created and the mature arteriovenous fistulas (AVF) and grafts (AVG).

The Physical Examination

Inspection Quick examination of an access and surrounding areas will reveal many clues of underlying problems. The skin overlying the fistula should be without signs of infection, bleeding, dermatitis, or aneurysmal dilatation. The arm and hand should be without edema. The cannulation sites should be well healed with minimal to no scabbing. As discussed below, observation of collapse of a dilated fistula upon raising the arm, the Arm Raising Test, is normally present, and a lack of collapse may suggest outflow stenosis. The arm, chest, neck, and face should be examined for presence of edema or dilated collateral veins, which may suggest outflow stenosis in the cephalic arch or central veins. Examination of entire extremity including the hands should demonstrate absence of skin changes, swelling, and abnormal coloration.

Palpation and Auscultation These are used to find new diagnostic findings as well as to confirm findings of inspection. The fistula is expected to be soft, compressible, and generally distended somewhat when the patient's fistula arm is dependent position but should collapse if the arm is elevated to a level above that of the heart (Arm Raising Test). Examples of palpation include that palpation of a hard nodule, expression of pus from infected access, temperature of skin, palpation of pulses in the distal arm, and evaluation of edema.

Thrill, Bruit, and Pulse Palpable buzz (thrill) and the auscultated sound (bruit) are a result of turbulent blood flow with eddy currents through the vascular access and can be used to diagnose underlying access problems, locations, and severity. The thrill is best evaluated using the palm of the hand, rather than the fingers. The thrill should be palpable over the length of the fistula but most pronounced over the anastomosis. The nature of the pulse at various sites is also very helpful in delineating problems with the access. In general terms, a thrill is more related to inflow of blood into the access than outflow, while pulse reflects the outflow of the blood. The thrill and pulse disappear with complete thrombosis or stenosis. These examinations are performed both unaugmented, that is, without any digital pressures on the access, and with aug-

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Table 21.1 Accuracy of physical examination in detection of arteriovenous fistulae stenosis in four prospective studies compared to confirmatory tests

Authors (year)	Number of patients enrolled	Confirmatory test	Location of stenosis	Sensitivity (%)	Specificity (%)
Asif et al. [3] (2007)	142	Angiography	Inflow	85	71
			Outflow	92	86
Campos et al. [4] (2008)	84	Doppler ultrasound	Presence of stenosis	96	76
Tessitore et al. [13] (2011)	119	Angiography	Inflow	70	76
			Outflow	75	93
Coentrao et al. [6] (2012)	177	Angiography	Inflow	98	88
			Outflow	97	92

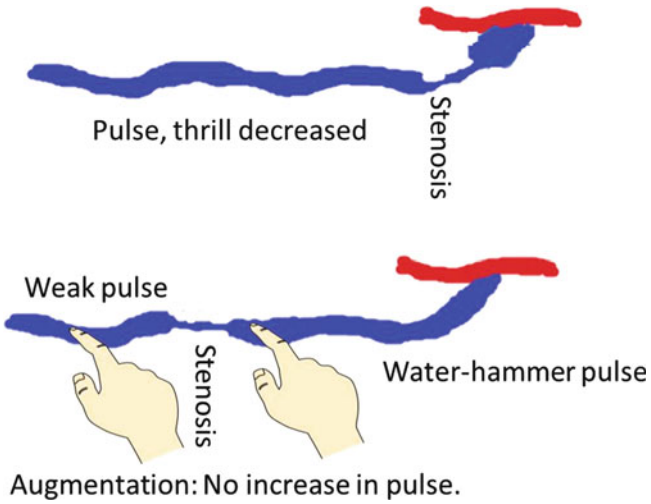

Fig. 21.1 An illustration of an arteriovenous fistula showing the artery, anastomosis, and body of the fistula. (**a**) An unaugmented palpation of an arteriovenous fistula with a juxta-anastomosis stenosis causing the pulse downstream of stenosis to become weaker, and the thrill is decreased while the upstream from obstruction the pulse is pronounced (water-hammer pulse). (**b**) Showing stenosis in the body of fistula. The pulse upstream from stenosis is strong (water hammer) in quality, and digital pressure (augmented palpation) will not increase the water-hammer pulse

mentation, after application of digital pressure on various sites of the access:

(a) *Thrill and bruit*: Good flow through the access is associated with strong thrill/bruit throughout the access and is present during the entire cardiac cycle (both the systole and diastole). As blood flow decreases, either due to stenosis or thrombus, the thrill/bruit becomes weaker. With further decreased flow due to significant obstruction, the thrill/bruit is felt/heard only during systole, becoming weaker or disappearing as flow becomes even slower. Change in the nature of thrill/bruit will reflect flow into the fistula and will change with augmentation as discussed below.

(b) *Pulse*: Palpation of pulse on the hemodialysis access is commonly utilized. Pulse indicates resistance to blood flow downstream from palpitation point. In a normal AVF, the pulse is generally soft and easily compressible. A hyperpulsatile hard pulse indicates increased resistance such as presence of stenosis downstream from the point of palpation. Palpation could be unaugmented or augmented.
- Unaugmented: When blood flow is satisfactory, palpation should reveal strong pulse throughout the AVF. With obstruction the pulse downstream of stenosis becomes weaker; however, upstream from obstruction becomes quite pronounced – often described as "the water-hammer pulse" (Fig. 21.1a).
- Augmented: Without any obstruction (stenosis), digital pressure will increase the force of pulse upstream of pressure. The presence of significant stenosis will result in a weak pulse downstream from stenosis, and digital pressure may further weaken it. The pulse upstream from stenosis, however, will already be strong (water hammer) in quality, and digital pressure will not further augment it (Fig. 21.1b).

Most AVGs are created in standard configuration; however, sometimes an element of creativity is needed in the creation or revision of some AVG. It is important to detect the flow direction in an AVG during the physical examination as the orientation of needles for hemodialysis must correspond to the direction of blood flow to avoid recirculation. This can be easily done by compressing the arteriovenous graft with the tip of the finger and palpating each side of the occlusion for a pulse. The side with the pulse is the arterial of the graft.

Hemodialysis Access Dysfunction Referrals

A detailed history is the first step in hemodialysis access dysfunction assessment. The next section is organized based on the common reasons; a patient with a hemodialysis access is referred to the internationalist for access assessment.

Table 21.2 Common history elements addressed when assessing a dialysis access

History assessment	Relevance
Frequent infiltration episodes in a newly established fistula	Failure to mature, access is too deep
Frequent infiltration episodes in a previously functioning fistula	Poor inflow – arterial or juxta-anastomosis stenosis Poor outflow – venous stenosis
Dialysis machine alarms (arterial alarm)	Poor inflow – arterial or juxta-anastomosis stenosis
Progressive arm swelling	Poor outflow – outflow or central venous stenosis
Dialysis machine alarms (venous alarm)	Poor outflow – outflow or central venous stenosis
Prolonged bleeding post dialysis	Poor outflow – outflow or central venous stenosis
Inadequate dialysis clearance	Hemodialysis access recirculation

Table 21.3 Common diagnostic elements in the physical examination used in assessing a dialysis access

	Exam finding	Relevance
Inflow problems	Weak or absent pulse distal to the AVF or AVG with hand pain	Steal syndrome
	Weak or absent pulse distal to the AVF or AVG with no hand pain, motor or sensory changes	Asymptomatic flow reversal
	Severe pain but normal pulse immediately after fistula or graft placement	Ischemic monomeric neuropathy
	Strong thrill for a short distance then thrill is absent	High-grade stenosis at the site of the strong thrill
	Good thrill that disappears after a short distance	Possibly collateral branches
Outflow problems	Arm edema	Indicates venous outflow problems in the outflow vein or central venous stenosis
	Collateral veins	Collateral veins are indicative of venous obstruction
	Pulsatile fistula	Indicates venous outflow problems in the outflow vein or central venous stenosis
	No thrill or bruit in the fistula	Thrombosed access
	Thinning of the skin, ulcerations of the AVF	Diffuse, progressive degeneration of the entire AVF

Table 21.2 summarizes the frequent complaints that accompany a dysfunctional access. Table 21.3 summarizes the diagnostic elements in the physical examination used in assessing a hemodialysis access.

Frequent Infiltration

Frequent infiltration is a common reason for referral after the creation of a new AVF but can also occur in a mature AVF. This usually presents as a hematoma that is localized or as in cases of posterior wall puncture where bleeding is not well controlled diffuse infiltration of tissue planes. Infiltration in a newly created an AVF that is too deep or due to poor maturation of the AVF. When an access is deep, the cannulation angle needed is a steep one, which significantly decreases the amount of the needle within the vessel. Any sudden movement by the patient can cause needle dislodgement and infiltration. Maturation of an AVF depends on two factors: adequate blood flow and adequate vein diameter. In ideal circumstances, inflow pressure is adequate to allow for fistula development even when upstream resistance is very low. Several factors can delay fistula maturation: low outflow resistance due to branches, low inflow pressure, high outflow resistance due to venous stenosis, or a combination of the above.

Ideally there would be one single cephalic vein extending from the wrist to the antecubital vein or shoulder. Unfortunately most of the time there are many accessory veins that divert flow from the main vein. Frequently the patient will present with repeated episodes of infiltration. At times, these veins can be identified on physical examination. However, deep branches may not be visible. Frequently the thrill will be present in the first few centimeters of the AVF, but then the thrill disappears or feels weak. One helpful maneuver to identify significant accessory veins is to occlude the arteriovenous fistula in the proximal arm/forearm. The thrill should disappear. If the thrill is still present, it would suggest the presence of significant accessory veins. Figure 21.2 illustrates the assessment for a venous tributary draining blood away from the main fistula. Ligation of these accessory veins would direct flow to the main channel and promote the development of a usable AVF [7].

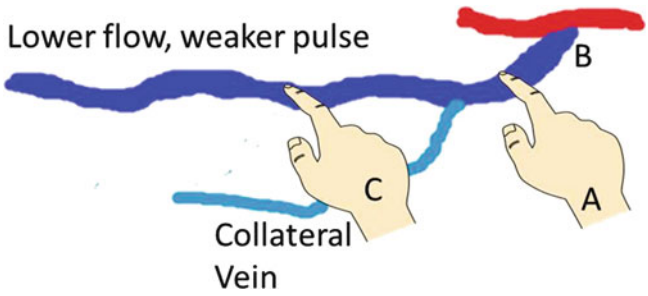

Fig. 21.2 The assessment for a venous tributary draining blood away from the main venous outflow of the fistula. Digital occlusion at point *A* leads to disappearance of the thrill in the body of the fistula and augments the pulse at point *B*. In the case of an accessory vein, pressure at point *C* will cause the thrill to disappear in the body of the fistula, but the thrill will continue at point *B* suggesting flow in the collateral vein

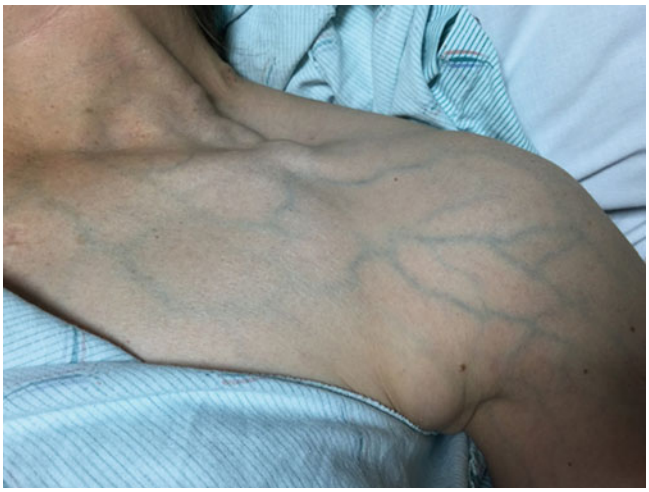

Fig. 21.3 Development of chest wall collaterals suggests clinically significant central venous stenosis

In terms of hemodynamics, low inflow pressure can arise from poor arterial inflow due to anastomosis stenosis or a stenosis in the arterial inflow. Early venous stenosis that impedes fistula maturation is usually located in the juxta-anastomotic area [8].

Low Inflow Pressures due to Fistula Stenosis or a Previously Functioning Fistula

The patient may present with frequent infiltration episodes or a compliance that the dialysis center is unable to sustain adequate blood flows for dialysis. Low inflow pressure can arise from poor arterial inflow due to anastomosis stenosis, stenosis in the juxta-anastomosis vein, or a stenosis in the arterial inflow. The thrill is frequently weak along the fistula or not palpable at all. The stenosis in the juxta-anastomosis vein can be diagnosed by palpation of the anastomosis and the distal vein. With stenosis, the caliber change in the vein is identified on palpation and appears as a fibrotic, indurated area, and a "water-hammer" pulse is felt at the anastomosis as opposed to the expected prominent thrill at the anastomosis [8].

Progressive Arm Edema

Progressive arm edema occurs in the setting of outflow venous stenosis, central venous stenosis, and less frequently due to lymphedema. The presentation of patients with central venous stenosis varies widely. It is often asymptomatic due to collateral formation prior to access placement. This, however, can be unmasked after placement of an AVF or AVG. Symptoms can range from mild to severe edema of the ipsilateral extremity. Persistent arm swelling is the hallmark of severe central venous stenosis. Marked ipsilateral face, neck, and breast edema may be apparent with multiple, dilated subcutaneous collateral veins over the chest wall or neck (Fig. 21.3). These findings if associated with a prior scar from a central venous catheter or pacemaker make the etiology obvious. Bilateral central vein stenosis or superior vena cava stenosis can produce a clinical picture of superior vena cava syndrome, associated with engorgement of the face and neck [9]. On exam, the AVF is firm and pulsatile with a typical water-hammer pulse. The AVF does not decompress with arm elevation.

Lymphedema due to hemodialysis access is rare, and minimal data are available about lymphatic complications of hemodialysis access. Lymphedema can occur as a result of disrupted small lymphatics during dissection to expose the arterial or venous structures or during tunneling through the subcutaneous tissue. In general, early lymphedema will resolve after a few days or weeks with elevation. Management of recalcitrant edema may require localized compression of the extremity with careful attention to the access site [10].

High Venous Pressures in an Arteriovenous Fistula or Graft

Venous pressure monitoring is based on the premise that resistance to flow in the AVF or AVG will increase proximal to a developing outflow stenosis. Similarly, significant venous stenosis will cause hemodynamic changes in the access that can be detected on physical examination. Unfortunately, it is not uncommon that a strong pulse or a strong thrill (both an indicator of venous stenosis) is often misinterpreted as a sign of "good access." The examiner should listen with the stethoscope over the

access paying attention to both pitch and duration of the bruit. As the degree of stenosis increases, the pitch of the bruit becomes more pronounced. To localize stenosis the head of the stethoscope can be removed, and the open end of the tubing can be used for auscultation. Listening continuously over the access, the stenosis is identified as a localized bruit or increase in the pitch of a bruit. In AVG, intragraft stenosis is more difficult to detect on a physical examination. A change in pulsation within the graft suggests an intragraft stenosis. Diffuse intragraft stenosis is also difficult to detect on physical examination.

Prolonged Bleeding After Needle Withdrawal

Prolonged bleeding after needle withdrawal frequently signifies outflow stenosis in the vein or central venous stenosis.

Localized Swelling of an Arteriovenous Fistula or a Graft

The presentation with localized swelling over an AVF or AVG could be due to a hematoma, seroma, aneurysm, or pseudoaneurysm. Differentiation between these conditions starts with a history.

Hematoma Hematoma usually arises from needle punctures during hemodialysis and are due to bleeding from needle puncture sites or prolonged after a dialysis session.

Seroma/Lymphocele Seromas are sterile fluid collections that can develop around AVG and almost never AVF. Lymphocele can occur as a result of disrupted small lymphatics during dissection to expose the arterial or venous structures or during tunneling through the subcutaneous tissue. These complications usually appear within the first month after access creation and are often close to the arterial anastomosis [10].

Aneurysms An aneurysm is a focal dilation of a vessel with true aneurysms involving all the layers of the vessel, while pseudoaneurysms represent a collection of blood and connective tissue outside the vessel wall, the result of a contained rupture. A normal AVF or AVG should be without aneurysms or pseudoaneurysms. When they do occur, they manifest as areas of bulging over the AVF or AVG and cannot be distinguished by physical examination alone. The skin should be examined for thinning, ulceration, or spontaneous bleeding (Fig. 21.4). Depigmentation and tightening of the overlying skin can also occur (Fig. 21.5). One should be able to pinch the skin over the fistula including an aneurysm between the examiner's index finger and thumb; the skin that is tissue-paper thin should prompt surgical evaluation. Ulceration or spontaneous bleeding of an aneurysm should be considered an indication for emergent surgical referral.

Pseudoaneurysms Pseudoaneurysms can develop in both AVF and AVG. With repetitive access of a single site, eventually a defect can form into the prosthetic graft. This can be sometimes detected by palpation of the graft where the defect can be easily felt. With time many of these defects will dilate to form a pseudoaneurysm. Color Doppler ultrasound can differentiate between aneurysms and pseoduaneurysms.

Erythema Over an Arteriovenous Fistula or a Graft

Infection accounts for 20 % of all AVF complications and is ten times lower than the rate of infection of AVGs [11]. Obvious physical findings of infection include erythema, swelling, tenderness, fluctuance, and pain. In some cases infection is not obvious, and signs are subtle as most AVF infections involve perivascular cellulitis manifesting as localized erythema and edema. Superficial infections appear as small, pustular lesions with minimal or no inflammation, swelling, or pain. Deep infections manifest with erythema, swelling, tenderness, and purulence. The AVF is frequently tender to touch, although pain is variable.

Erythema associated with new graft placement can be confusing as edema, erythema, and pain at the site of the newly tunneled AVG are not unusual. In this case, erythema is usually localized over the tunnel and within 1 cm from the tunnel. The experienced examiner should be able to distinguish the above pattern from infection (Fig. 21.6).

Poor Recirculation

The most common cause of recirculation is the presence of high-grade venous stenosis leading to backflow into the arterial needle. Simply occlude the graft between the access needles and observe the arterial and venous pressures on the hemodialysis machine. With a normal arteriovenous graft little change should be seen. If recirculation is due to venous outflow obstruction, the pressure will rise in the venous return because the lower-resistance, recirculation route is occluded. If recirculation is due to poor inflow (arterial stenosis or insufficiency), the main pressure will drop as the recirculation route is cut off.

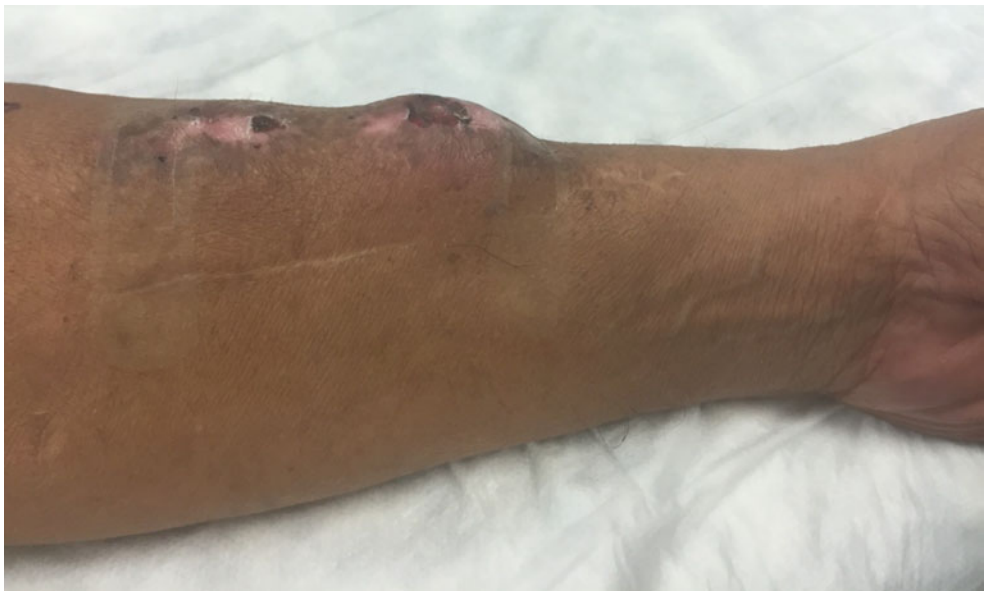

Fig. 21.4 Left forearm radiocephalic arteriovenous fistula with bilobed aneurysmal degeneration presenting with skin thinning and ulceration

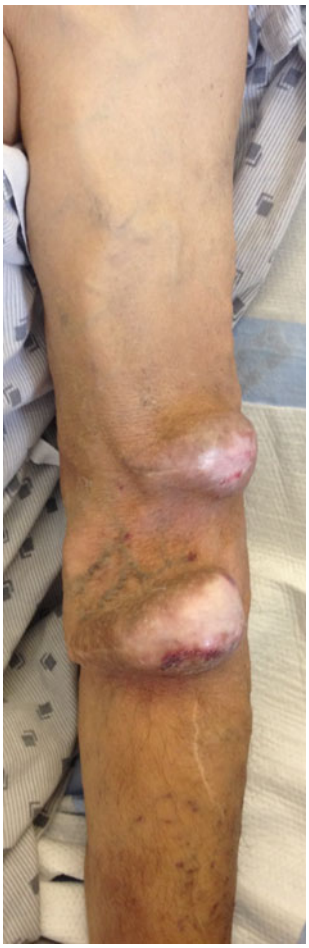

Fig. 21.5 Left brachiocephalic arteriovenous fistula with large aneurysmal degeneration. Note the depigmentation and tightening of the skin overlying the aneurysms

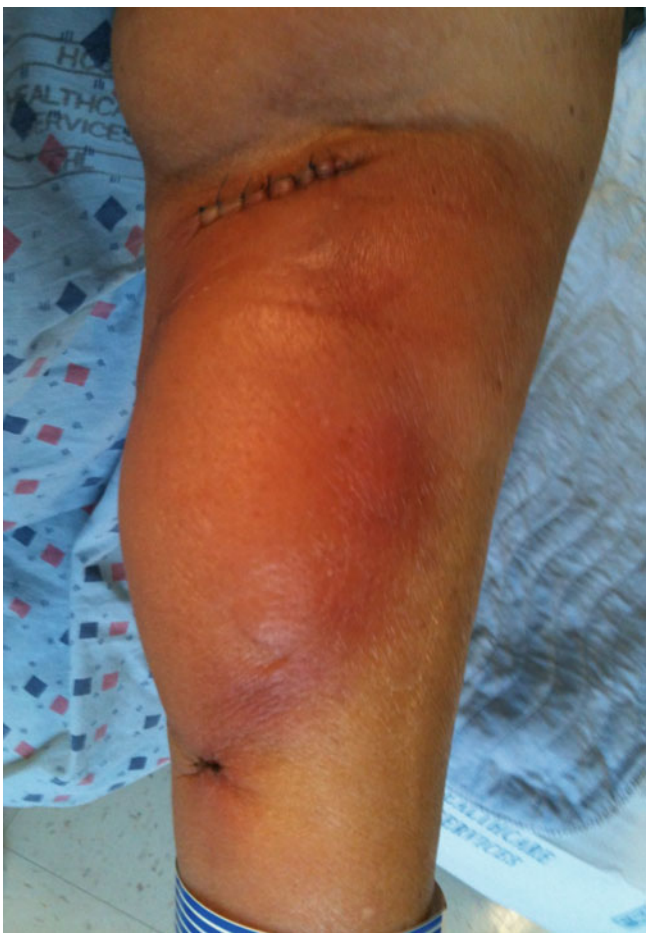

Fig. 21.6 Erythema and edema associated with new graft placement. Note that this is localized over the tunnel site only

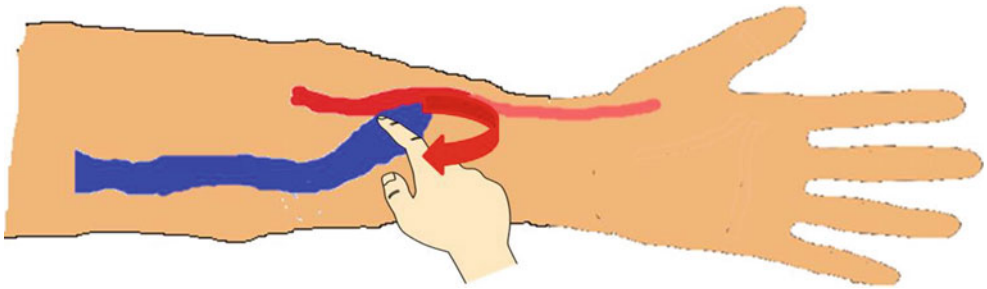

Fig. 21.7 Steal syndrome: Increased arterial flow into the vein reduces distal flow to the hands causing symptoms. Pressure on anastomosis occluding venous flow improves symptoms

Hand Pain

While hand pain is not usually associated with a failing hemodialysis access, it is not uncommon to be referred to patients who have a functioning hemodialysis access and hand pain. Thus it is important to understand the etiology and associated physical exam findings of a patient who has an AVF or AVG and who is also presenting with hand pain.

Hand pain can occur due to ischemia, neuropathy, or both. Hand ischemia may develop after the creation of an access. Often preexisting arterial insufficiency causes this complication that may require urgent intervention. Excessive diversion of blood through the fistula may also contribute to hypoperfusion (Fig. 21.7). On physical examination, the hand may be cold, pale, or cyanotic. Pain or paresthesia may be present, and in severe cases necrosis of skin may develop.

Peripheral neuropathy occurs in up to 70% of patients with ESRD [12]. This could be multifactorial, and it is imperative that the astute clinician be familiar with the types of peripheral neuropathies seen in this patient population.

Ischemic Monomelic Neuropathy Classically presents immediately after creation of the hemodialysis access in the presence of good perfusion and affects all three forearm nerve trunks with pain, paresthesias, numbness out of proportion to physical findings, as well as weakness and paralysis in the radial, ulnar, and median nerve distribution. This is most likely to improve when corrected immediately.

Entrapment Neuropathy Involves a unilateral involvement of nerve entrapment: this focal mononeuropathy may be amenable to focal surgical intervention via nerve decompression such as carpal tunnel release of the median nerve or cubital tunnel release and ulnar canal release of the ulnar nerve.

Uremic Polyneuropathy Classically presents as bilateral symmetrical distal sensory neuropathies and worsen with the duration of the disease. The typical clinical findings usually begin in the lower extremity but eventually may involve all four extremities. Symptoms initially manifest as a burning pain in the sole of the foot with sensations of numbness or tingling; this is followed by loss of peripheral reflexes and vibration sense. Symptomatic uremic polyneuropathy develops gradually in most individuals; however, occasionally it will develop in an acute form. Autonomic nerve fibers are involved but usually produce minimal symptoms [10].

Diabetic Neuropathy The most prevalent manifestation is a distal, symmetrical, and sensory neuropathy, often described as having a stocking or glove distribution; the more debilitating form consists of burning or lancinating pain. It usually develops insidiously, continues to progress, and rarely improves. Sensory and autonomic findings are more prominent than motor impairment. 200 diabetic autonomic neuropathies are manifested as gastroparesis, impotence, nocturnal diarrhea, loss of sphincter control, or postural hypotension.

Conclusion

The combination of inspection, palpation, and auscultation yields invaluable information about the status of vascular access. With practice healthcare provider can develop these skills accomplishing the physical exam as second nature when caring for patients with hemodialysis access.

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Point-of-Care Ultrasound for Creation and Maintenance of Hemodialysis Access

22

Gale L. Tang

Introduction

Ultrasound is a valuable tool for assessing patients at all phases of dialysis access creation and maintenance. This chapter specifically covers point-of-care (POC) applications and focuses on clinician-performed ultrasound examinations for the purpose of guiding decision-making and interventions. As such, POC examinations are not intended to replace formal studies done in the vascular laboratory that follow more detailed protocols. Rather, these brief and focused examinations serve to supplement the information gained from formal studies as well as to allow the practitioner to perform image-guided therapy. Acquiring the skills needed for POC ultrasound is extremely helpful for anyone involved in dialysis access creation and maintenance.

The advent of relatively inexpensive portable ultrasound machines allows clinicians to use ultrasound as an extension of the routine physical exam in multiple practice settings such as the clinic or office, the preoperative holding area, the operating room, the interventional suite, and the emergency room. This is particularly important in the United States where the prevalence of obesity remains high at 34.9 % of US adults older than 20 years of age as this can directly impact the evaluation of hemodialysis access [1]. Examination of theoretically "superficial" venous structures can be challenging in the upper arm in normal individuals and nearly impossible in obese patients.

Formal studies obtained in the vascular lab, which is often not colocated with the clinic, may not answer critical questions. From a patient standpoint, having to visit and then potentially revisit multiple sites is inconvenient and may lead to decreased patient satisfaction and compliance—an important metric that is being increasingly used as a quality measure and may eventually affect reimbursement. Furthermore, confirmation of anatomy prior to interventions can direct therapy and increase efficiency of intervention. Unfortunately, POC ultrasound is generally not reimbursable when used as an adjunct to a formal study. Clinician time is also a limiting factor. However, if adequate images and a description of the use of ultrasound guidance are documented in the patient's medical record, the CPT code 76937 can be used to bill for ultrasound-guided vein access.

Equipment

Major advances in portable ultrasound machines have been made over the last 10 years in terms of image quality, image acquisition speed, specialized features, durability, portability, and affordability [2]. In addition to being significantly less costly than full-sized units, the newer laptop-sized portable units facilitate point-of-care usage, while sacrificing very little in terms of image quality and special features such as color flow and Doppler modes. Several of the currently available machines are shown in Fig. 22.1.

For virtually all dialysis access POC applications, a linear 10-5 transducer is adequate. Occasionally a higher frequency probe may be useful to give additional detail for more superficial structures in the forearm. Rarely a lower frequency probe may be necessary for morbidly obese patients, especially if the femoral vein is being used as a conduit. Ergonomics, such as raising the patient to a convenient height and positioning the ultrasound machine so that the controls are reachable and the screen is easily visible, for the point-of-care sonographer are important to improve the speed and accuracy of the exam. Likewise the patient should be positioned comfortably with the upper extremity supported in order to facilitate stable images in both transverse (short axis) and longitudinal (long axis) views.

A basic understanding of ultrasound "knobology" is helpful to optimize imaging. The practitioner should at the very least know how to adjust image depth, focus (if available), and time-gain

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Fig. 22.1 Laptop-sized portable ultrasound units with high-quality imaging facilitate point-of-care applications. Clockwise from *top left*: Terason uSmart 3300, Siemens Acuson X300, Sonosite S Nerve and M-Turbo, Mindray HUC5-3D, and Chison Q5

compensation in B-mode. Many of the newer machines have "auto-gain" and "optimal time-gain compensation" features to help quickly optimize the image. Being able to obtain Doppler spectra and measure peak systolic velocity (PSV) and end-diastolic velocity (EDV) as well as add color flow are helpful adjuncts to assess for stenosis. The practitioner should know how to use the measurement calipers to measure length. Furthermore, knowing how to measure volume flow in the mid-brachial artery as well as within the fistula (discussed later in this chapter) is extremely helpful when assessing fistula maturation, as well as troubleshooting fistulas with marginal maturation, failing access, and for evaluation of patients with steal syndrome [3]. Lastly, for documentation and billing purposes, the ability to print pictures and/or interface with the electronic medical record is useful.

Preoperative Assessment

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines recommend vein mapping prior to access creation secondary to available evidence showing that preoperative vein mapping increases the rate of arteriovenous fistula creation [4, 5]. The American Institute of Ultrasound in Medicine (AIUM) in conjunction with the American College of Radiology (ACR) and Society of Radiologists in Ultrasound (SRU) recently published practice guidelines for the performance of preoperative vein mapping [6]. This formal exam is generally performed within the vascular laboratory and consists of an arterial exam documenting arterial size, aberrant arterial anatomy, calcification, and waveforms throughout the upper extremity and including a modified duplex Allen's test for assessment of the palmar arch. A venous exam is also performed documenting the depth and diameters of the superficial veins (cephalic and basilic), any stenosis, as well as the phasicity and patency of the more central veins. If no suitable superficial vein is noted, then the diameter of the brachial vein and axillary vein should be documented to determine whether the patient is a candidate for arteriovenous graft (AVG) placement.

Point-of-care ultrasound examinations for preoperative assessment are less detailed and more focused. Localization

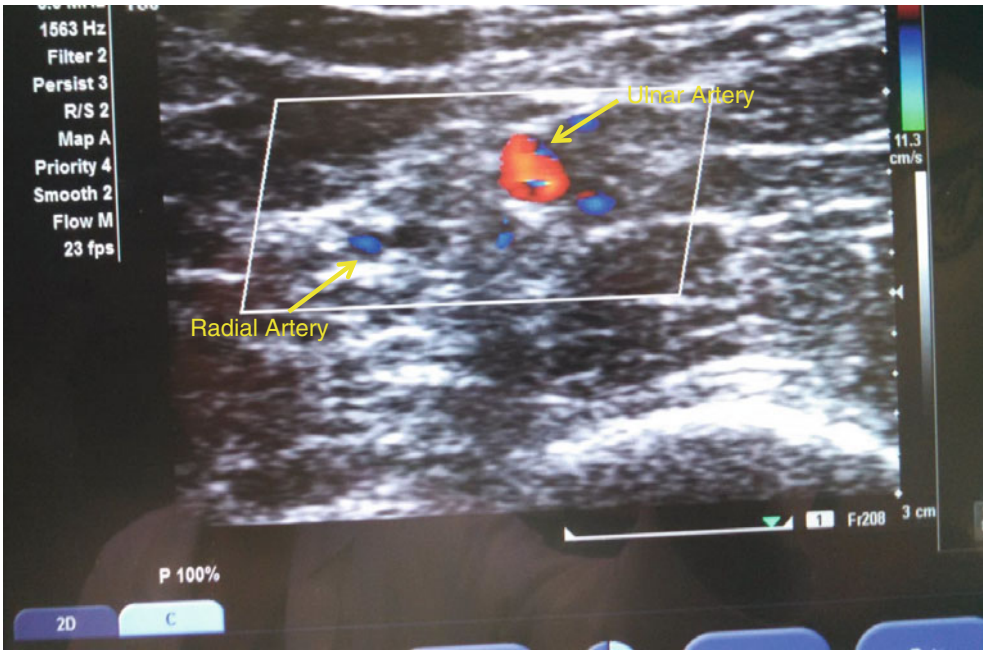

Fig. 22.2 Transverse view of the antecubital fossa of a patient with an aberrant high takeoff of the left radial artery. The relatively long course and small caliber of the aberrant radial artery make it less suitable for use as an inflow source for dialysis access creation even when the patient has a normal radial pulse

of aberrant arterial anatomy can be used in both preoperative planning as well as in counseling the patient as to the risk of non-maturation or steal (Fig. 22.2). Similarly, depth assessment may lead to discussion with the patient about the potential need for a secondary procedure such as superficialization. Occasionally, the vascular lab exam is not as complete as suggested by the AIUM. In this case, point-of-care ultrasound can be used to answer focused questions to avoid sending the patient for a second trip to the vascular laboratory. For instance, the forearm basilic vein or the diameter of the brachial vein may not have been examined but may be suitable for arteriovenous fistula creation or graft placement. A patient may have an adequate forearm cephalic vein, but an inadequate upper-arm cephalic vein documented on the formal vein mapping. Point-of-care ultrasound can determine if the patient has a large communicating branch to the basilic vein or to the deep system, which will allow for radiocephalic fistula maturation in this situation or if radiocephalic fistula should not be attempted due to inadequate outflow. The clinic-based point-of-care exam is not intended to replace, but rather complement and supplement the information provided by the formal vein mapping.

Perioperative Assessment

Temperature, emotional state, and hydration status may affect measured vein diameter, a critical predictor for fistula maturation [5, 7]. It is also well recognized that regional and general anesthesia increase superficial venous diameter [8, 9]. Preoperative POC ultrasound may lead to an alteration in the operative plan. A POC exam may identify a vein of adequate size not seen or thought to be too small on preoperative vein mapping that can then be used for fistula creation as opposed to placing an arteriovenous graft. The vein diameter and compressibility should be checked throughout the length of the vein in this instance to confirm that the vein is adequate throughout its course into the deep system. The POC exam may also identify a suitable median antecubital branch communicating with either the upper-arm cephalic or the basilic vein. Preoperative identification of this may alter the medial or lateral extent of the antecubital incision necessary for upper-arm fistula creation. Large branch veins close to the arteriovenous anastomosis may also be identified and preemptively ligated to improve fistula maturation.

Occasionally, intraoperative POC ultrasound assessment can be helpful to identify technical problems with a newly created arteriovenous or graft anastomosis or an injury to the arterial system proximal or distal to the site of the newly placed access. For instance, loss of the radial pulse even with compression of the newly created access should prompt an intraoperative duplex exam or other evaluation such as angiography. Similarly, if the patient is noted to have symptoms of hand ischemia immediately postoperatively, especially after arteriovenous graft placement, a high-flow volume (>1400 ml/min) measured within the graft may prompt immediate banding or other revision as opposed to ligation of the access [10].

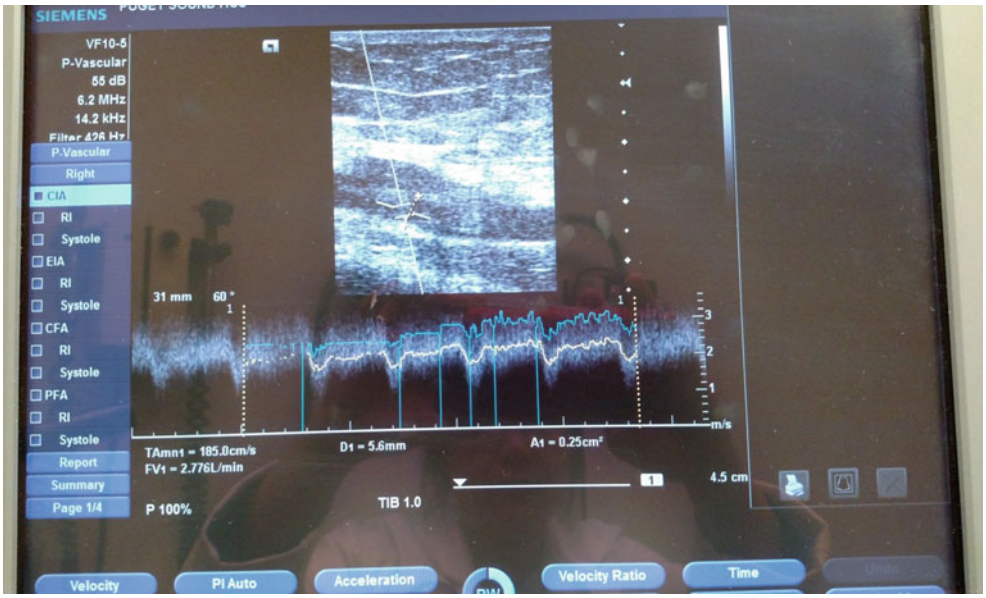

Fig. 22.3 Measurement of mid-brachial arterial flow volume using point-of-care exam

Marginal Maturation

The Society for Vascular Surgery (SVS) published practice guidelines for hemodialysis access creation and maintenance in 2008 [11]. These guidelines correspond with the NKF KDOQI guidelines for adequate fistula maturation [4]. A mature fistula should have adequate length (ideally > 6 cm) and diameter for cannulation (ideally > 6 mm), a flow rate > 500 ml/min, and be superficial enough to be cannulated with the standard 12 mm long dialysis access needle (generally no deeper than 6 mm below the skin) [4, 11]. Primary failure rates for arteriovenous fistulas, as defined as inability to use the created access successfully for hemodialysis by 3 months after creation, have been reported to be as high as 30–70 % [12]. A recent meta-analysis reported a pooled estimate for primary failure to be 23 %, with increased rates in more recent publication dates [13]. Arteriovenous fistulas have higher patency rates than arteriovenous grafts only when primary failure rates are excluded [14]. Therefore, minimizing primary failure rates by aggressive reintervention in fistulas with marginal maturation is worthwhile [15–19].

POC ultrasound is helpful to assess fistulas with marginal maturation on clinical exam. Fistulas with a minimum diameter of 4 mm and flow rate >500 ml/min by 2 months postoperatively can be expected to have a 95 % chance of being usable for hemodialysis, whereas fistulas with a vein diameter below 4 mm and flow rate <500 ml/min only have a 33 % chance of becoming usable for hemodialysis [11, 20]. Mid-brachial artery flow volume can be used as a surrogate for fistula flow volume, with a brachial artery flow volume > 800 ml/min being associated with 98 % freedom from revision and 600–800 ml/min being associated with 90 % freedom from revision in a recent study. As the brachial artery is easily identifiable, has relatively constant diameter, and can be studied with a more appropriate Doppler angle then the more superficial fistula, a brachial artery flow volume can be performed within 5 min, making it ideal for POC study (Fig. 22.3) [3]. If the POC machine being used does not have the capability to measure flow volumes, a brachial artery diameter ≥ 4.5 mm, PSV > 150 cm/s, and EDV/PSV ratio > 0.4 are associated with a volume flow > 800 ml/min [3]. Figure 22.3 shows the brachial artery volume flow measurement in a young patient with a high-flow fistula.

Flow rates through the fistula increase within 2 weeks of access creation [21], with the increase in vein diameter stabilizing after 2 months [20]. Therefore, it is reasonable to assess fistulas at 4–6 weeks after the creation to determine whether a correctable problem exists that will improve the maturation rate [16]. POC ultrasound is well suited for this purpose, as the common correctable problems are easily identified with ultrasound. Special attention should be paid to the anastomosis and juxta-anastomotic vein as a frequent location of intimal hyperplasia/stenosis. The remainder of the venous outflow should be assessed for size; if it is diffusely small, then balloon-assisted maturation can be considered [22]. Focal stenoses can be treated either with endovascular or surgical angioplasty. Large accessory veins near the arteriovenous anastomosis should also be identified for possible ligation (Fig. 22.4). The depth of the fistula should be assessed to determine if superficialization is necessary. Inadequate arterial inflow is rarely the cause of failure of maturation, especially if the patient had adequate preoperative vein mapping, but should be checked as it may be correctable.

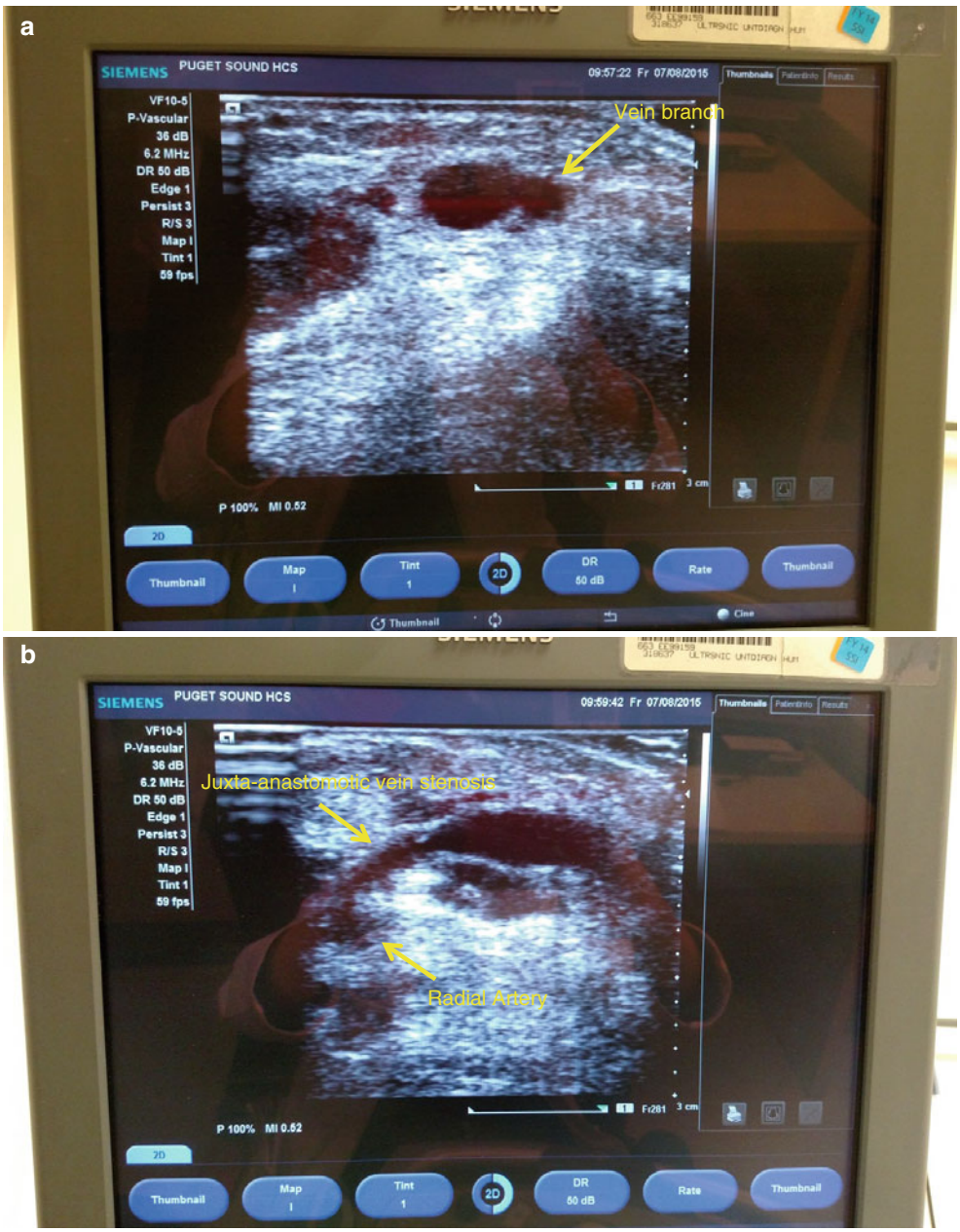

Fig. 22.4 (**a**) Large vein branch (*arrow*) preventing ideal fistula maturation in a forearm radiocephalic fistula. (**b**) Juxta-anastomotic vein stenosis in the same fistula also preventing maturation

Individually, these problems may be identifiable with clinical exam alone; however, ultrasound is useful to evaluate the entire circuit; this is important as the prevalence of multiple lesions leading to failure of maturation has been reported to be between 34 and 71 % [17, 18]. All problems should be identified prior to revision to avoid failure of revision to lead to a functioning access. For instance, ligation of a large accessory branch will not assist with maturation if a venous outflow stenosis is also present. Clinical judgment is needed to determine whether a point-of-care examination is sufficient or if more formal evaluation of the access is needed via either the vascular lab or angiography. Correction of access-related problems can lead to a significantly higher rate of access maturation [15–19].

POC ultrasound can also be useful for assessment of AVGs postoperatively. Identification of a focal fluid collection should lead to a delay prior to cannulation to decrease the risk of infection of a postoperative hematoma or seroma. A low flow volume (<600 ml/min) within a recently placed arteriovenous graft is concerning for early graft failure and should prompt further evaluation and possible reintervention [23, 24].

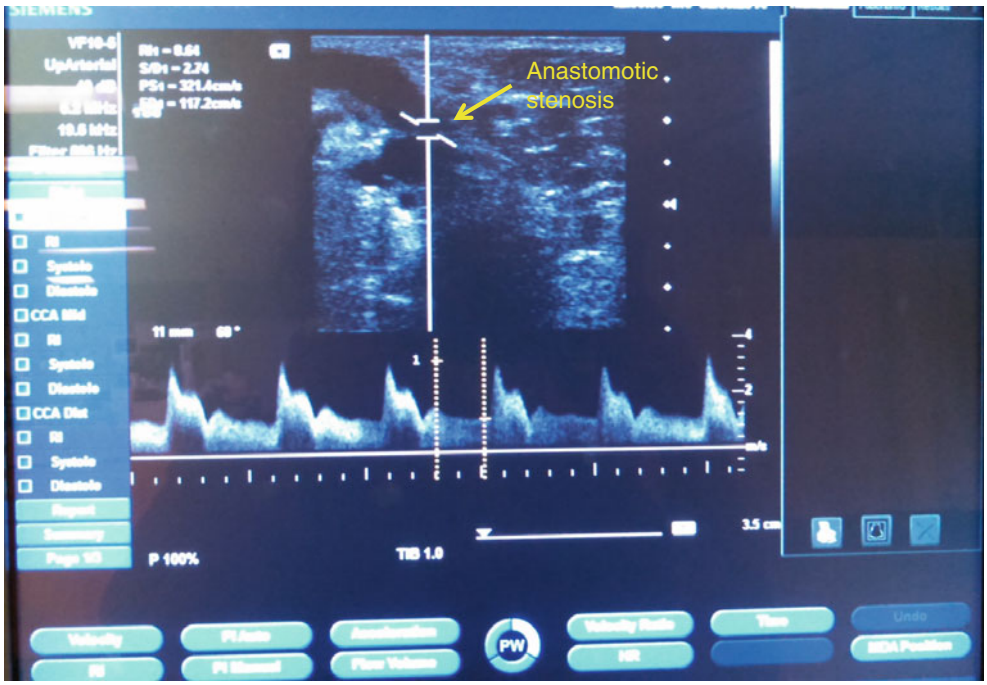

Fig. 22.5 Point-of-care exam showing anastomotic stenosis with PSV 321 cm/s and velocity ratio of 3.9

Assessment of Failing Access

Salvage of failing access leads to higher patency rates than salvage of thrombosed access [11]. The use of ultrasound for dialysis access surveillance is controversial, as prophylactic angioplasty has not been definitively shown to extend clinical patency [11]. In any event, it is uncommon for patients to be referred for evaluation by an interventionalist in the absence of some clinical sign of impending access failure, unless a defined monitoring or surveillance program is in place. Signs predictive of impending access failure include difficulty in cannulation or thrombus aspiration, elevated venous pressure (>200 mmHg), access recirculation of ≥12 %, a palpable water-hammer effect, shunt collapse, or perigraft fluid/mass. As 80 % of the lesions leading to access failure are occlusive in nature, POC ultrasound can be helpful to the access interventionalist to assist in pre-intervention planning [11].

Similar to the non-maturing access, venous stenosis is a common cause of access failure. In AVGs, the most likely location is at the venous anastomosis, followed by the venous outflow tract, and more rarely the draining central veins. Autogenous fistulas may have stenosis anywhere along the length of the native vein [11].

A 50 % stenosis is considered indicative of a hemodynamically significant stenosis within the access. Duplex criteria for 50 % stenosis include a focal velocity increase with a velocity ratio pre to within the stenosis of >2.0. A PSV of >300–400 cm/s, EDV > 240 cm/s, or a visualized segment with <2 mm residual lumen is also suggestive of a significant stenosis. Because of significant turbulence in the anastomosis, a hemodynamically significant stenosis at the anastomosis is defined as a focal velocity increase with a velocity ratio > 3.0 or PSV >400 cm/s (Fig. 22.5) [6]. Given that POC exams may not result in ideal Doppler angles to measure PSV or EDV accurately, focusing on color bruits indicating turbulence and velocity ratios may be of more use to the POC sonographer. Similarly, assessment of the central veins is difficult with ultrasound, so this should be deferred to angiography.

In contrast to the non-maturing access, arterial inflow problems are more common among failing access, especially as renal disease and diabetes accelerate atherosclerosis although venous stenosis is still the most common reason for failure [25]. Therefore examination of the axillary, brachial, or radial artery waveforms may be informative, especially in patients with steal symptoms. Heavy calcification, small arterial diameter, and focal velocity elevation are suggestive of arterial inflow problems, whereas loss of end-diastolic flow in the inflow artery suggests access thrombosis or high-grade stenosis.

POC ultrasound can also be used to differentiate between fistula aneurysms and pseudoaneurysms, as well as determine the distance to the skin, as fistula erosions warrant urgent intervention (Fig. 22.6). Mobile thrombus seen within an aneurysmal inflow artery is worrisome for distal embolization; this is easily apparent during live duplex imaging and less apparent with other imaging modalities.

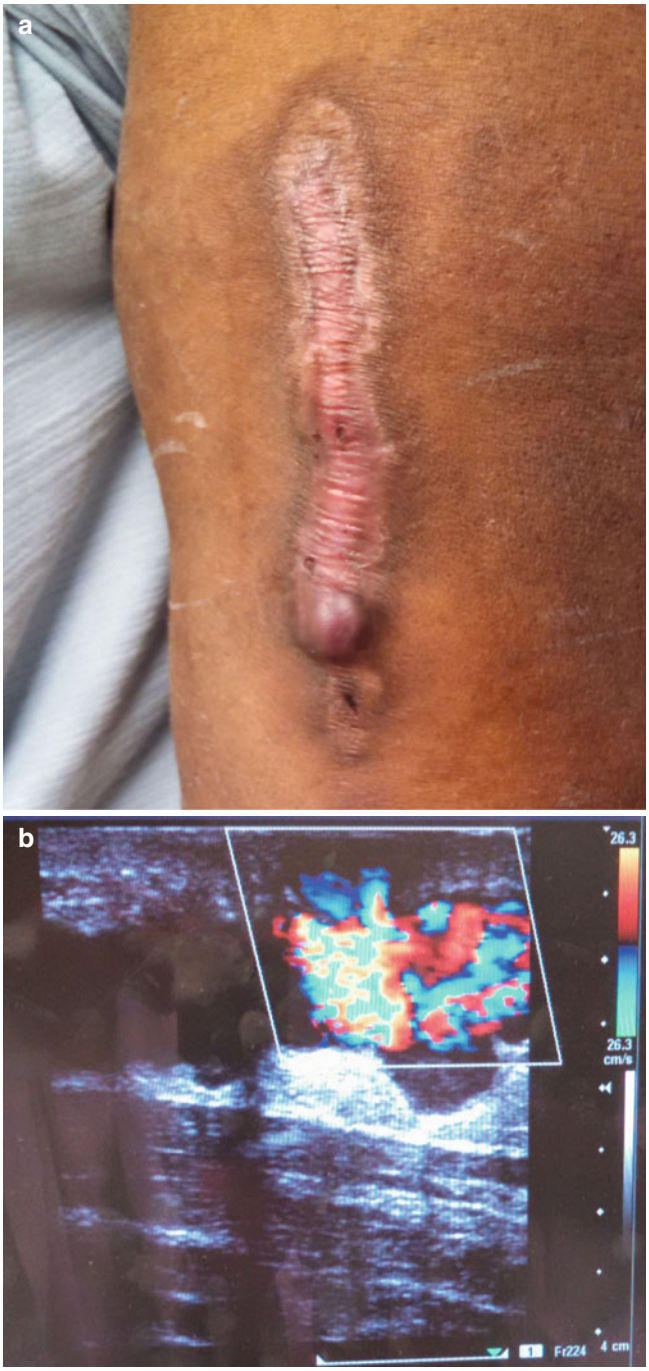

Fig. 22.6 (**a**) Superficialized brachiocephalic fistula with thinned skin. (**b**) Pseudoaneurysm of cephalic vein underlying thinned skin

Guiding Intervention

Several groups have published on the safety and effectiveness of duplex ultrasound to guide endovascular access interventions in an office-based setting [26–28]. Avoidance of iodinated contrast and ionizing radiation, as well as the ability to assess physiologic flow rates, and directly visualizing puncture sites, vessel size, results of intervention, and complications are the major advantages of duplex ultrasound [27]. In addition, tumescent anesthesia may be injected under ultrasound guidance to minimize the need for sedation [28]. The avoidance of contrast is especially important in patients with chronic kidney disease who have not yet initiated dialysis or for patients with a documented contrast allergy. Office-based procedures are also less costly and more cost effective than hospital-based procedures [26]. A vascular technologist performed the duplex ultrasound in the published reports. However, POC ultrasound could be used for this purpose assuming adequate skill in performing ultrasound by the interventionalist.

Retrograde vs antegrade access and the actual site of access should be guided by ultrasound. As the wire is easily visible, ultrasound can be used to confirm crossing of stenoses, as well as to guide balloon sizing. Volume flow measurement and post-dilation vessel diameter can be obtained to assess the success of the intervention. Complications such as rupture, access thrombosis, and vessel spasm can also be directly visualized.

Surgical interventions can likewise be guided by POC ultrasound. Pre-incision localization of branches to be ligated or vein stenoses with ultrasound facilitates small incisions. This is especially important to allow the fistula to be used immediately after revision so as to avoid tunneled line placement while the revision site heals. Furthermore, with the assistance of ultrasound localization, branch ligation can be easily performed in an office-based setting, avoiding the OR.

Conclusions

POC ultrasound is a critical tool for both surgeons and interventionalists involved in creation, maintenance, and salvage of hemodialysis access. It is useful in all phases of management. The small investment in time to become facile in the duplex applications necessary for access assessment is amply repaid by improvement in patient outcomes.

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Duplex Examination of the Hemodialysis Access

23

R. Eugene Zierler

Introduction

According to the National Kidney foundation (NKF)-Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines, the detection of hemodialysis access dysfunction involves monitoring, surveillance, and diagnostic testing [1]. The term *monitoring* refers to evaluation of the access site by physical examination to identify signs that suggest dysfunction, while *surveillance* is the periodic evaluation of the access site using tests that require special instrumentation for evidence of dysfunction that may not be apparent on physical examination alone. *Diagnostic testing* is prompted by a specific abnormality or medical indication and typically involves specialized tests that are intended to diagnose the cause of access dysfunction. Techniques used for surveillance include direct measurements of access site flow rates and pressures during dialysis to detect abnormal trends over time. Diagnostic testing typically involves direct imaging with catheter angiography and may be combined with an intervention. Duplex ultrasound scanning can be used for both surveillance and diagnostic testing of hemodialysis access sites.

Failure to maintain satisfactory hemodialysis access site function and patency is common, with loss of primary patency in up to 40 % of cases at 1 year for both autogenous vein fistulas and prosthetic grafts [2–4]. The causes of access site dysfunction include failure of autogenous vein maturation, access site thrombosis, pseudoaneurysms, venous hypertension producing limb swelling, and arterial steal resulting in hand ischemia (Table 23.1). Inadequate arterial inflow and impaired venous outflow can also threaten access site function, and high-output cardiac failure is a rare but serious complication. The rationale for surveillance of hemodialysis access sites is that the various problems leading to access dysfunction develop over variable time periods and can be detected at an early stage when surgical or endovascular interventions are likely to be most effective in restoring normal function. Whether a routine surveillance program actually prolongs overall access site, survival remains controversial, although it appears to reduce the risk of access thrombosis in selected cases, and it may decrease access-related costs and hospitalizations [1, 5–7].

Duplex Ultrasound Scanning

Instrumentation

A standard duplex ultrasound system is required for examination of hemodialysis access sites with high-resolution B-mode imaging, color-flow Doppler, and spectral waveform analysis. A selection of transducers with a choice of operating frequencies and "footprints" is necessary for scanning of the inflow arteries, the superficial venous or prosthetic conduit (segment to be cannulated for dialysis), and the outflow veins. These include a midrange-frequency linear array transducer (e.g., L7-4) for general applications and a high-frequency transducer (e.g., L12-5, L10-5 intraoperative, L15-7 intraoperative) for assessing superficial vessels. A small curved array transducer (e.g., C8-5) is excellent when scanning around the clavicle.

Examination Protocol

Prior to scanning, the autogenous vein or prosthetic graft should be palpated to detect the presence or absence of a "thrill"—the normal vibration felt over an access site produced by high-velocity fistula flow. The presence of a

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strong pulse without a thrill suggests a venous outflow obstruction. Using the thrill as a guide, the course of the vein or graft can be traced on the skin to help direct the duplex examination. Alternatively, a stethoscope can be used to detect a bruit over the course of the vein or graft. An operative report or diagram of the access site is also helpful in planning the access site evaluation. A dialysis access duplex examination is best performed on a non-dialysis day to avoid reduction in blood pressure as a potential source of error.

The duplex examination of a dialysis access site can be divided into three main parts: (1) arterial inflow, (2) conduit, and (3) central venous outflow (Table 23.2). Examination of the conduit is different for autogenous vein fistulas and prosthetic grafts. In an autogenous fistula, the conduit is the superficial vein to which the inflow artery is connected by a single anastomosis; however, with prosthetic grafts, the conduit is the graft itself, and there are two anastomoses to evaluate.

Table 23.1 Causes of hemodialysis access site dysfunction

Failure of autogenous vein maturation
Thrombosis
Inadequate arterial inflow
Impaired venous outflow
Infection
Hematoma, seroma, lymphocele
Pseudoaneurysms
Arterial steal (hand ischemia)
Venous hypertension (limb swelling)
High-output cardiac failure

Arterial Inflow

Arterial inflow may be inadequate due to atherosclerotic occlusive disease, dissection, or other arterial conditions that narrow the upper extremity arteries. Doppler spectral waveforms from the inflow artery to a widely patent autogenous fistula or prosthetic graft are characterized by increased peak systolic velocity (PSV) with low pulsatility (high diastolic flow)—features typical of a "low-resistance" flow pattern (Fig. 23.1a). However, with a poorly functioning or occluded access site, the inflow arteries will display a typical "high-resistance" multiphase flow pattern similar to that of a normal peripheral artery (Fig. 23.1b). Significant arterial stenosis at any level in the vasculature supplying the access site may reduce the pulsatility and PSV within the autogenous fistula or prosthetic graft and lead to access failure.

The subclavian, axillary, brachial, radial, or ulnar arteries proximal to the access site should be evaluated for stenosis. Flow patterns in the native arteries distal or peripheral to the anastomosis should also be recorded to document distal perfusion to the hand. Distal to the arterial anastomosis, the flow waveform may return to a high-resistance pattern or it may show alternating or retrograde flow direction suggestive of an arterial steal, as discussed later in this chapter. Spectral waveforms for all PSV measurements should be obtained using a Doppler angle of 60° between the ultrasound beam and the vessel wall. If a 60° angle is not possible, a smaller angle is acceptable; however, larger angles approaching 90° should be avoided.

Table 23.2 Protocol for duplex examination of dialysis access sites

1. Arterial inflow
Scan the subclavian and axillary arteries, documenting the presence of atherosclerosis or other abnormalities
Scan the brachial, radial, and ulnar inflow arteries, documenting the peak systolic velocity prior to the anastomosis Record the velocity in the artery peripheral to the anastomosis to evaluate for steal
2. Conduit
A. Autogenous vein fistula
Document the location of the fistula anastomosis and identify the involved artery and vein
Measure the diameter of the anastomosis
Record peak systolic velocity at the anastomosis
Evaluate the forearm and/or upper arm outflow vein throughout its course for evidence of venous stenosis, thrombosis, or other abnormalities
B. Prosthetic graft
Identify the arterial anastomosis; record peak systolic velocity at the anastomosis
Scan the proximal, mid, and distal segments of the graft, evaluating for patency and stenosis with spectral waveform analysis. Use B-mode and color-flow Doppler imaging to look for pseudoaneurysms and other anatomic defects
Identify the venous anastomosis; record peak systolic velocity at the anastomosis. Evaluate for venous stenosis at and immediately distal to the anastomosis
3. Central venous outflow
Scan the innominate, subclavian (supra- and infraclavicular), and axillary veins, evaluating for central venous outflow obstruction (thrombosis or stenosis)

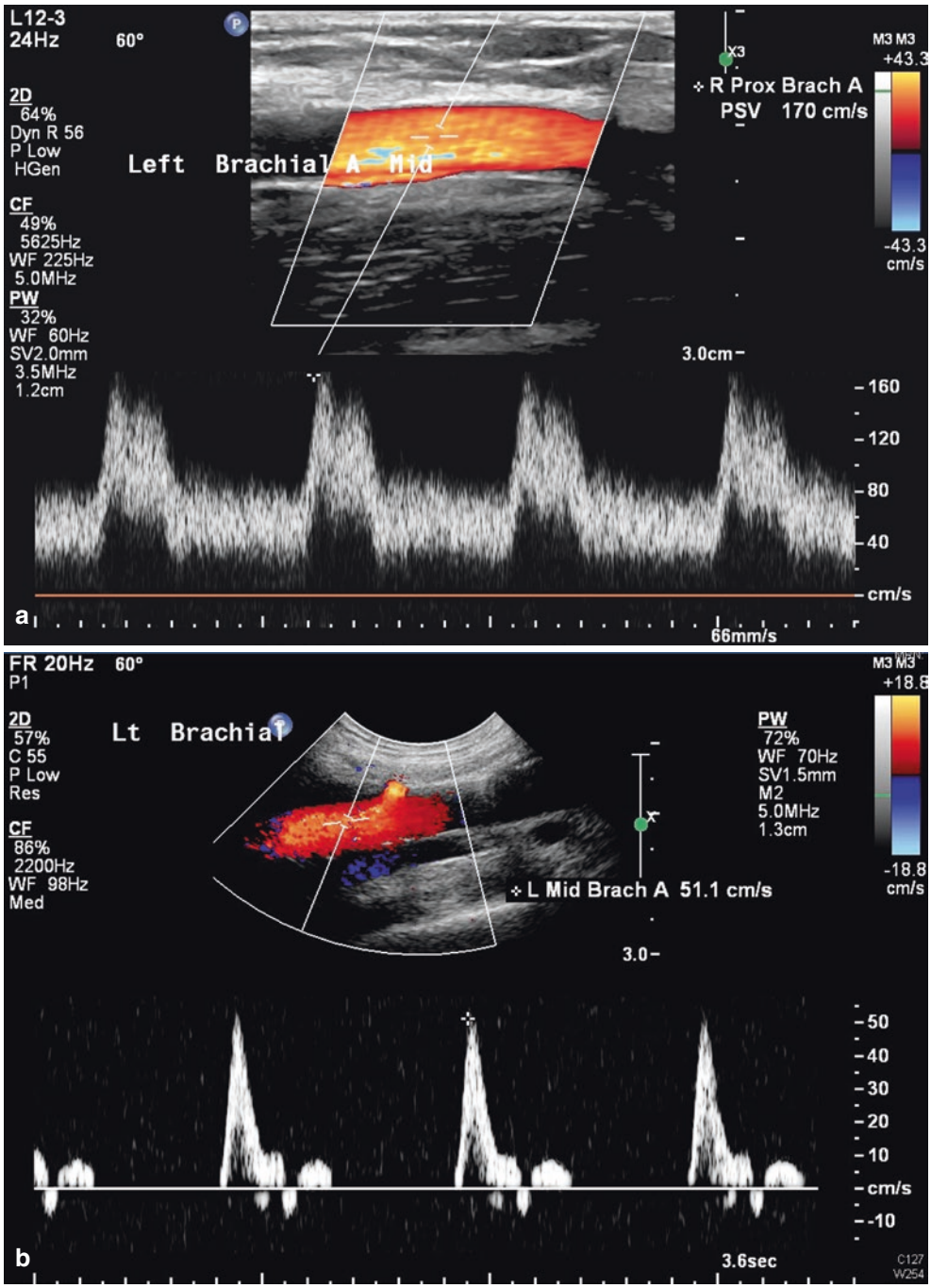

Fig. 23.1 (**a**) Spectral waveform from a brachial artery supplying a widely patent hemodialysis access site shows a low-resistance flow pattern characterized by a relatively high peak systolic velocity (PSV) of 170 cm/s and antegrade flow throughout diastole. (**b**) Spectral waveform from the brachial artery of a patient with an occluded access site shows a PSV of 51 cm/s with a high-resistance multiphasic flow pattern

Conduit

Autogenous Vein. A direct surgical connection between an inflow artery and an autogenous vein requires a single anastomosis. Autogenous vein fistulas are most commonly created at the wrist (radiocephalic fistula), antecubital space (brachiocephalic fistula), or the upper arm (basilic vein transposition fistula). The cephalic vein is preferred because it is more superficial than the basilic vein. If the basilic vein is used, it is usually transposed and brought closer to the skin surface for accessibility. After scanning the arterial inflow, evaluation of an autogenous fistula continues with the arterial-venous anastomosis followed by the superficial venous outflow vessel.

The site of the anastomosis is identified and the adjacent artery and vein segments are scanned. The diameter of the arteriovenous anastomosis is measured and is typically in the range of 4–5 mm (Fig. 23.2), since larger diameters have a higher risk of causing an arterial steal. The PSV at the anastomosis is measured from Doppler spectral waveforms, recognizing that relatively high velocities are

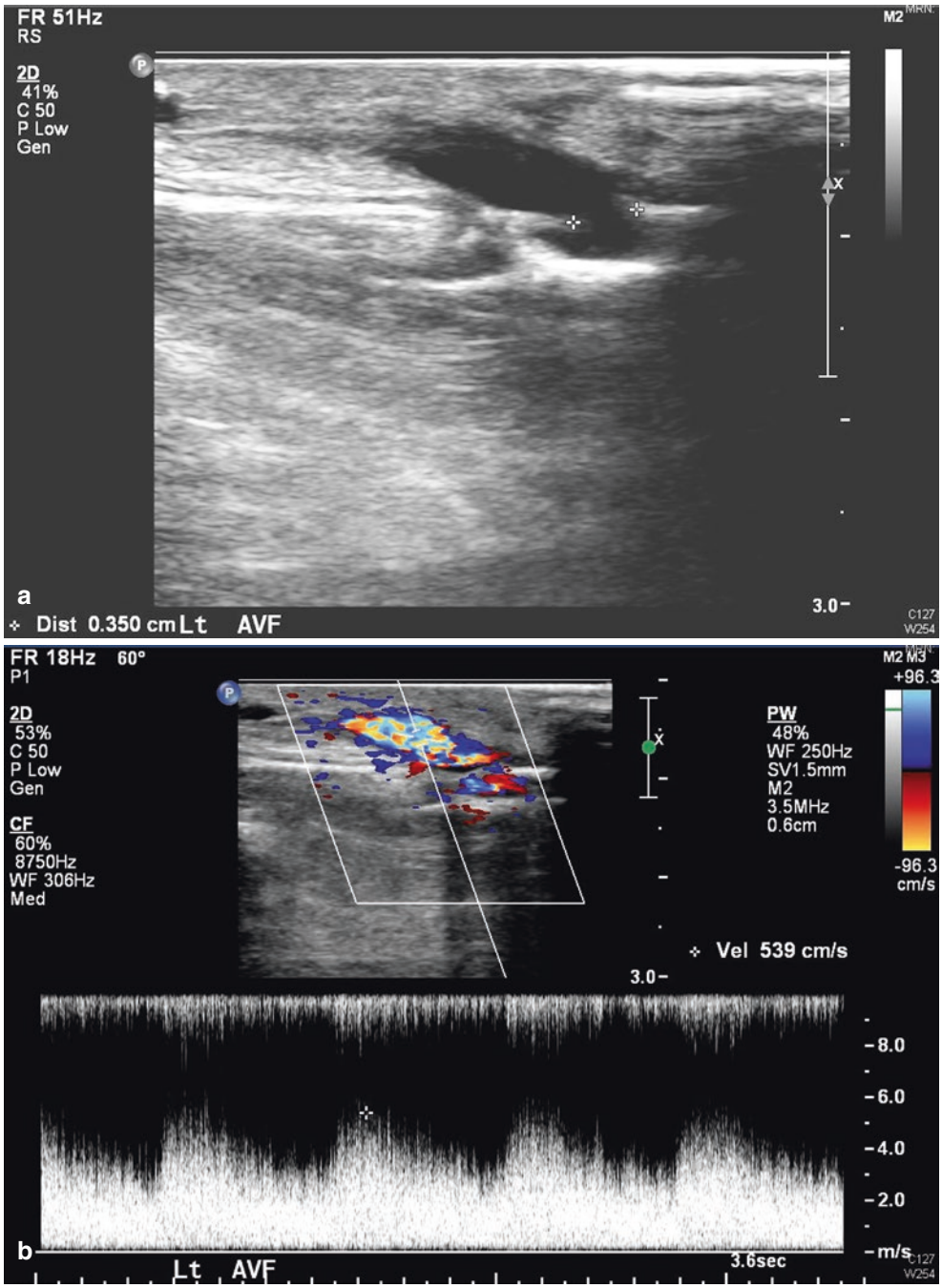

Fig. 23.2 (**a**) B-mode image of an arteriovenous anastomosis with a diameter of 3.5 mm. (**b**) Spectral waveform obtained at the anastomotic site with a peak systolic velocity (PSV) of 539 cm/s and spectral broadening indicating turbulent flow

common at anastomotic sites followed by turbulence due to caliber change and angulation.

Because high velocities are common at an arteriovenous anastomosis, one method of identifying anastomotic stenosis by duplex ultrasound is based on the PSV ratio (Vr) which is defined as the maximum PSV within the anastomosis divided by the PSV in the inflow artery approximately 2 cm proximal to the anastomosis. A Vr of 3.0 or greater and a PSV of 400 cm/s or greater are suggestive of a stenosis of at least 50 % diameter reduction at the anastomosis [8, 9]. However, B-mode confirmation of an intraluminal defect at the anastomosis should also be obtained, since the geometry of the vessels may cause a velocity increase without a true stenosis (Fig. 23.3).

The main superficial venous outflow in an autogenous fistula is usually through either the cephalic or the basilic vein. The entire length of the outflow vein is evaluated with B-mode, color-flow Doppler, and Doppler spectral waveforms. B-mode imaging in long-axis and transverse views will help identify intraluminal defects such as thrombus,

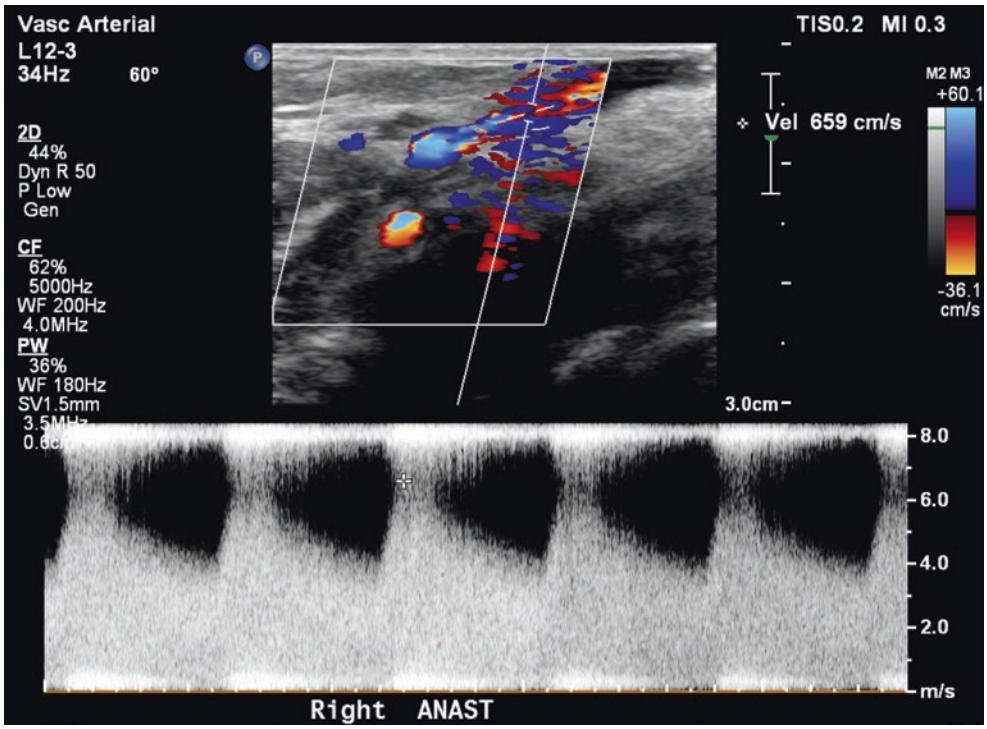

Fig. 23.3 A peak systolic velocity of 659 cm/s is recorded at this arteriovenous anastomosis, which is consistent with a stenosis, although the actual velocities may be higher. A color bruit in the adjacent tissue is also suggestive of a stenosis

chronic webbing, a fibrotic valve, or caliber change (Fig. 23.4). Color-flow images may show aliasing along the length of the outflow vein which helps to quickly identify focal velocity increases signifying a possible stenosis. Doppler spectral waveforms are also obtained along the length of the outflow vein. Within the outflow vein of the fistula, PSV is typically in the range of 150–300 cm/s, although velocities are highly variable. Some laboratories use a twofold focal velocity increase (Vr of 2.0) with associated poststenotic turbulence as a threshold to indicate a significant stenosis within the autogenous vein fistula [9]. Occlusion is identified by the presence of intraluminal echoes with no obtainable color Doppler flow or Doppler spectral waveforms.

Prosthetic Graft. Access sites created with prosthetic grafts have two anastomoses—arterial and venous—and may be created from a variety of materials, with expanded polytetrafluoroethylene (ePTFE) being the most common. The evaluation of a prosthetic graft can be considered in three parts: (1) the arterial anastomosis, (2) the prosthetic conduit, and (3) the venous anastomosis. A loop graft is often created to provide more access site lengths for cannulation. The arterial anastomosis is performed with the graft directed peripherally, and the graft then makes a loop coursing back centrally to the venous anastomosis. With a loop graft, the arterial and venous anastomoses are usually located at the same level in the upper extremity, typically near the antecubital fossa. A straight graft runs directly back toward the heart from the arterial anastomosis to the outflow vein, and the venous anastomosis is located more proximally in the upper extremity.

The duplex evaluation of a prosthetic graft continues after the inflow arteries are assessed, measuring the diameter of the arterial anastomosis and the maximum PSV at that site. As with autogenous vein conduits, high velocities are common at the arterial anastomosis of a prosthetic graft, and flow disturbances related to angulation are frequently present; however, the diameters of graft anastomoses are less variable than those of autogenous vein anastomoses. Although velocities at the anastomotic sites of prosthetic grafts are extremely variable, the general threshold criteria for stenosis listed previously for autogenous vein fistulas can be applied to grafts. A PSV of 400 cm/s or greater and a focal velocity increase with a Vr of 3.0 or greater are consistent with a significant (≥50 % diameter reduction) anastomotic stenosis [9].

An initial B-mode image evaluation of the prosthetic graft in transverse and long-axis views will identify any intraluminal abnormalities that may be masked by the color-flow display. Abnormalities in the soft tissues around the graft, such as fluid collections, may also be identified by B-mode imaging. Color-flow Doppler is helpful in detecting anatomic defects such as pseudoaneurysms (Fig. 23.5). The prosthetic graft should be examined throughout its length using the pulsed Doppler and spectral waveforms for focal increases in PSV which may be due to intraluminal thrombus, neointimal hyperplasia, or stenosis at a revision site. Velocities in prosthetic grafts are quite variable; however, some criteria for significant (≥50 % diameter reduction) stenosis that have been applied include a PSV of 300–400 cm/s or greater, end-diastolic velocity (EDV) of 240 cm/s or greater, and Vr of 2.0 or greater [8, 9].

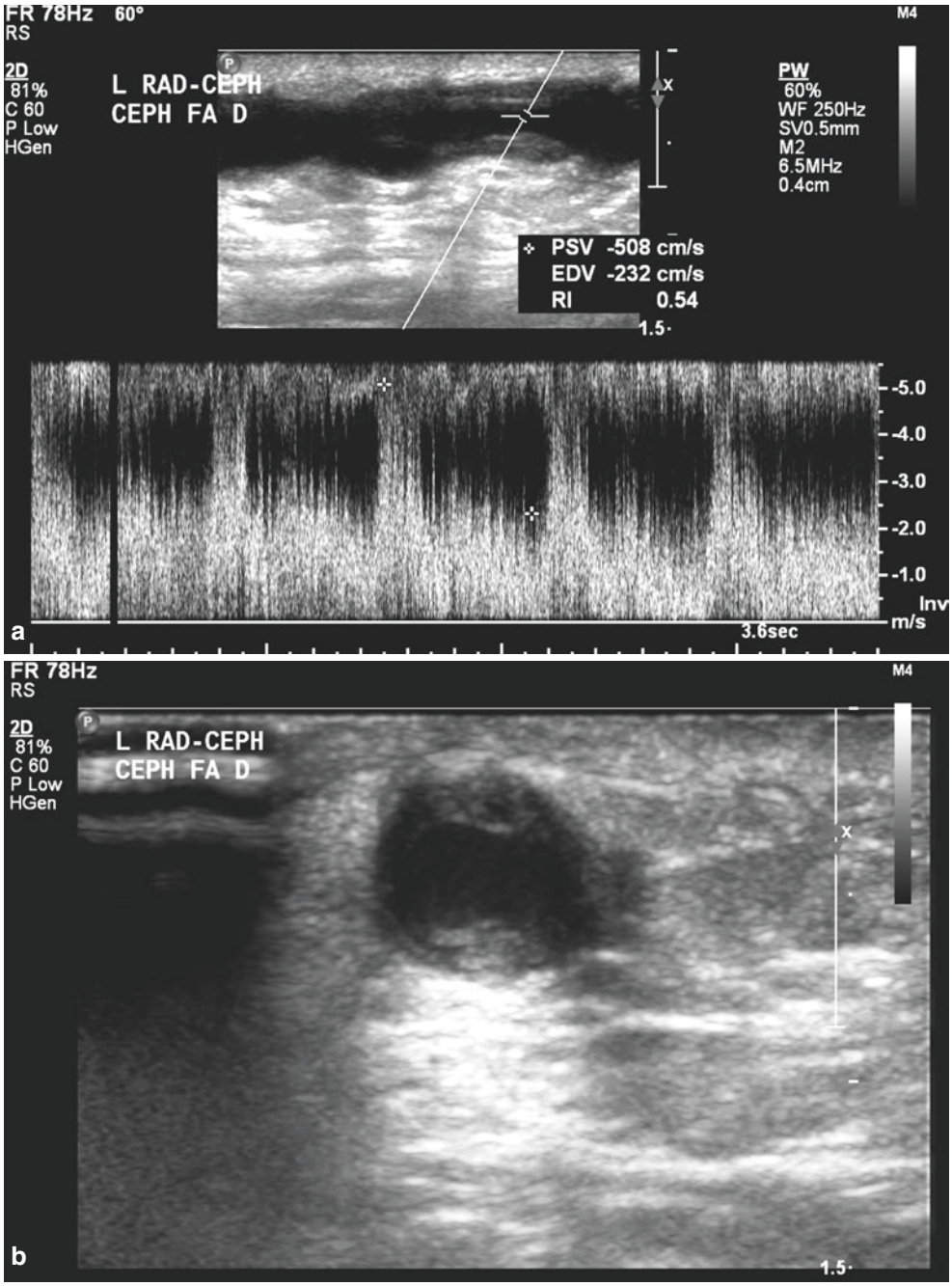

Fig. 23.4 B-mode images in long-axis (**a**) and transverse (**b**) views showing thrombus in the cephalic outflow vein of an access site. Peak systolic velocity (PSV) is 508 cm/s at the site of maximum luminal narrowing

Graft occlusion is suggested by the absence of a palpable thrill or audible bruit over the graft on physical examination. Duplex confirmation of graft occlusion is based on the presence of intraluminal echoes on B-mode imaging and absence of flow on Doppler spectral waveforms and color-flow Doppler (Fig. 23.6). Some synthetic graft materials, including PTFE, contain small amounts of air that impede the transmission of ultrasound for a period of time after implantation. This causes acoustic shadowing across the lumen of the graft and prevents direct interrogation by Doppler. In this situation, Doppler spectral waveforms from the adjacent inflow artery and outflow vein can provide indirect evidence of graft patency. With a patent prosthetic graft, the inflow artery will show a low-resistance flow pattern, and the flow pattern may return to a high-resistance waveform in the artery distal to the anastomosis.

The venous outflow anastomosis should be identified and its diameter and maximum PSV measured. A common site for a stenosis is at or just beyond the venous anastomosis of a prosthetic graft, as indicated by a focal velocity increase with poststenotic turbulence.

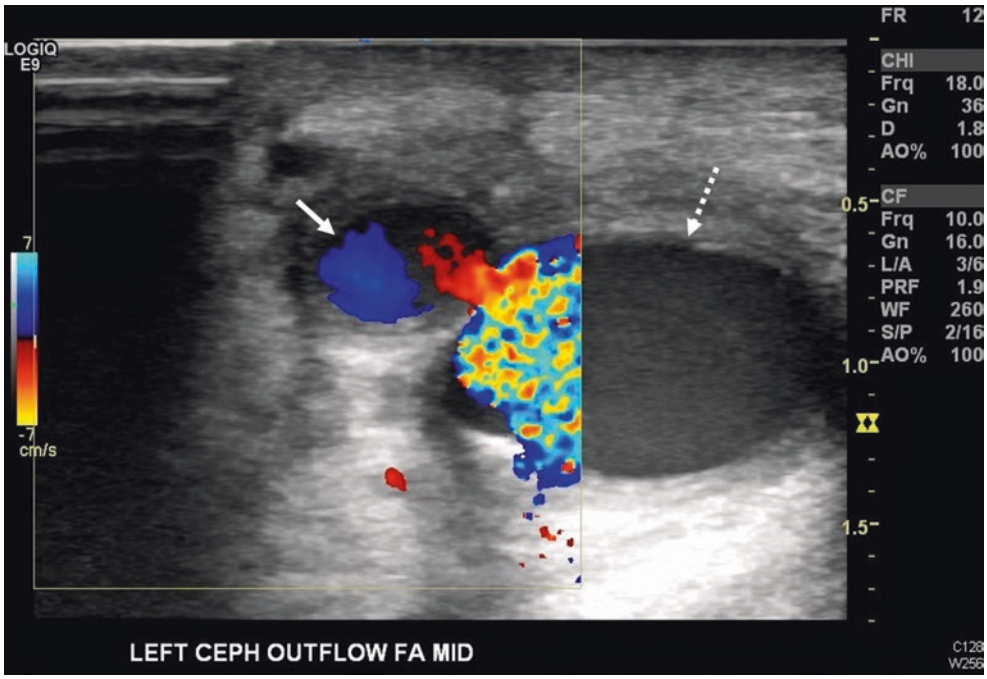

Fig. 23.5 Color-flow Doppler image of a small pseudoaneurysm (*solid arrow*) originating from a cephalic outflow vein (*dashed arrow*) of an access site

Central Venous Outflow

Duplex evaluation of the upper extremity outflow veins can provide information on the presence or absence of central venous obstruction as well as the status of the autogenous vein fistula or prosthetic graft. Obstruction in the central veins is a common finding in long-term dialysis access patients, particularly those with a history of multiple central venous catheters. The flow patterns in the innominate and subclavian veins provide indirect information about graft or fistula outflow. With a functioning access site, spectral waveforms from the innominate and subclavian veins will show "arterialized" pulsatility (Fig. 23.7); if the access site is occluded, the central vein flow pattern will be non-pulsatile and more phasic with respiration.

A central outflow vein stenosis produces a focal velocity increase in the "arterialized" vein segment. The peak vein velocity (PVV) ratio has been defined as the poststenotic velocity divided by the pre-stenotic velocity, and a value >2.5 has been shown to correlate with a central venous stenosis severe enough to result in a pressure gradient [10]. Some central venous occlusions may be difficult to visualize directly with duplex scanning due to their location under the clavicle or in the mediastinum. The presence of visible, well-developed venous collaterals around the shoulder is suggestive of a central vein stenosis or occlusion.

Interpretation and Reporting

The approach to performing and interpreting duplex ultrasound evaluations of hemodialysis access sites follows the same principles as other duplex examinations of peripheral arteries and veins. However, the access site evaluation presents unique challenges due to the variety of vascular anatomy involved and the difficulty in establishing specific threshold velocity criteria for stenosis due to the wide variability in the velocities encountered. Both absolute velocities and velocity ratios have been used as the basis for classifying the severity of stenosis associated with access sites. While it is difficult to set threshold criteria that can be strictly applied in all cases, some guidelines are summarized in Table 23.3.

A well-functioning hemodialysis access conduit (autogenous vein or prosthetic graft) should have a high-velocity, low-resistance flow pattern on spectral waveform analysis with antegrade or forward flow throughout the cardiac cycle (Fig. 23.8). In general, the PSV at an arterial anastomosis should not exceed 400 cm/s, and PSV in the conduit is typically in the range of 150–300 cm/s. The reported sensitivities for the duplex ultrasound detection of significant access conduit stenosis in comparison to contrast fistulography have varied from 75 to 95 %, with specificities ranging from 60 to 97 % and a positive predictive value of approximately 80 % [1, 5, 8, 9]. While assessment of flow velocities plays an important role in the evaluation of a hemodialysis access site, the volume flow rate is the best single indicator of access function. The minimum volume flow rate that will support successful dialysis is about 600 mL/min [1, 8].

Documentation of flow directions associated with access sites can be confusing if the terms "proximal" and "distal" are used. It is better to replace these terms with the less ambiguous "central" and "peripheral." When scanning an autogenous vein fistula, flow in the artery up to the

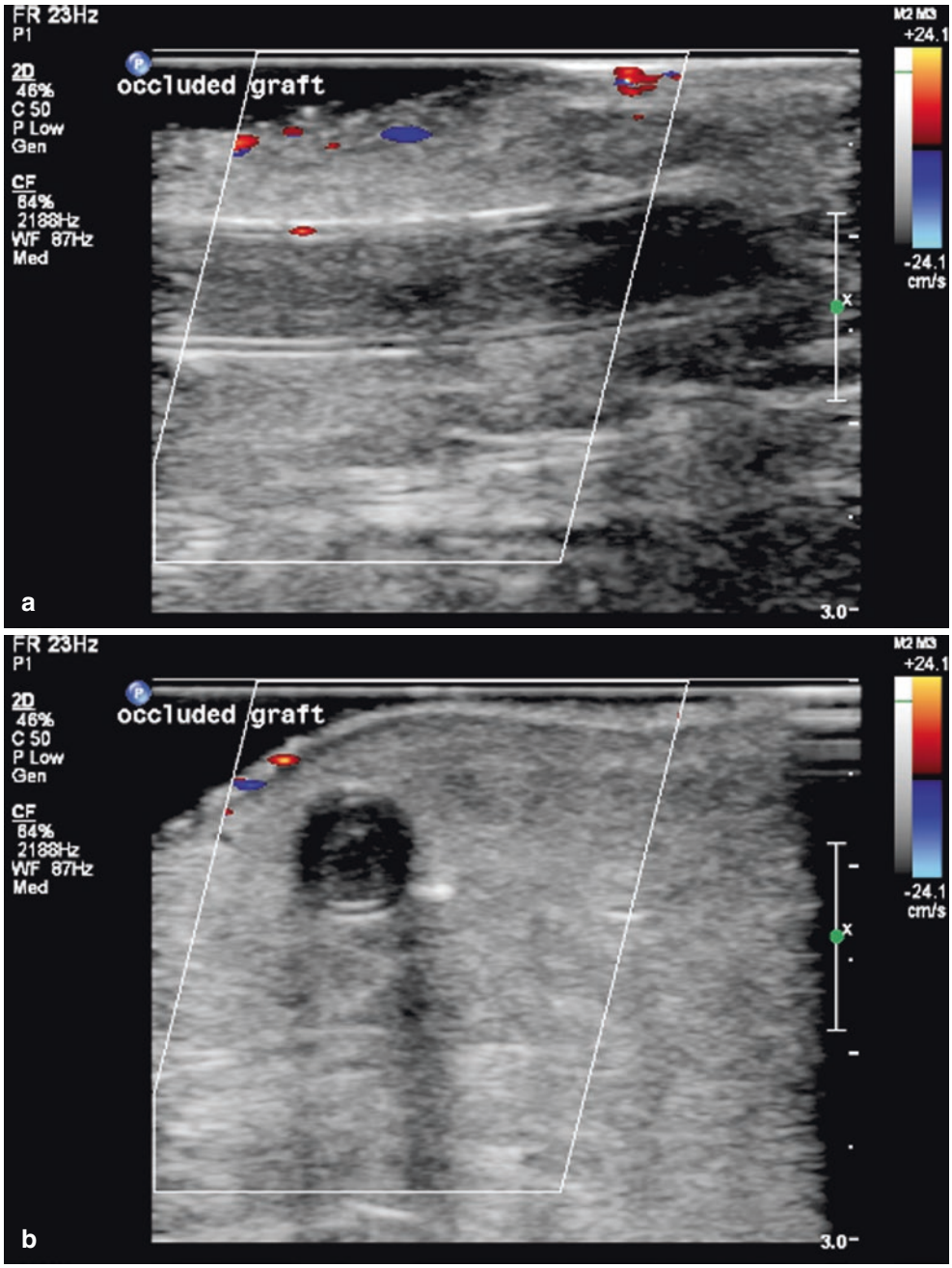

Fig. 23.6 B-mode and color-flow Doppler images of an occluded prosthetic graft in long-axis (**a**) and transverse (**b**) views. Intraluminal echoes and lack of flow confirm the diagnosis of graft occlusion

anastomosis is in a peripheral direction, and flow in the venous conduit is directed centrally. Similarly, with a prosthetic graft, flow is in a peripheral direction in the inflow artery and in a central direction in the outflow vein. Flow direction in the artery distal to an arterial anastomosis should be peripheral; if it is central, then flow is away from the hand and an arterial steal is present.

The Current Procedural Terminology (CPT) code for the hemodialysis access duplex examination is 93990 which includes evaluation of the arterial inflow, the access conduit, and the venous outflow. The Centers for Medicare and Medicaid Services (CMS) provides reimbursement for non-invasive vascular studies of hemodialysis access sites when they are medically necessary due to the presence of signs or symptoms of access site dysfunction. These include difficult cannulation for dialysis, thrombus aspiration after cannulation, elevated venous pressures on dialysis (>200 mmHg), and elevated recirculation time of 12 % or greater. There is no reimbursement by CMS for routine duplex ultrasound surveillance of access sites in the absence of signs or symptoms. In addition, if both a duplex scan and a contrast fistulogram are performed on the same patient, CMS limits reimbursement to one examination unless documentation supports the medical necessity of both studies.

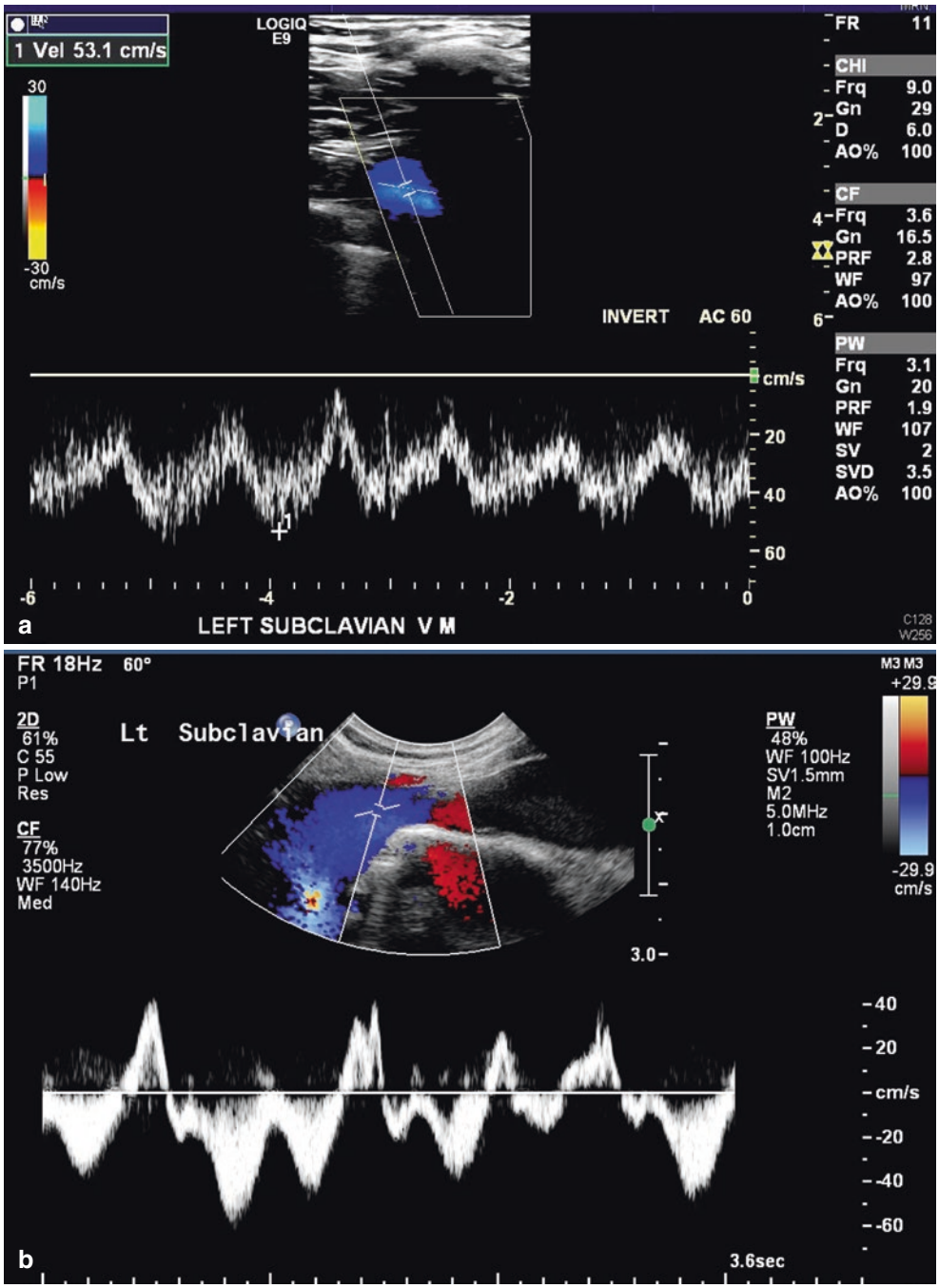

Fig. 23.7 (**a**), Spectral waveforms from the subclavian vein on the side of a well-functioning access site show "arterialized" pulsatility with minimal respiratory phasicity. (**b**) In a limb without an access site, spectral waveforms from the subclavian vein show respiratory phasicity along with some pulsatility, typical of normal upper extremity central veins

Assessment of Access Maturation

The maturation process of an autogenous vein conduit involves three components that are necessary to produce a functional hemodialysis access site: (1) adequate diameter and length for cannulation with dialysis needles, (2) sufficient volume flow for effective dialysis, and (3) superficial location that allows safe and repetitive puncture. These anatomic and hemodynamic parameters can be assessed with duplex scanning, and problems that may interfere with maturation can be identified. Both diameter and flow rate should increase in the immediate postoperative period, and maximal levels are attained in 4–8 weeks. The reasons for failure of an autogenous vein conduit to mature include the presence of large venous side branches that divert flow, stenosis at the arterial anastomosis, and narrowing of the outflow vein or more central venous outflow obstruction. General requirements for adequacy of maturation parameters are a conduit diameter greater than 5 mm, depth (distance from the skin surface) less than 6 mm, accessible conduit length of at least 10 cm, and calculated volume flow rate of 600 mL/min or greater (Fig. 23.9) [8, 11].

Duplex scanning of autogenous vein fistulas during the maturation period and prior to initiation of dialysis is helpful to ensure that they are maturing or determine the cause of non-maturation. Aggressive intervention soon after access placement may promote successful maturation and permit salvage of some conduits that may not otherwise have matured. Possible interventions include ligation of venous side branches, repair of venous or arterial stenoses, vein angioplasty (balloon-assisted maturation), and vein superficialization [12]. While prosthetic graft conduits do not mature like autogenous veins, the same general anatomic and flow parameters can be applied, and duplex scanning prior to use for dialysis will identify prosthetic graft access sites that may need revision to support successful hemodialysis [13].

Volume Flow Measurements

If all the anatomic parameters associated with an access site are consistent with successful hemodialysis, the main hemodynamic requirement is a sufficient volume flow rate.

Table 23.3 Classification of hemodialysis access site stenosis by duplex scanning

Interpretation	Velocity parameters and flow pattern	B-mode and color-flow image
Normal	Arterial anastomosis PSV 200–400 cm/s Mid-conduit PSV 150–300 cm/s High-velocity, low-resistance, pulsatile conduit flow pattern	Widely patent lumen throughout the access site
≥50 % diameter stenosis	Arterial anastomosis PSV ≥400 cm/s Arterial anastomosis Vr ≥3.0 Conduit lesion PSV ≥300 cm/s Conduit lesion Vr ≥2.0 Conduit lesion EDV ≥240 cm/s Mid-conduit PSV (away from lesion) <150 cm/s Low-velocity, high-resistance, dampened conduit flow pattern *proximal* to lesion Low-velocity, low-resistance, dampened conduit flow pattern *distal* to lesion Significant central venous stenosis PVV ratio >2.5	Severe reduction in lumen diameter with residual diameter <3 mm
Occlusion	No Doppler spectral waveform in conduit	No color-flow image in conduit Thrombus in conduit lumen on B-mode image

PSV peak systolic velocity, *Vr* velocity ratio, *PVV* peak vein velocity, *EDV* end-diastolic velocity

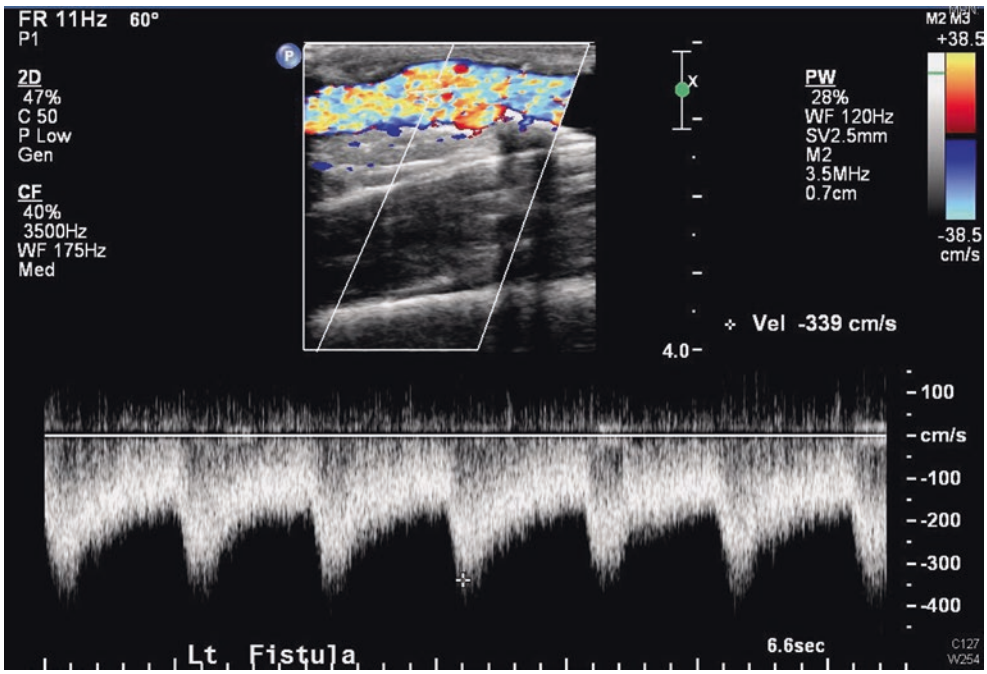

Fig. 23.8 Spectral waveforms from a well-functioning cephalic vein access conduit show a high-velocity, low-resistance flow pattern with antegrade flow throughout the cardiac cycle. The peak systolic velocity (PSV) is 339 cm/s

Functioning autogenous vein fistulas and prosthetic grafts typically have volume flow rates in the range of 800–1200 mL/min, and flow rates of less than 500 mL/min are generally considered indicative of impending access site failure. Autogenous vein fistulas tend to require less flow to remain patent than prosthetic grafts. Volume flow measurements are more predictive of access site function than PSV, although focal increases in PSV are better for detecting stenosis. However, even if there is evidence of a greater than 50 % diameter reduction associated with an access site, intervention may not be necessary if the volume flow rate remains adequate for dialysis [5, 8].

The volume flow rate in the inflow artery, conduit, or outflow vein associated with a hemodialysis access site can be calculated using velocity and vessel diameter measurements obtained by duplex scanning [8, 14]. Most current duplex ultrasound systems include the capability to determine volume flow based on the following relationship:

$$Q = v \times A \times 60\text{s} = v \times \pi \left(d^2 \right) / 4 \times 60\text{s}$$

where Q = volume flow (mL/min), v = time-averaged and spatially averaged velocity across the vessel lumen (cm/s), A = cross-sectional area of the vessel at the site of velocity measurement (cm^2), and d = lumen diameter (cm). Multiplying by 60 s is necessary to express Q in mL/min. The pulsed Doppler sample volume must be expanded to include the entire vessel diameter in a long-axis view, and spectral waveforms are recorded with a Doppler angle of 60° or less. The time-averaged velocity is measured over at least two or three cardiac cycles and assumes laminar flow and a circular vessel cross section (Fig. 23.10). Experimental validation of duplex ultrasound volume flow measurements has shown an absolute error of 13 % and a high degree of correlation with timed blood collection [14].

Accurate volume flow measurements require a regular or uniform flow pattern. Because variations in lumen diameter, vessel tortuosity, and turbulence are more likely to occur in a venous conduit or outflow vein, it is often better to measure volume flow in the inflow artery—usually the brachial artery—or in a straight section of a prosthetic conduit. For upper extremity access sites originating from the brachial or radial arteries, the inflow brachial artery is the best choice for volume flow measurements due to its consistent location and constant diameter (Fig. 23.10b). In this setting, more than 90 % of the brachial artery flow will travel through the low-resistance access conduit [8]. A comparison of volume flow measurements obtained by duplex scanning from both the inflow brachial artery and the access conduit in 75 patients showed a high degree of correlation for both autogenous veins and prosthetic grafts [11]. If a decrease in volume flow is noted in the outflow vein relative to the inflow brachial artery, there may be large venous side branches that are diverting flow away from the main venous conduit.

The relationship between velocity parameters and calculated volume flow allows a rapid ultrasound assessment of access site function which can be performed as a "point of care" examination. The hemodynamic and anatomic duplex ultrasound results from 148 access sites were compared with access maturation or need for revision prior to initiation of hemodialysis [11]. Measurements of brachial artery PSV and EDV were used to define three categories of access site flow

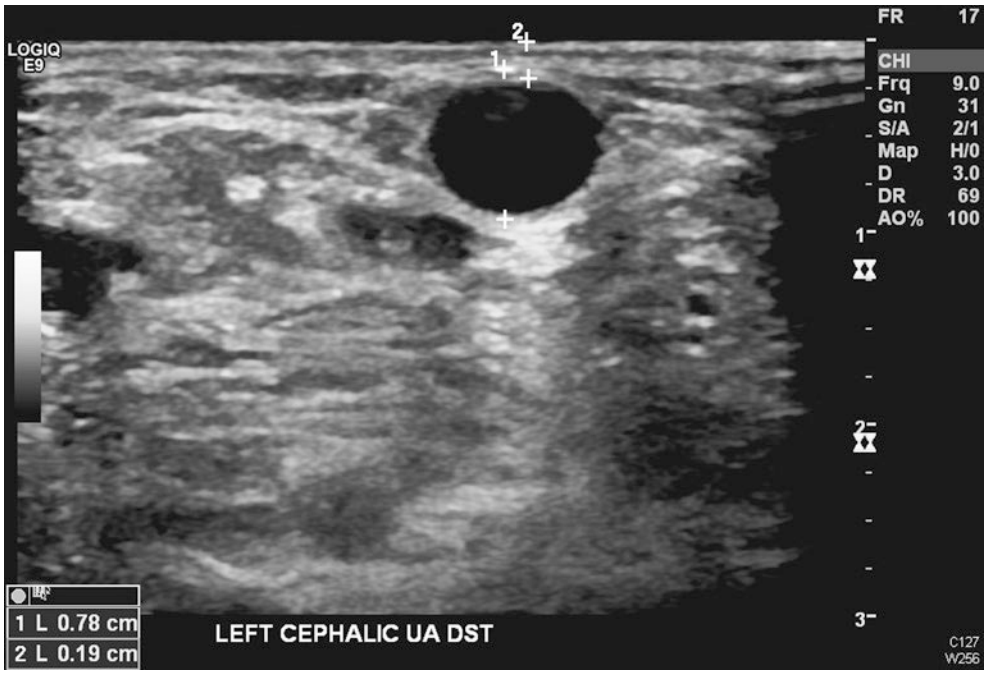

Fig. 23.9 Measurement of maturation parameters. B-mode image of a cephalic vein access conduit showing a diameter of 7.8 mm and depth from the skin surface of 1.9 mm

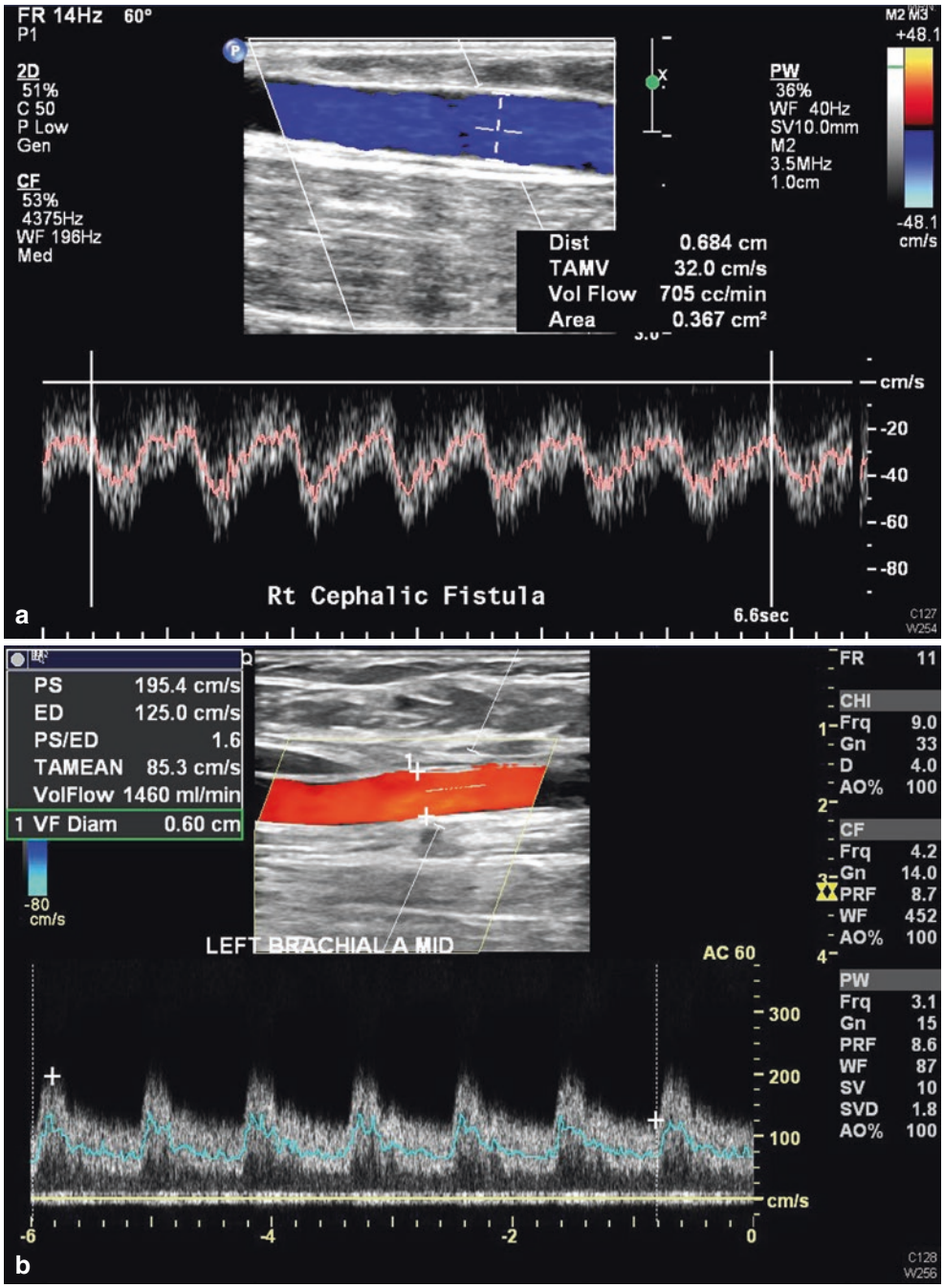

Fig. 23.10 (**a**) Duplex ultrasound volume flow measurement in a cephalic vein access conduit. The pulsed Doppler sample volume is expanded to include the entire vessel diameter in a long-axis view, spectral waveforms are recorded with a Doppler angle of 60°, and the time-averaged mean velocity is measured over multiple cardiac cycles. The vessel diameter is 0.68 cm (area 0.37 cm^2), time-averaged mean velocity is 32 cm/s, and calculated volume flow is 705 cc/min. (**b**) Similar volume flow measurement from the inflow brachial artery for a hemodialysis access site. The vessel diameter is 0.60 cm, time-averaged mean velocity is 85 cm/s, and calculated volume flow is 1460 ml/min

in patients with a brachial artery diameter of 4.5 mm or more: *Low* (<600 mL/min) – PSV <100 cm/s, EDV/PSV ratio <0.2; *Acceptable* (600–800 mL/min) – PSV <150 cm/s, EDV/PSV ratio 0.2 to 0.4; and *High* (>800 mL/min) – PSV >150 cm/s, EDV/PSV ratio >0.4. The EDV/PSV ratio is an indicator of outflow resistance, with higher values representing the low resistance expected in a normally functioning access site. In addition to the hemodynamic parameters of PSV and EDV, the anatomic parameters of conduit diameter, conduit depth from the skin surface, and superficial conduit length are important in the rapid ultrasound assessment for access site maturation. Access sites with calculated volume flow rates of less than 600 mL/min and those with unfavorable anatomic parameters are likely to require revision prior to successful use for dialysis [11].

Assessment of Access Complications

An access site that has matured and provides adequate flow rates through a conduit that is readily cannulated for dialysis is still at risk for a variety of complications. The most

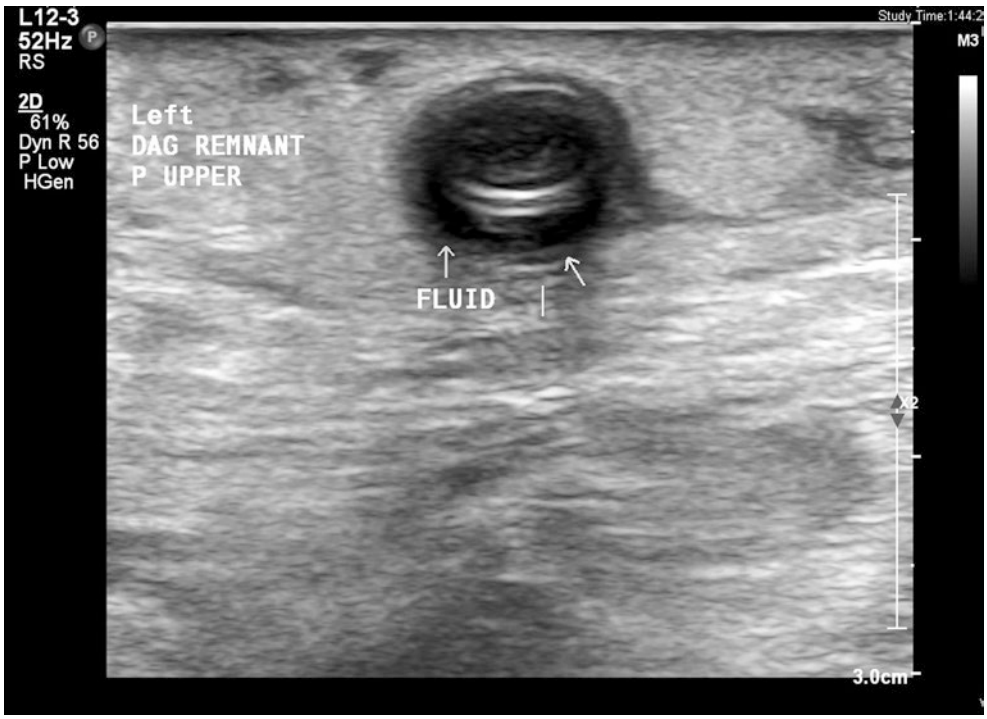

Fig. 23.11 Fluid collection adjacent to an occluded prosthetic access conduit. The B-mode image shows a hypoechoic area deep to the prosthetic graft (*arrows*)

common mode of failure for dialysis access sites is progressive narrowing of the venous outflow by intimal hyperplasia at or within a few centimeters of the venous anastomosis, but a stenosis can occur anywhere from the inflow artery and arterial anastomosis to the venous or prosthetic conduit and the central veins. Vein valves and puncture sites are particularly prone to intimal hyperplasia. Outflow venous stenosis causes reduced flow and increased pressure in the access conduit which may be associated with a reduced thrill and increased pulsation on physical examination. Progressive venous outflow obstruction eventually results in elevated pressure in the venous circuit of the dialysis machine. The detection of stenotic lesions by duplex scanning has already been discussed. Other problems associated with hemodialysis access sites that can be evaluated by duplex ultrasound are infection, arterial steal, pseudoaneurysms, congestive heart failure, and venous hypertension.

Infection

Infection is one of the most common complications associated with hemodialysis access sites and may result in perigraft fluid or an abscess cavity [15]. Nonvascularized fluid collections are apparent on B-mode imaging as irregular hypoechoic areas surrounding or adjacent to the access conduit or the anastomotic segments (Fig. 23.11). An abscess contains pus and typically has internal septations and debris which result in a heterogeneous ultrasound appearance. A seroma is a pocket of clear fluid that appears uniformly anechoic, while a hematoma contains red blood cells which appear hypoechoic or heterogeneous on ultrasound. Because of these features, it is difficult to distinguish between a hematoma and an abscess based on ultrasound imaging alone.

Arterial Steal

An arterial steal develops when the artery supplying the access site is unable to provide adequate flow to both the fistula and the distal arterial circulation. In this situation, flow preferentially follows the low-resistance path through the access conduit, resulting in decreased arterial pressure and flow in the distal extremity. In severe cases, there is retrograde flow (away from the hand) in the radial or ulnar artery peripheral to the anastomosis. A clinically significant steal rarely occurs unless there is occlusive disease in the arterial system proximal or distal to the arterial anastomosis of the access site: proximal stenosis reduces inflow, while distal stenosis makes the hand more susceptible to ischemia when inflow is decreased. Arterial steal is more common in diabetic patients who are particularly prone to occlusive disease in the upper extremity arteries.

Patients may present with coolness, pain, numbness, or weakness in the hand, especially while dialyzing, or they may develop digital tissue necrosis. When a symptomatic arterial steal is suspected, a complete duplex ultrasound examination of the access site should be performed to identify hemodynamically significant stenoses involving the arterial inflow, the conduit, or the venous outflow vessels. The

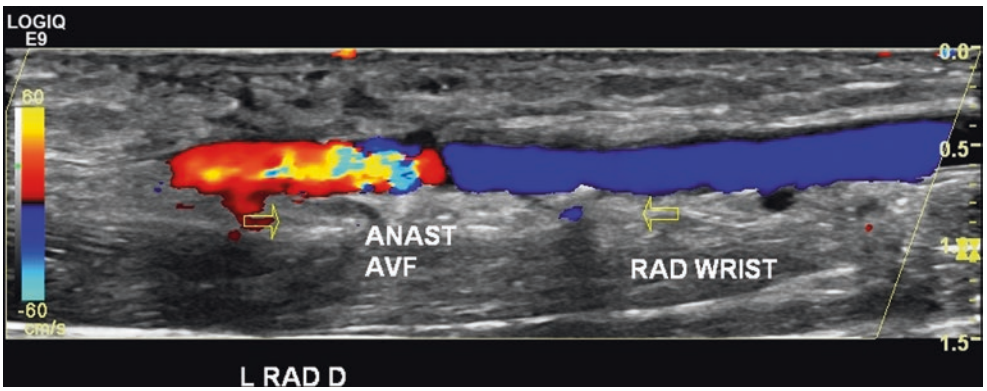

Fig. 23.12 Color-flow Doppler image of a radial artery with a radial artery to cephalic vein anastomosis (ANAST AVF). The color-scale indicates antegrade flow up to the anastomotic site with retrograde flow (away from the hand) in the radial artery distal to the anastomosis (*blue color*). *Arrows* indicate direction of flow

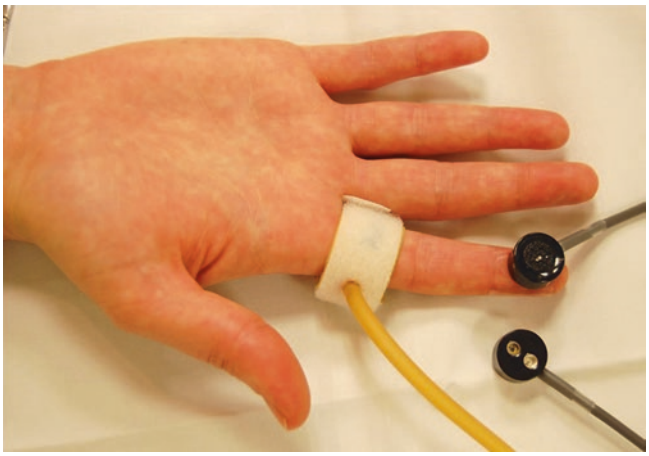

Fig. 23.13 Measurement of digit pressure with a finger cuff and a photoplethysmograph (PPG) for flow detection (From Moneta [19], used with permission)

direction of flow, flow velocity, and flow pattern in the arteries peripheral to the arterial anastomosis should also be documented (Fig. 23.12). Some evidence of flow diversion in these arteries can be identified by ultrasound with most access sites, such as a decrease in antegrade flow velocity, dampening of the flow waveform, or retrograde flow, but these remain asymptomatic in the majority of cases. The incidence of symptomatic arterial steal is lowest with forearm access sites (0.25–1.8 %) and highest with access sites originating directly from the brachial artery (4–9 %) [15]. Access sites with high flow rates are also more likely to produce a symptomatic arterial steal.

Measurement of digit pressures with a finger cuff and a photoplethysmograph (PPG) for flow detection is a useful diagnostic test for assessing the presence and severity of arterial steal (Fig. 23.13). Digit systolic blood pressure is normally within 20–30 mmHg of brachial systolic pressure, and a ratio of finger systolic pressure to brachial systolic pressure of greater than 0.80 is considered normal. Digit pressures of less than 60 mmHg are consistent with clinically significant or symptomatic hand ischemia. Pressure measurements obtained without and with temporary manual compression of the access conduit can provide an estimate of the hemodynamic severity of an arterial steal. If digit pressures are abnormally low with the access site patent but normalize with access compression, the presence of a significant pressure steal is confirmed. This provocative examination is best carried out by two examiners, with one performing the manual compression and the other obtaining the digit pressures.

Pseudoaneurysms

A pseudoaneurysm associated with a hemodialysis access site is a cavity with active flow outside the wall of a blood vessel or prosthetic graft that presents as a localized pulsatile mass. Pseudoaneurysms develop if an access puncture site does not seal when the needle is removed, and they are more common with prosthetic conduits than with autogenous veins. The communication between this cavity and the vessel or graft lumen is referred to as the "neck" of the pseudoaneurysm, and the diagnosis is confirmed by duplex examination showing the active flow cavity and connecting neck. On the color-flow Doppler image, a pseudoaneurysm has a swirling appearance as the flow enters the pseudoaneurysm cavity, and the neck shows a "to-and-fro" flow pattern in the spectral waveforms (Fig. 23.14). Pseudoaneurysms can also occur at an anastomosis and may be associated with infection, particularly in the presence of a prosthetic conduit and a perigraft fluid collection.

High-Output Cardiac Failure

High-output cardiac failure is characterized by increased cardiac output combined with physical findings of systemic

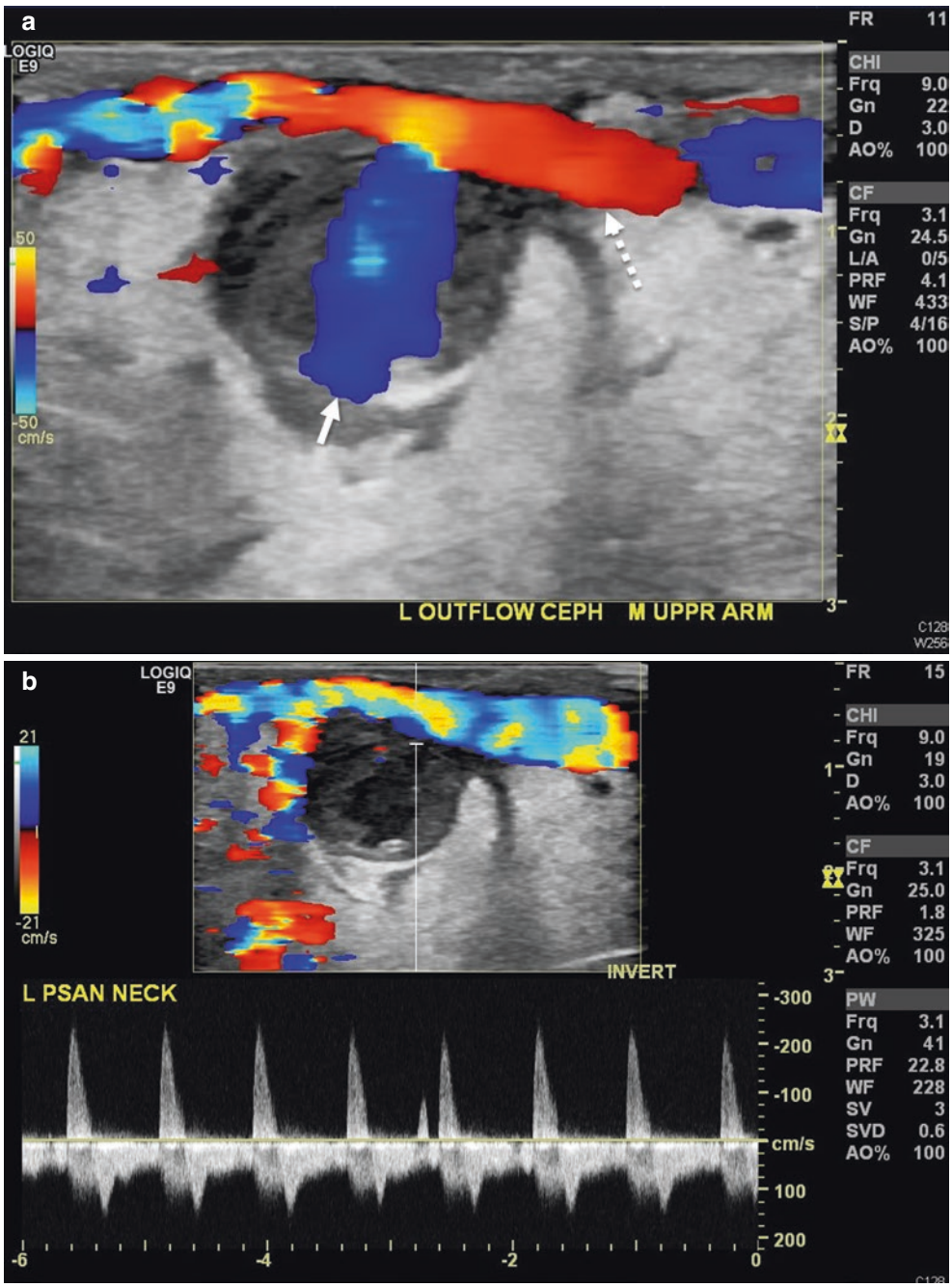

Fig. 23.14 A pseudoaneurysm originating from the cephalic outflow vein of an access site. (**a**) Color-flow Doppler image shows flow in the pseudoaneurysm cavity (*solid arrow*) and the adjacent cephalic vein conduit (*dashed arrow*). (**b**) The "neck" of the pseudoaneurysm between the vein lumen and the flow cavity shows a "to-and-fro" flow pattern in the spectral waveform

venous or pulmonary congestion. Although symptoms of heart failure are common in patients requiring hemodialysis and are usually due to intrinsic cardiac disease, a small proportion of these patients will have cardiac failure secondary to relatively high flow rates through their dialysis access site [15]. Access flow rates of greater than 3000 mL/min or a ratio of access flow to total cardiac output of greater than 0.30 are consistent with high-output cardiac failure, although there are no absolute thresholds that can be applied to all patients. A decrease in cardiac output during transient occlusion of the access site is suggestive of this diagnosis and can be demonstrated as a drop in the pulse rate with temporary compression of the access conduit—the Nicoladoni-Branham sign [16]. When high-output cardiac failure occurs, it is typically associated with large upper arm access sites, particularly those with autogenous vein conduits. The strongest evidence in support of a diagnosis of high-output cardiac failure is clinical improvement in response to procedures designed to decrease access flow rates, such as ligation or banding [15].

Venous Hypertension

The combination of a high access site flow rate and central venous obstruction can lead to elevated venous pressure with ipsilateral arm and hand edema, reddish-purple skin discoloration, and prominent chest wall venous collaterals. Central venous stenosis and extremity venous hypertension are more common in patients who have had multiple venous lines, including pacemaker wires and temporary dialysis catheters. In the absence of high flow rates from an access site, a central venous stenosis is often asymptomatic, and a stenosis may be "unmasked" by placement of an access site. This highlights the importance of a careful assessment of the upper extremity central outflow veins prior to creation of an access site. If the central veins cannot be evaluated completely by duplex ultrasound due to their location under the clavicle or the sternum, and a central venous stenosis is suspected, additional imaging should be considered.

Patients with signs or symptoms of extremity venous hypertension and those with increased venous pressures during dialysis should be evaluated for venous outflow obstruction, as discussed previously. Findings within the venous or prosthetic conduit may be normal, but a significant venous stenosis may be found beyond the venous anastomosis. The most common locations for venous outflow stenoses are adjacent to the venous anastomosis in the native outflow vein, the transposed basilic vein where it turns down into the brachial vein, the cephalic vein where it joins the deep venous system, and within the proximal subclavian or innominate veins. The Doppler flow pattern in the outflow veins of a well-functioning dialysis access site is characterized by regular pulsatility without the respiratory phasicity and dynamic vein wall motion seen in normal upper extremity veins (Fig. 23.7a).

Conclusions

Several systematic reviews of the randomized trials comparing routine screening or surveillance to clinical monitoring alone for maintenance of hemodialysis access sites suggest a possible benefit of surveillance followed by intervention to prolong patency; however, the overall quality of evidence was noted to be very low [5, 7, 17]. This benefit may be greater for autogenous vein conduits than for prosthetic grafts [17]. While acknowledging the limitations of the available evidence, the Society for Vascular Surgery (SVS) clinical practice guidelines recommend "regular clinical monitoring (inspection, palpation, auscultation, and monitoring for prolonged bleeding after needle withdrawal) to detect dysfunction" of dialysis access sites and "performing a duplex ultrasound study or contrast imaging study in accesses that display clinical signs of dysfunction or abnormal routine surveillance" [5]. Sequential measurements and documenting abnormal trends in flow rates or velocities over time may be helpful in identifying those access sites that should be considered for intervention.

A baseline duplex ultrasound assessment of a new access site prior to first use for dialysis is valuable to verify adequate volume flow and conduit anatomy [8]. In those cases where these maturation parameters are unfavorable, the duplex findings can serve as a guide for revision of the access site. With appropriate training, ultrasound screening for access site maturation can be performed as a "point of care" test, with referral to the vascular laboratory for a complete duplex examination when abnormalities are detected [11]. Once an access site is established and being used for dialysis, subsequent duplex examinations are generally performed when signs or symptoms of access dysfunction occur. This includes clinical suspicion for complications such as infection, arterial steal, and venous hypertension.

The recommendations summarized above are generally consistent with the "appropriate use criteria" produced by the American College of Cardiology Foundation [18]. These criteria are based on expert opinion and consensus regarding use of diagnostic imaging tests for a variety of indications or "clinical scenarios" with ratings of *appropriate*, *may be appropriate*, or *rarely appropriate*. For evaluating an access site that has failed to mature, duplex ultrasound was rated as *appropriate* at more than six weeks after placement, with a rating of *may be appropriate* within six weeks of placement. Duplex ultrasound was rated as an *appropriate* test for most clinical scenarios related to upper extremity symptoms in the patient with a mature access site, including the presence of a mass, arm swelling, or signs of digital ischemia. Duplex ultrasound was also rated as *appropriate* for signs of dysfunction or occlusion in a previously mature access site, including difficult cannulation, low volume flow, and loss of a palpable thrill. Routine duplex surveillance of a well-functioning access site in an asymptomatic patient with no signs of access dysfunction was rated as *rarely appropriate*.

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Part V

Hemodialysis Access in Special Populations and Ethical Issues

Considerations in Pediatric Hemodialysis Access

24

Beatriz V. Leong, Sarah M. Wartman, and Vincent L. Rowe

Background

The International Pediatric Fistula First Initiative (IPFFI) was established in 2005 with the aim of addressing the lack of arteriovenous fistula (AVF) use in the pediatric population [1]. The IPFFI was a collaborative effort with the Midwest Pediatric Nephrology Consortium, whose aim was to increase awareness among providers (nephrologists, surgeons, and dialysis staff) that fistulae are the best access in the pediatric hemodialysis population.

Currently, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) recommends placing permanent hemodialysis access in all patients with end-stage renal disease (ESRD) aged 0–19 who are greater than 20 kg and are not expected to receive kidney transplantation within one year. Thus anyone who is expected to be on dialysis greater than one year and meets the age and size criteria should have a permanent arteriovenous fistula placed.

Although most pediatric patients who initiate renal replacement therapy meet these criteria, approximately 90 % of children start treatment via central venous catheter instead of an AVF. Furthermore up to 80 % of pediatric patients with central venous catheters (CVC) have a "permanent" catheter in place [2]. Additionally as many as 50 % of the permanent catheters are placed in the subclavian vein as opposed to the internal jugular vein, exacerbating associated central vein stenosis that occurs with prolonged catheter-based hemodialysis [3].

Incidence of ESRD and Trends in Renal Replacement Therapy in the Pediatric Population

According to the United Stated Renal Data System (USRDS) reports, the incidence of ESRD in the pediatric population aged 0–19 years was 1,161 and was up to 1,462 in 2013; while the cummulative prevalence of children with ESRD as of December 31,2013 was 9,921 [4]. This is compared to the incidence of 117,162 adult patients in the 2013. The reported incidence of ESRD in the pediatric population appears to have peaked in 2003 and has been steadily decreasing since that time. Since the initiation of data collection in 1992, the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) reports no significant change in the pattern of incidence of ESRD in pediatric population when looking by age, race, or gender; thus, these rates are anticipated to remain stable [2]. The USRDS reports hemodialysis is the most common index treatment for new-onset ESRD in the pediatric population. Other less common treatments are preemptive kidney transplantation and peritoneal dialysis.

Evaluating trends of index treatments for ESRD, there has been a shift toward patients being treated with hemodialysis initially compared to peritoneal dialysis, presumably because of readily available CVCs. The USRDS data shows that hemodialysis has consistently been the most common form of index treatment for ESRD patients, the majority initiating HD therapy via CVCs. Elaborating on index treatment for the year 2013, 816 (55.8%) of patients diagnosed with ESRD started treatment with hemodialysis, 367 (25.1%) initiated ESRD treatment with peritoneal dialysis, and 267 (18.3%) did so with index transplantation [4]. Compared to adults where index transplantations are rare and most initiate treatment with hemodialysis, there is a wider distribution of index treatment types in the pediatric population. The index treat-

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ment for adults, in 2013, was hemodialysis in 88.4% of patients, peritoneal dialysis in 9.0% and only 2.6% of adults initiated ESRD care with index transplantation. As many as 37 % of newly diagnosed children with ESRD undergo transplantation within 1 year of starting ESRD care, and of the 9,921 pediatric patients receiving ESRD care in 2013, 6,739 (67.9%) have undergone a kidney transplantation. It is difficult to explain to the parents that their child needs a permanent AVF when they are likely to proceed to transplantation prior to initiation of dialysis or after a short course of dialysis with a temporary HD catheter.

The total number of pediatric patients undergoing hemodialysis in 2011 was 3,363 patients or 42 % of all those receiving ESRD treatment. According to the NAPRTCS 2011 data of those 3,363 patients on HD, 78 % were receiving HD via external percutaneous catheters, 0.3 % via external AV shunts, 11.8 % via internal arteriovenous fistula, and 6.7 % via internal AVG. Of the external percutaneous catheters, the majority were placed in the subclavian vein (51.1 %), 43.7 % in the jugular vein, and 4.2 % in the femoral vein. Interestingly, despite the recognized measures and efforts to increase arteriovenous fistula placement, the use of external percutaneous catheters for HD at initiation of therapy has increased from 73 % in 1992 to >90 % of all HD access in 2010. Meanwhile in the same time period, the use of internal arteriovenous fistula for HD at initiation of treatment has decreased significantly from 12 % in 1992 to ~ 1 % in 2010.

Morbidity and Mortality of ESRD in the Pediatric Population

ESRD in the pediatric population, as it does in the adult population, confers an increased morbidity and mortality on those affected compared to the general population. The five-year survival for all pediatric ESRD patients evaluated from 2003 to 2007 was reported as 89 % with the youngest age groups having the lowest overall survival. The one-year survival for ESRD patients aged 0–1 years old is 88.9 %; it increases slightly with age being 95 % for ages 2–5, 97.5 % for ages 6–12, and 98.2 % for those older than 12. The three-year survival for these patients by age group is 75.1 %, 89.6 %, 94.3 %, and 95.4 %, respectively. Finally the five-year survival for those ages are 75 %, 86 %, 90 %, 94 %, respectively. Broken down by modality of treatment, the reported survival is highest for transplant patients which have a five-year survival of 95 %, followed by peritoneal dialysis patients whose 5-year survival is 81 %, and finally 76 % for hemodialysis patients.

The causes of mortality for pediatric ESRD patients are multiple; however, the most commonly cited cause is cardiopulmonary complications, responsible for 21 % of all deaths. Characterized by age, cardiopulmonary disease claims 22.8 % of all deaths in children aged 0–1 years old, 18.3 % for those aged 2–5, 19.1 % of ages 6–12, and 22.1 % of deaths in children 13 or older. The next most common culprits of mortality in pediatric ESRD patients are infections, of which bacterial infections account for 11.1 % of deaths. By age, infectious causes are responsible for 14.6 % of deaths for children 0–1 years old, 9.9 % for those aged 2–5, 5.7 % for those aged 6–12 years old, and 12.9 % of deaths among children aged 13 or older.

Morbidity in ESRD pediatric patients is another serious issue, leaving room for improvement. Pediatric ESRD patients average 1.5 hospitalizations per patient per year. Comparing the two latest USRDS reporting blocks 2002–2006 and 2007–2011, there was an increase in all-cause hospitalizations of 17.2 %. When grouped by mode of renal replacement therapy for the same time block periods, there was an increase in cardiovascular-related hospitalizations by 33.9 % among hemodialysis patients and by 24.5 % among peritoneal dialysis patients, while transplant patients had a decrease in cardiovascular-related hospitalization of 7.8 %. In terms of infectious-related hospitalization, there was a decrease of 4.9 % among hemodialysis patients, while both peritoneal dialysis patients and transplant patients had an increase in infection-related hospitalization by 4.3 % and 25 %, respectively.

Etiology of ESRD on the Pediatric Population

The USRDS compiles a broad table depicting the categories and individual diagnoses responsible for ESRD in children. This data shows little change in the etiologic patterns for ESRD in the latest reporting period compared with previous years. The current reports include data from 2008 to 2012 and compare it to previous reporting period of 2003–2005. The leading group of disorders responsible for ESRD in patients aged 0–19 is cystic/hereditary/congenital disorders accounting for 38.3 % of cases in the current time period (compared to 33.5 % in previous time period). This is followed by glomerular diseases which are responsible for 23 % of ESRD (24.7 % previously) and secondary causes of glomerulonephritis attributed to 11.3 % of patients (11.4 % previously). The most common individual diagnosis causes of ESRD include renal hypoplasia/dysplasia (11.9 %), congenital obstructive uropathies (8.8 %), specifically of the uteropelvic junction (0.7 %), uterovesical junction (0.9 %), focal glomerular sclerosis (12.4 %), and lupus erythematosus (5.7 %).

African American children have a significantly higher percentage of certain nephropathies related to systemic diseases. African American children make up 90 % of all children affected with sickle cell nephropathy. Human immunodeficiency virus (HIV)-related nephropathy patients

in the current reporting period are 100 % African American which is an increase from 86.4 % in previous reporting years. Finally among those affected by lupus nephropathy, 59 % are African American (increased from 50.4 % in previous years) (Fig. 24.1).

Patient Selection

Despite having the knowledge that fistulae are better than catheters, many parents and/or patients still select catheters over fistulae in the pediatric population. This may be as a result of a multiple issues, preconceived notions, or unintentional provider bias [5]. The selection of access for initiation of treatment depends largely on what information is provided by caregivers but also relies on preconceived notions about ESRD, parent and caregiver biases, and the age and maturity of the child. When evaluated by vascular surgeons, many of these children already have CVCs in place and have initiated hemodialysis. Regardless, there should be a complete discussion of the benefits of AVF over CVCs, and ample time for making an informed decision should be given.

While anecdotally there are many factors that limit placing AVF in children, few studies have been done to study these barriers. A recent publication by Chand and colleagues describes some of these barriers and identifies communication issues between providers as a major issue, in addition to lack of standardized referral practices for CKD patients, lack of standardization as to whom the patients should be referred to, and finally lack of early communication between surgeons and interventional radiologists and dialysis staff (nephrologists, nurse practitioners, dialysis nurses) regarding problematic fistulae [5]. Similarly, few studies have assessed the psychosocial aspects of decision-making in choosing a form of dialysis access in the pediatric population. As one might imagine, for younger patients the decision is up to the parents and caregivers, which may place a huge burden on them. Once a child is able to express desires and dislikes, even without necessarily completely understanding all the options, the decision is often left up to them or at least made with their preference in mind. In our own practice, some of the reasons given a patient might not want a fistula include fear of needles, inability to wear jewelry at the site of an AVF, inability to participate in sports, ugly appearance of fistulae, and desire for the fistula to remain unseen. Parents also voice concerns with fistula placement which include the uncertainty of knowing what is best for their child despite receiving all the data supporting fistulae over catheters and the hope that a more "permanent" solution is approaching and that the "bridge to transplant" could be accomplished with a central venous catheter. In another survey by Brittinger and colleagues, assessing the pediatric patients' discomfort with cannulation, 39 % of patients reported no discomfort, 39 % had tolerable discomfort, and 22 % reported great discomfort. Interestingly, 95 % of the participants reported they would prefer not to revert to central venous catheter for access [6].

Larger studies are needed to identify barriers to fistula placement, and even further projects are needed to address these barriers and offer solutions. Despite having the knowl-

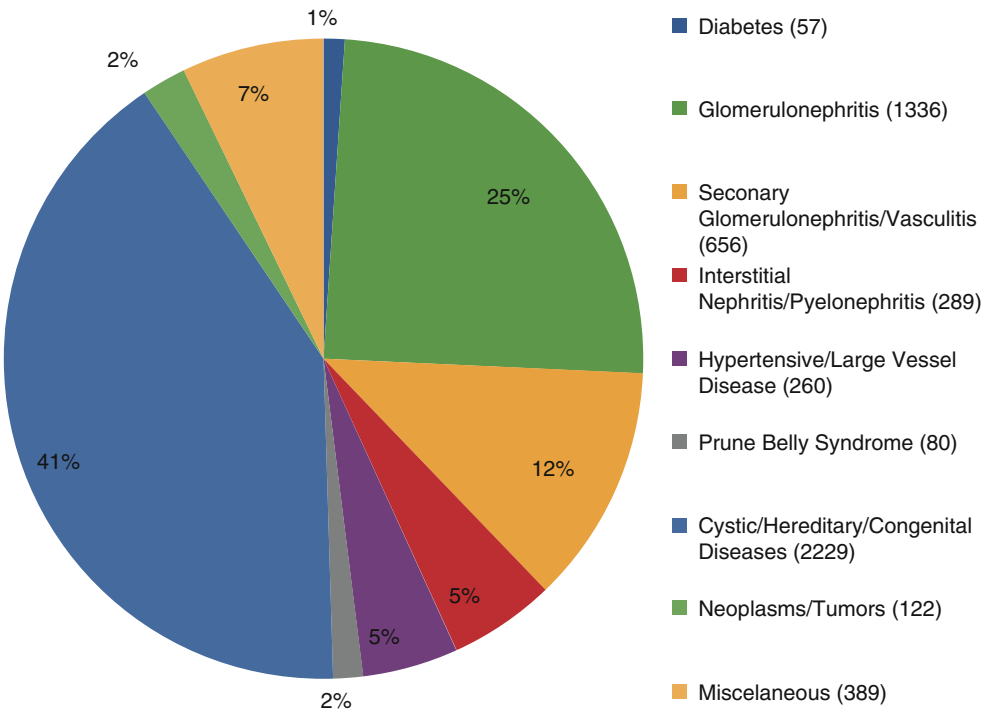

Fig. 24.1 The reported major etiologies of end-stage renal disease in pediatric population, with respective proportions of each etiology

edge that autogenous access is better than CVCs, many patients and families still select CVCs over AVFs for access. As providers we use CVCs first in 90 % of the pediatric population, and thus both patients and their caregivers may be resistant to change or to undergo another (more invasive) procedure once a central venous catheter is in place. Efforts to educate families at an earlier stage, before initiation of any treatment, should be pursued. A campaign to place AVF in patients months before they start dialysis is ideal; thus, nephrologists and surgeons should communicate frequently and early about these patients such that AVF surgery can be completed in a timely fashion.

Central Venous Catheter Use in the Pediatric Population

Several studies have investigated the reasons for CVC preference among pediatric patients undergoing hemodialysis. Fadrowski and colleagues retrospectively analyzed a cohort of 1,284 patients from 2001 to 2003 [7]. In this cohort, 755 (59 %) had a central venous catheter. The reasons given for choosing a central venous catheter included "small body size" in 142 (18.8 %), having "maturing" AVF/AVG in 53 (7 %) patients, and a "transplant scheduled" in 83 (10.9 %) of patients. Among these 755 patients, 32.2 % did receive a transplant within the year. In another retrospective cohort study published in 2006 by the same group looking at ESRD patients aged 12–18 years old receiving HD for the year 2000, the authors quantify the increased risks attributable to CVCs compared to patients with arteriovenous fistula [8]. The authors included 418 patients, 41 % of whom had an arteriovenous fistula or graft and 58 % had central venous catheter. Data analysis revealed an increased relative risk among central venous catheter patients with regard to all-cause hospitalization (RR 1.84 CI 1.38–2.44), hospitalizations due to infections (RR 4.74 CI 2.02–11.14), and complications of vascular access (RR 2.72 CI 2.00–3.69).

The durability of CVCs, while improved in recent years with smaller profile catheters, still remains inferior to AVF and averages between 4 and 10 months and in some cases is under 1 month. Several groups have published data on the longevity of CVCs and investigated the reasons they fail [9–11]. Central venous catheter durability ranges from 0 to 62 % at 1 year, and failure is attributed to infection (17 %), thrombosis (33 %), extrusion (5.4 %), and kinking (which is more common in smaller catheters). In general, cuffed catheters carry a lower risk of infection and have a longer durability (months) when compared to non-cuffed catheters.

One of the major long-term complications of central venous catheter placement is central venous stenosis. In an attempt to minimize this complication, NKF-KDOQI has delineated management in the event that a central venous catheter is placed in children [12]. The recommendation lists, in order of preference, the right internal jugular vein, right external jugular vein, left internal and external jugular veins, subclavian veins, femoral veins, and finally translumbar and transhepatic access to the IVC.

The prevalence of central venous stenosis associated with a history of subclavian central venous catheter placement is 25–50 % [3, 13–15]. In a recent case report, the author brings to light the fact that central vein stenosis might be grossly underdiagnosed, and as surgeons we likely are only seeing the cases that are significantly stenotic enough to cause symptoms [15]. In this report, however, it is not only hemodialysis-related access which was identified as a risk factor for developing central venous stenosis but rather the use of both tunneled and non-tunneled dialysis catheters, peripherally inserted central catheters (PICC), as well as other CVCs and ports. The length and duration of the catheter and multiple catheters are two factors most closely associated with developing central venous stenosis. A 2012 retrospective review evaluated failure rates of arteriovenous fistulae in adult patients with a history of ipsilateral vs. contralateral catheters [14]. Their results indicate that while maturation times and primary failure rates were similar in both groups, there was a lower cumulative fistula survival at 2 years in patients with ipsilateral catheters compared to contralateral catheters (54 % vs. 74 %). This result is echoed in other publications in the adult population [3, 15, 16]. This phenomenon however has not been demonstrated in the pediatric population. In a study by Wartman and colleagues, catheter history did not affect patency of arteriovenous fistulae after surgery [17]. Thus if a pediatric patient has had a central venous catheter, this does not become a contraindication for ipsilateral arteriovenous fistula creation, although if central venous stenosis is clinically suspected, it should be ruled out as this could confer long-term complications.

Central Venous Catheter Technical Considerations

Central venous catheters may be either non-tunneled or tunneled. These can be placed percutaneously under moderate sedation and local anesthetic; however, tunneled catheters in the pediatric population often require general anesthesia to ensure patient compliance.

Major challenges in establishing central venous access for hemodialysis in children are that there are no evidence-based rules for selection of catheter size and that the pre-curved catheters commercially available for children are limited to larger sizes. Larger catheters offer higher volumes during dialysis, but the size of the child and his or her vessels limits the size of the catheter that can be used. Catheters that are smaller mean that the length of dialysis sessions has to be

longer with slower flows. A useful formula that has proved safe in selecting catheter size is [Size (Fr) = Age +/− 2]. Taking the age of the child and converting it to the diameter, in French measurement, with adjustments after physical examination of the child to reduce the size if the patient is small for age or increase size if the child is larger than peers the same age. Pre-curved catheters available for the adult populations make percutaneous and subcutaneous tunneling possible; however, these catheters are largely not available in the smaller sizes for the youngest of pediatric ESRD patients. In these patients placing a tunneled central venous catheter usually means forcing the curve during placement and making one or more counter incisions over the access vessel for accurate and precise placement.

AV Access Use in the Pediatric Population

AVF is the preferred form of access for pediatric patients undergoing hemodialysis as AVFs have superior outcomes when compared to CVCs. In a recent retrospective review, 93 pediatric patients aged 3–19 (mean 14 years old, 70 % male, weight ranged between 12 and 131 kg) undergoing fistula operations were reviewed. In this review, 82 % of the patients were already receiving hemodialysis at the time of surgery for an average time span of 18 months. Most of the patients (78 %) had a history of central venous catheter placement, and 24 % of these patients had multiple catheters placed. The group performed 101 fistula procedures: 43 radiocephalic AVF, 29 brachiocephalic AVF, 20 basilic vein transpositions, and 9 femoral vein transpositions. The primary and secondary patency rates were 83 % and 92 %, respectively, at 2 years and 65 % and 83 %, respectively, at 4 years. Older age was shown to correlate with improved primary patency [17].

Many others have published on the feasibility of placing arteriovenous fistulae in pediatric populations with good outcomes. Bagolan and colleagues described their experience placing Cimino fistulae in children and reported a 4-year follow-up with 63.5 % patency and a complication rate of 35 % of which thrombosis was the most common [18]. A retrospective review in a single institution demonstrated that IPFFI is feasible in a pediatric population and also reported on the successful use of the operating microscope in small children [19].

Arteriovenous Fistula Access: Technical Considerations

As with central line placement, the NKF-KDOQI publishes guidelines for a structured approach for the placement of AVF access [12]. The recommended order for arteriovenous fistula in the pediatric population is as follows: radiocephalic AVF, followed by brachiocephalic AVF, and lastly basilic vein transposition. The techniques for standard radiocephalic, brachiocephalic, and basic vein transposition AVFs are widely described and discussed in different chapters in this book. When applied to the pediatric populations, there are some additional considerations. As in the adult population, planning of access starts with a complete history including previous central venous access use and a thorough physical exam with a detailed vascular exam and vein mapping on all patients. Vein mapping should then be evaluated by the operating surgeon for suitability of vein size. A size cutoff of 2.0 mm is acceptable in forearm veins, and 2.5 mm cutoff for upper arm veins has been shown to have success rate in maturation [17].

Vein imaging should also be routinely performed intraoperatively once the patient is placed under anesthesia. One of the attributes unique to pediatric vessels is their intense vasospastic response with handling. To reduce this response, tourniquet occlusion can be used for arterial control during fistula construction in lieu of arterial clamping. Additionally, based on surgeon preference an operating microscope might be used; however, loupe magnifications should be the standard of care in all pediatric fistulae. Standard end-to-side anastomosis using a continuous running monofilament suture is recommended in the pediatric population, while interrupted suture placement is not necessary.

Finally, transposition (brachial or femoral) can be performed in either one- or two-stage procedure. Groin fistulae have also been successfully placed in pediatric populations, in the setting of unavailable upper extremities or patient preference as described by Gradman and colleagues. The technique for this is similar to that described in adults [20]. The reported primary patency for the femoral vein transposition was 100 % and 96 % at 1 and 2 years, respectively, and secondary patency reported to be 100 %.

Future Outlook

In order to optimize the care and future of patients with ESRD, we propose to minimize interventions in children as much as possible. This means that all those involved in the care of a child progressing toward ESRD are mindful and plan ahead in order to foresee what the child will need in the future. Early referral to well-trained experts for thorough discussion on types of dialysis and treatment options, in addition to referral to vascular surgeons, is essential. Planning ahead can potentially prevent urgent use of short-lived, morbid, and potentially damaging CVCs. Given the information available to patients over the Internet or from personal acquaintances, one must be mindful of preexisting biases to ensure that each family gets accurate and complete

information. As our own experience with obtaining consent has demonstrated, decisions are often made by young teens or children who may not have gathered all of the necessary information to make the best decision. As permanent tunneled catheters may have longer durability and as the time to transplant is shorter compared to that in adults, children who present to a surgeon with a preexisting CVC may potentially avoid a second procedure if transplant comes prior to AVF placement.

If a child must have a central venous catheter because of acute presentation or personal preference, central venous catheter guidelines should be followed: placement in the internal jugular vein is preferred over the subclavian vein, and simultaneous referral to an access surgeon is recommended.

Fistulae in the pediatric population, including in very small children, are both technically feasible and have good long-term outcomes. Taking into consideration certain technical differences in the pediatric population, vascular surgeons can be equipped with the tools needed to be successful in fistula creation. Finally, remembering that diseases in children are psychosocially challenging for all involved, each child and his or her family must be given complete and accurate information, in addition to ample time to process this information, and support in making a decision.

Conclusion

The current state of establishing pediatric hemodialysis access is complex and has yet to become standardized. Both USRDS and NAPRTCS data indicate that a large majority of patients initiate dialysis treatment with CVCs despite published and peer-reviewed data indicating that arteriovenous fistulae are superior to catheters. CVCs are associated with more complications, hospitalizations, and shorter access life span when compared to arteriovenous fistulae. Since the initiation of the IPFFI, there has been little progress in the campaign to create fistulae first in children. A handful of barriers to fistula placement have been identified but remain to be addressed. The USA lags behind the international community in pediatric-arteriovenous fistula placement and use. Given that the majority of the pediatric population will likely outlive at least one transplant and return to dialysis, providers should avoid using CVCs given the long-term complications that can hinder the patient's access options in the future. CVCs should be reserved for urgent needs or for those who have a transplantation scheduled. Finally, educational material like that used in IPFFI should be widely distributed nationally and not limited to providers but also shared with patients. Each dialysis center should standardize their referral patterns and follow-up practices and, wherever possible, a vascular surgeon or a surgeon with expertise in microvascular anastomoses should be selected.

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Hemodialysis in the Morbidly Obese

25

Marlin Wayne Causey and Niten Singh

Introduction

The American population has had significant growth in two often overlapping patient populations over the past 20 years – obesity and end-stage renal disease (ESRD). Unfortunately, the coexistence of these two diseases is often interrelated due to the higher incidence of hypertension and diabetes in obese patients and the association with renal disease. Over the past 25 years, the United States has had a robust and steady growth of obesity and it has even been dubbed an epidemic [1]. Given the increasing proportion of the population becoming obese and its association with ESRD, hemodialysis access surgeons must become adept in techniques that create functioning hemodialysis access to minimize renal replacement that is performed through tunneled dialysis catheters [2]. Successful hemodialysis access creation is challenging, particularly in obese patients, as they have deeper anatomic vasculature, higher rates of wound infections, and a relative proinflammatory and prothrombotic state [3]. The National Kidney Foundation has established clinical guidelines aimed at using an evidence-based approach to improving outcomes for kidney disease and successful hemodialysis access [4]. The creation and maintenance of successful arteriovenous fistula (AVF) access in obese patients are often difficult as their obesity increases the depth of all anatomic structure, particularly their superficial veins for repetitive dialysis cannulation.

Even with a successful arteriovenous fistula (AVF) creation that subsequently matures, obese patients may find that the fistula cannot be consistently and reliably punctured by dialysis technicians who need dual access through an arterial and venous needle cannula. In patients with obesity, adjuvant techniques are needed for successful creation of functioning hemodialysis access. Given the depth of functioning arteriovenous fistulas, obese patients not uncommonly receive prosthetic grafts for access as these may be placed in an accessible subcutaneous plane. Patient selection and access choice based on anatomic information are paramount for successful hemodialysis access creation, and the appropriateness of individual access sites is important in providing a functional access site. In general, hemodialysis access is typically categorized as having a goal of achieving a mature, dialysis-capable autogenous fistula in the nondominant arm as distally as possible. The "rule of 6 s" is commonly used as criteria for access cannulation in that a matured and adequate vein is 6 mm in diameter, has a flow rate of 600 mL/min, and is at or less than 6 mm in depth (though unsuccessful and difficult access may reduce this distance even more) [5]. A major factor limiting the creation of successful autogenous fistulas in obese patients is having the fistula mature at a depth greater than 6 mm. Successful permanent hemodialysis access in obese patients often requires modifications or adjuncts to existing procedures in the creation of reliable hemodialysis access. It is for this reason that many surgical techniques have been targeted at this problem and this is therefore the focus of this chapter.

Dialysis Access in the Morbidly Obese

When creating arteriovenous fistulas in the upper arm, either brachiocephalic or brachiobasilic AVFs, surgical adjuncts are frequently needed in the obese patient. While surgical superficialization of brachiobasilic AVFs is routine practice, the need to superficialize brachiocephalic AVFs in larger arms or in those with anatomically deep cephalic veins is not uncommon. Once a fully matured autogenous arteriovenous

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fistula has been created, several techniques are available for superficialization.

Elevation Technique

This technique involves dissection of the arterialized vein (fistula) in the upper arm, closure of the subcutaneous tissue underneath the fistula, possible fistula transposition, and closing the overlying skin [6, 7]. This technique may be utilized with a number of different AVF configurations. Most commonly utilized for brachiocephalic AVFs, this technique has also been described with success using radiocephalic AVF, brachiobasilic AVF, and even femoral vein fistulas.

The fistula elevation procedure (FEP) begins with a longitudinal incision over the venous portion of the AVF that is desired for access. This venous portion of the fistula is then completely mobilized so that it may be elevated out of its anatomic bed. Once the vein is completely mobilized, the subcutaneous tissue is closed under the fistula (over the previous anatomic bed) with the fistula being placed in a subcutaneous position just underneath the skin. A subcuticular skin closure is then performed on the skin over the fistula. Once healed, the superficialized fistula is then accessed through the surgical scar.

Surgical Lipectomy

This is another less commonly employed technique in which pockets of subcutaneous fat are removed directly over the fistula through skip incisions and placed away from potential access sites and is less invasive than the elevation procedure [8]. In this technique, two transverse skin incisions are made directly over the vein, 8 cm apart. The adipose packet overtop of the vein is removed for 4 cm in each direction so that a total of 16 cm of adipose tissue is removed overtop of the vein. In this technique, skin hooks are used to elevate the skin, and dissection of the adipose is performed from the adipose subcuticular junction of the skin down to the periadventitial plane of the vein. The fat pad is then excised, a drain placed into the resultant empty space, and the incision closed with subcuticular absorbable sutures. This technique has been described for both arm radiocephalic AVFs and forearm radiocephalic AVFs. It is described to only use one incision for the forearm fistulas when only a short (8 cm) segment needs to be superficialized [9]. Access should not be performed for at least 30 days given the resultant dead-space creation and the possible risk of hematoma, to ensure appropriate healing of the skin to the underlying empty space.

Minimal Incision Superficialization Technique

Minimal incision superficialization technique (MIST) is a technique that has demonstrated utility in treating patients with matured AVFs in which the only correction needed is superficialization and may be used in all fistula configurations in the arm [10]. This technique is done by first performing an ultrasound and marking the anatomic location of the native vein and major venous branches that need ligation. A straight-line mark is helpful to later aid in the creation of the linear tunneling segment. Two small curvilinear incisions (2–3 cm) are made near the proximal and distal portion of the fistula with an ideal segment of vein between these incisions being around 10–12 cm. The proximal and distal venous fistula segments are isolated, and dissection is then carried along the superficial fascia along the entire course of the anterior surface of the fistula. The venous part of the fistula is then dissected circumferentially with ligation of branches using 6-0 monofilament ligatures. Vein orientation is ensured and often aided by marking the anterior surface to prevent twisting during the tunneling. Once the vein is fully dissected, the fistula is divided obliquely at the distal incision 1–2 cm from the anastomosis and brought out of the proximal incision. The fistula is then checked for retained valves, and if any are present, they are lysed with a valvulotome. The fistula is then tunneled in a subdermal plane in the previously marked straight-line section of the arm while maintaining proper orientation. The vein is then anastomosed to the beveled section of the vein, which minimizes anastomotic narrowing. The incisions are then closed in layers.

Suction Lipectomy (Liposuction)

The elevation and surgical lipectomy techniques involve significant surgical incisions, and as mentioned previously, the patients with obesity have higher rates of surgical site infections and delayed wound healing. Derived from the lipectomy procedure, suction lipectomy (liposuction) evolved as a less-invasive manner to reduce the skin to fistula distance utilizing the same surgical principle of keeping the incision away from the fistula and removal of excess adipose to minimize fistula depth [11]. The goal of the liposuction superficialization technique is targeted at the latter goal to attempt to superficialize a matured brachiocephalic AVF that is too deep for successful, consistent, and repetitive hemodialysis access.

While all of these techniques are possible for superficialization, liposuction is the least invasive, has the shortest incision length, and likely requires the least amount of surgical time. Liposuction superficialization requires proper patient selection with the plan for superficialization during the pre-

operative evaluation, utilization of continuous and direct ultrasound guidance, and adequate suction lipectomy to reduce the skin to fistula distance, thereby creating an adequately superficialized AVF.

The necessary supplies for liposuction superficialization are a linear array ultrasound transducer and the supplies listed in Fig. 25.1. This procedure may be performed under almost any type of anesthetic: general, regional, or local anesthesia. The initial description of this procedure was under general anesthesia, but any type of anesthetic that provides the ability to manipulate and remove subcutaneous fat is possible [11]. This procedure is also possible without the assistance of a plastic surgeon, though the operating surgeon must be facile at ultrasound-guided procedures.

The procedure begins with ultrasound visualization of the AVF, and an indelible marker is used to mark its course (Fig. 25.2). Ultrasound-guided tumescence technique is performed with a Klein pump, 18-gauge needle, and the tumescent solution (50 mL of 1 % lidocaine mixed with 1:100,000 units of epinephrine) in order to infiltrate the subcutaneous tissue overlying the AVF. This provides analgesia (lidocaine) and also some vasoconstriction (epinephrine) of smaller blood vessels for hemostasis and a less-systemic lidocaine effect. Adequate tumescence is confirmed by ultrasonic evidence of separation of the skin from the AVF accompanied by a firm turgor to the soft tissue (Fig. 25.2). The key principle is to infiltrate directly over the AVF and in the medial and lateral adipose tissue to allow for liposuction directly over the fistula and along the sides in order to create a visual and palpable "adipose valley." Essential to the procedure is facility with ultrasound techniques as continuous ultrasound visualization of the 18-gauge needle tip to avoid iatrogenic injury to the AVF.

Once tumescence is deemed technically successful, liposuction superficialization is performed under ultrasound guidance. A small incision is made proximal to the area of interest and away from the AVF (this ensures that a surgical infection would not be directly over the fistula). A 2-mm aspiration cannula attached to a 30-mL syringe is introduced into the subcutaneous soft tissue, and the overlying adipose tissue is aspirated under direct ultrasound guidance while keeping continuous negative pressure on the 30-mL syringe. The cannula tip is visualized in real time using ultrasound guidance while the surgeon's operative hand moves in a back and forth manner, similar to the technique when liposuction is performed in other anatomic locations. This adipose aspirate is removed directly overtop the fistula and in a radial manner suctioning the adipose tissue medially and laterally to create an "adipose valley" (Figs. 25.2 and 25.3). Adequate liposuction occurs when the AVF is easily palpable, and the fistula depth is decreased based on the ultrasound appearance and measurements.

The key to success during suction lipectomy is to perform the aspiration while continuously visualizing the tip of the cannula under ultrasound guidance. Loss of ultrasonic visualization has the potential to cause iatrogenic injury to the AVF. The lipoaspirate is adequate when there is an adequate "adipose valley" so that the fistula is easily palpable under the skin and should be visible through the skin. A post-procedure ultrasound will demonstrate a significant depth decrease of ideally 4 mm or less (Fig. 25.4). A completion ultrasound is performed to assess for injury to the fistula which would be seen with color flow Doppler and B-mode duplex (extravasation, hematoma, or pseudoaneurysm). Should these complications arise, management is dictated on ultrasound findings. Active extravasation from the fistula will likely require suture repair, while an isolated hematoma may respond to compression if there is no communication with the fistula (best visualized with color flow Doppler). Again, all of these complications are greatly minimized, and perhaps eliminated, by continuous ultrasound visualization of the cannula. Once the AVF is adequately superficialized, a sterile dressing is applied and the upper arm wrapped firmly in an elastic bandage while avoiding AVF compression. The elastic bandage is left in place for 72 h to provide continuous compression (not restrictive) and removed on the third post-procedure day. At 1 week, the arm is examined and AVF depth is assessed by ultrasound. Another ultrasound is performed at 4 weeks to assess for

18-Gauge needle
Klein pump (HK Surgical, Inc, San Clamente, California)
50mL of 1% lidocaine with 1:100,000 U of epinephrine
Bag of 950mL of Normal Saline
2mm Coleman Aspiration cannula (Byron Inc., Ruscon, Arizona)
30-mL syringe
Portable ultrasound (capable of M and B mode)
4-0 monofilament suture
Surgical dressing with ace bandage

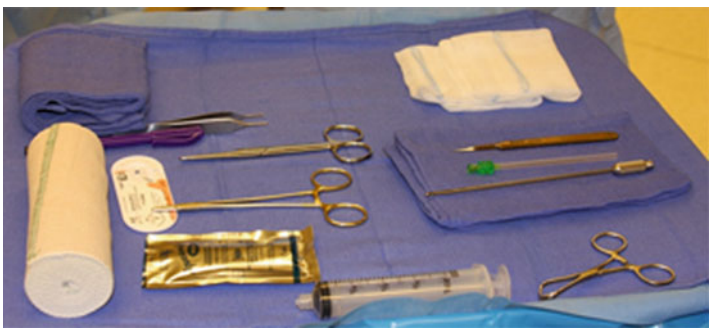

Fig. 25.1 Recommended supplies for the liposuction superficialization procedure

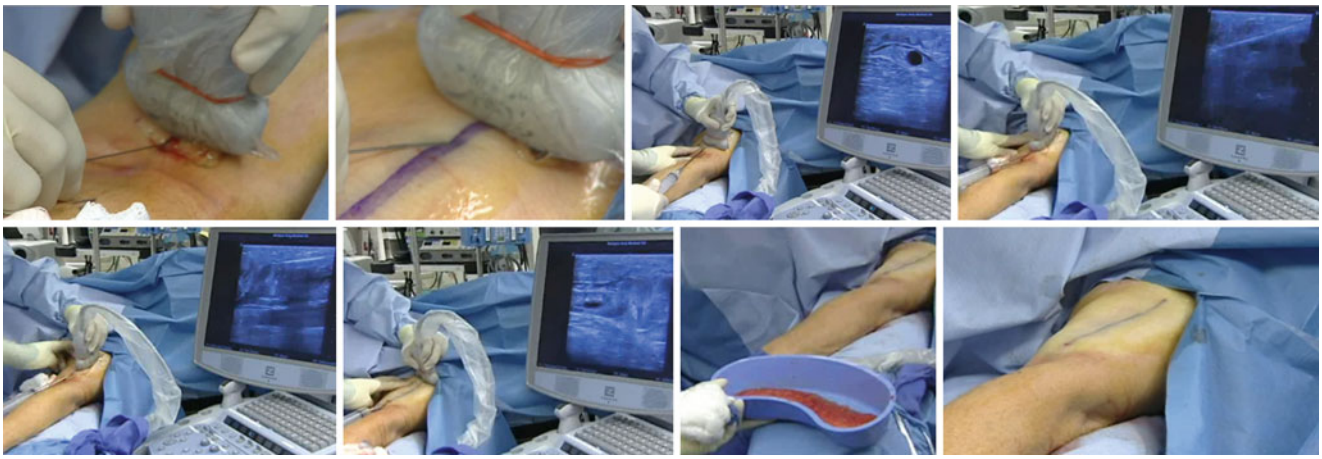

Fig. 25.2 Demonstration of infiltration of tumescent anesthetic solution. Adequate infiltration occurs when there is firm turgor in the subcutaneous tissue overlying the fistula and for 2 cm medially and laterally. Suction lipectomy being performed under direct and continuous ultrasound guidance. Not that when visualized in the long axis of the fistula that the tip of the cannula is easily visualized both directly and with acoustic shadowing. The *bottom middle image* demonstrates an axial view of the fistula which is often helpful in performing liposuction of the adipose tissue medial and lateral to the fistula so as to create a "valley." The *bottom right* pictures demonstrate adequate lipectomy when the fistula is easily palpable

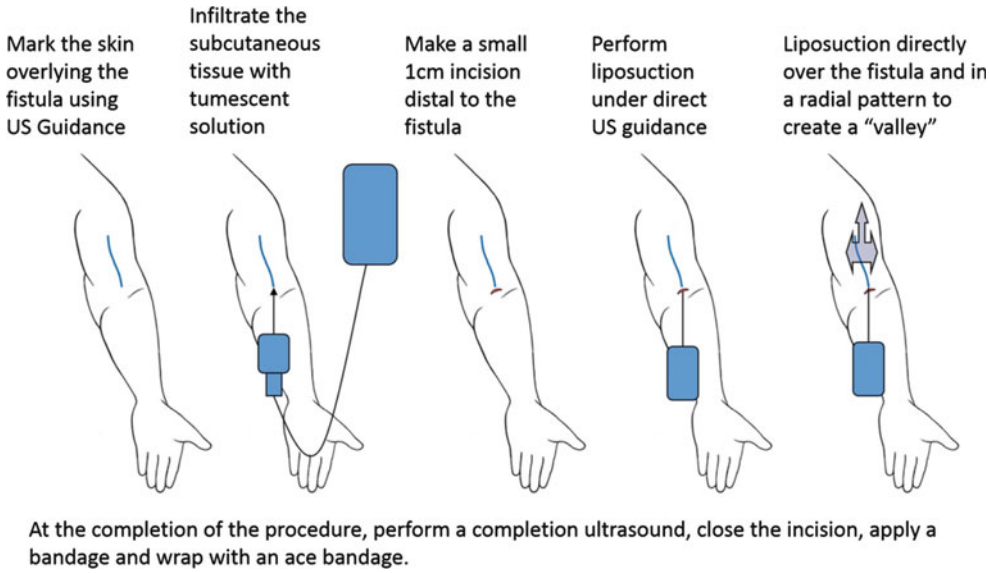

Fig. 25.3 Schematic of the setup and overall technique when performing liposuction superficialization

maturity and depth and clinical exam for wound healing, if necessary. Attempts at hemodialysis access may now be attempted if the arm is healed, the AVF mature, and the superficialization successful.

Data involving technical variations and outcomes of liposuction superficialization are mostly case reports. There are several other adjuncts that deserve mention such as the use of an endoscopic vein-harvesting device which serves as a shield for the fistula during adipose aspiration [12]. Another technique involves decremental liposuction cannulas beginning with a 4-mm cannula and progressing to smaller diameters as the subcutaneous tissue volume decreases [13]. Published outcomes for this technique are very sparse, but one retrospective study found that liposuction superficialization of radiocephalic and brachiocephalic AVFs led to an 85 % successful two-needle (17-gauge) cannulation rate at 33.7 days post-procedure. Increased body mass index correlated with a higher rate of surgical site infections and delays in successful cannulation [14].

Dialysis Access Grafts in Patients with Obesity

When autogenous access creation is not possible, arteriovenous grafts (AVGs) are necessary for successful hemodialysis access. Dialysis access comes in many different

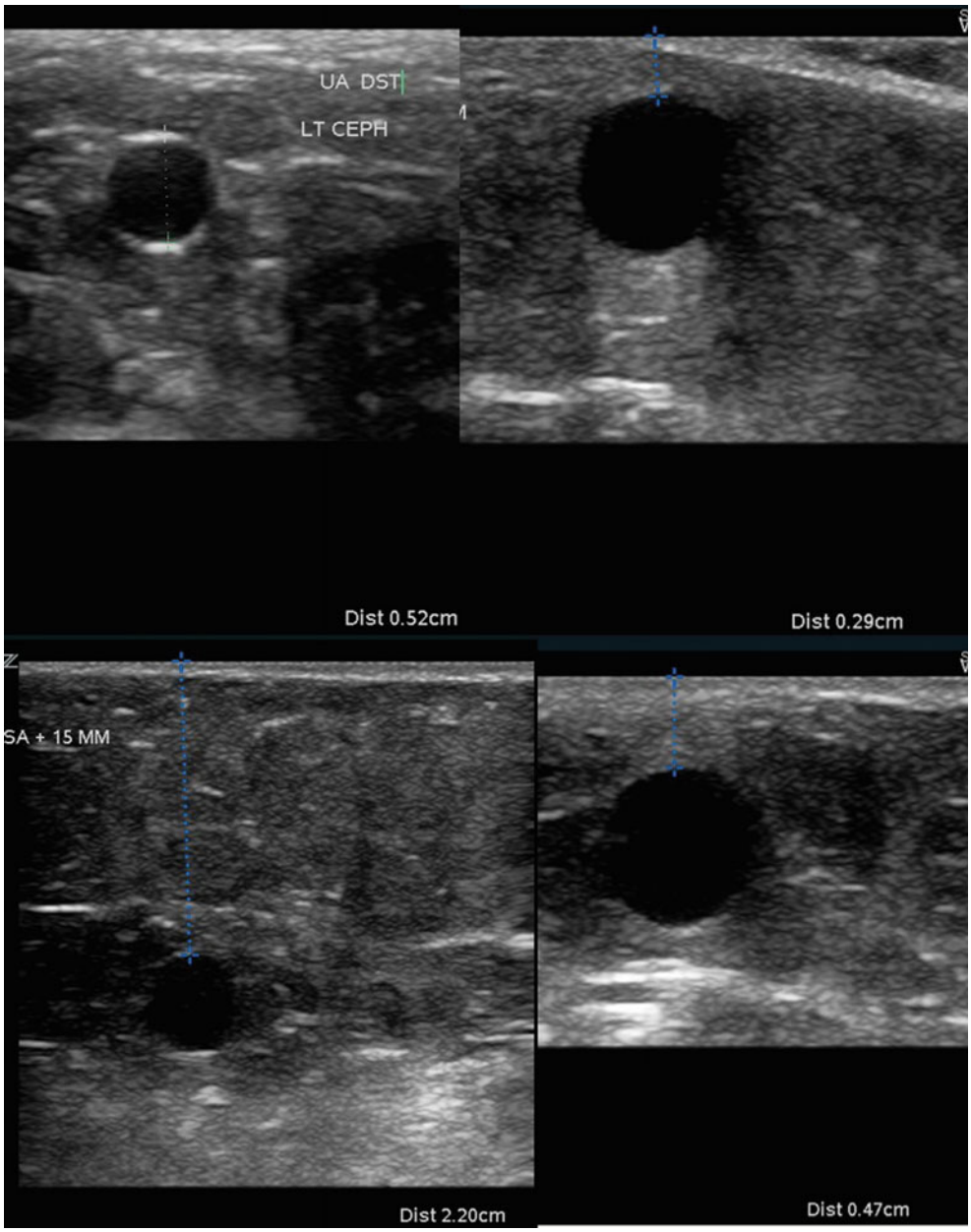

Fig. 25.4 Ultrasound of the fistula is seen before (*left*) liposuction superficialization and at 1-week ultrasound (*right*)

configurations, and the specifics for hemodialysis-graft creation are described in other chapters. AVGs are not the preferred method of permanent dialysis access and should be reserved for patients with anatomic constraints. However, it is necessary to place AVGs in obese patients, and there are some procedural adjuncts that are useful when creating permanent hemodialysis access. One consideration in the patient with obesity is to perform a forearm-loop graft. This type of graft has several advantages. First, there is commonly less adipose tissue present in the forearm than in the upper arm. Given the decrease in adipose tissue in the forearm, this is often an advantageous graft in patients with good-quality brachial vein but failed or poor-quality superficial arm veins. It is often advantageous to perform a diagnostic venogram of the upper extremity to identify dialysis vein targets, particularly in the deep veins of a large arm as anatomic depth may limit visualization. A venogram should be used with caution when patients are not on dialysis.

When placing hemodialysis access in the upper arm of obese dialysis patients, standard dialysis graft surgical techniques should be performed. There are, however, two special techniques that should be performed as an adjunct during the first operation. The first, similar to AVG placement in other populations, is to ensure that the tunnel is created in a subcutaneous plane that can be easily accessed by dialysis technicians. Given the increase in the wound complications in patients with obesity, keeping the skin

incision away from the tunnel is very important. One useful technique is to make tunneling counter incisions lateral to the proposed tunnel. The subcutaneous tissue is mobilized medial to the incision and this used as the proposed site of the tunnel. Using this method, if there should be a surgical site infection, the incision will be away from the prosthetic graft. The second adjunct is to push down the adipose tissue over the tunneling device once it is in place so as to even further minimize the amount of adipose tissue between the skin and the graft. By manually compressing the skin over the tunneler, a modest amount of adipose displacement is possible, and this will serve to further superficialize the tunneled graft.

Central Vein Stenosis in Patients with Morbid Obesity

Endovascular techniques in the patients with morbid obesity require no further adjunctive procedures with the exception of understanding that increased radiation is necessary to image structures in patients with obesity.

When central vein stenosis becomes refractory to endovascular techniques or has progressed to the point of hemodialysis access loss, alternate methods of dialysis access in the arm are necessary as lower hemodialysis creation in obese patients should be avoided if at all possible. The reasons for avoiding lower extremity placement are decreased cleanliness of the area, increased intertriginous folds, and sometimes difficulty in maintaining a semi-recumbent and comfortable fistula during dialysis sessions. For these reasons, the Hemodialysis Reliable Outflow (HeRO, Cryolife, Kennesaw, GA) graft should be considered when dealing with central vein stenosis in the obese patients.

One situation for which the HeRO graft is well suited is when there is a functioning upper arm arteriovenous fistula access. If this is near the antecubital fossa, a HeRO graft may be originated from the already preexisting fistula. In patients with an obese arm, a percutaneous approach to the axillary vein is beneficial to avoid dissection and dead-space creation in obese arms and minimize the extent of the incision and potential for wound infection from an axillary incision. In order to do this, the arterial origin should be dissected and isolated; once this is done, a 3-cm incision is made at the point that the HeRO graft central components will be placed. The vein is access with a micropuncture needle and a 5-Fr sheath placed with placement of a soft guide wire into the inferior vena cava, contrast confirmation, and switching to a stiff wire (Fig. 25.5). Once in place, the HeRO graft central components are placed into position, and the graft is connected using the supplied-coupling components. Since this is often the pri-

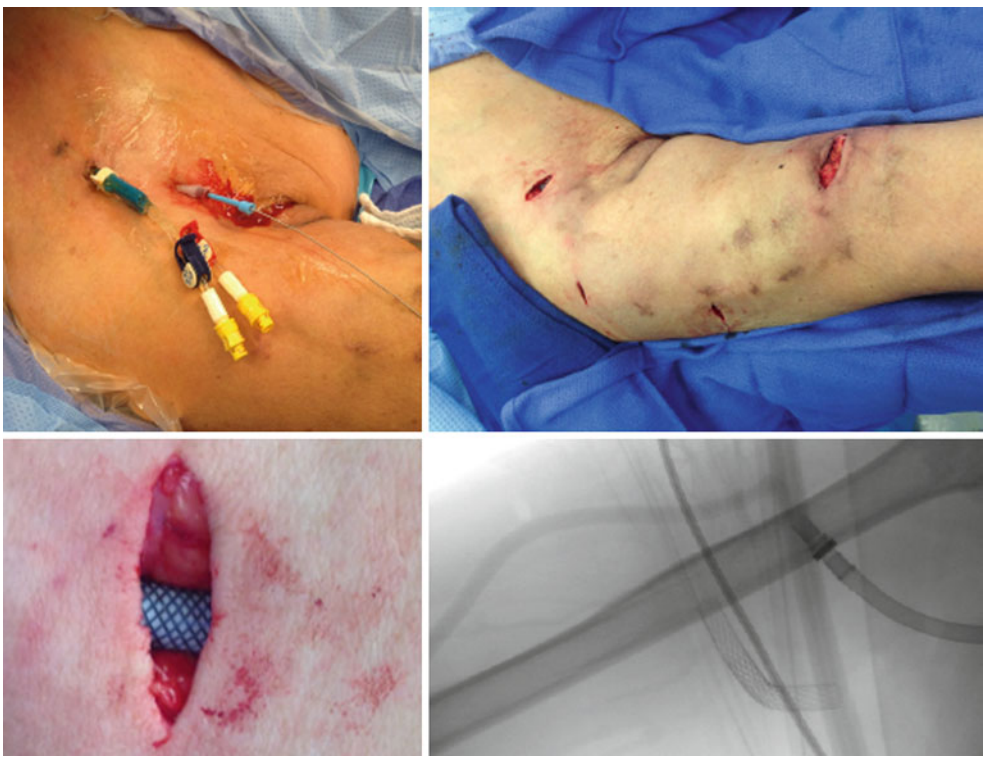

Fig. 25.5 Placement of a Hemodialysis Reliable Outflow (HeRO) graft in an obese patient using a percutaneous method. In this case, the central components were placed through a percutaneous axillary vein technique and the proximal portion anastomosed to the brachial artery just above the antecubital fossa

mary access for patients, it may be useful to sew an immediate access graft (such as AccuSeal, W. L. Gore, Flagstaff, AZ) to the supplied graft to allow for immediate access. The graft should be brought through the tunnel and fluoroscopy performed to confirm proper central positioning and the arterial anastomosis completed (Fig. 25.5). Pressure may be required at the venous access site for hemostasis, and it is for this reason and the increased depth in the obese neck that heparin administration should be minimized or even eliminated.

Conclusions

Obesity presents many challenges in the creation of successful hemodialysis access. Patients with obesity have deeper anatomic structures, and the additional subcutaneous adipose tissue requires modification of existing procedures and adjunctive procedures for superficialization. Liposuction superficialization of brachiocephalic fistulas provides an adjunct technique in the armamentarium of superficialization procedures. Success in this technique requires proper patient selection, continuous ultrasound guidance for tumescent infiltration and suction lipectomy, and adequate lipectomy to create an "adipose valley" and palpable fistula. Other adjuncts have been described for this technique such as fistula protectors and the use of different, graduated cannula diameters. Initial reports have demonstrated high rates of successful two-needle cannulation using this technique, but complications may limit success in high body mass index patients. However, compared to other described techniques for brachiocephalic fistula superficialization, this is the least invasive. When autogenous fistula creation is not possible, grafts are necessary, and special adjuncts particularly with tunneling technique are required. When patients present with central venous stenosis or occlusion, alternative upper extremity hemodialysis access is preferred over lower extremity access. In these situations, HeRO grafts have a role in the successful creation of functioning dialysis access, and the use of an immediate access graft, appropriate tunneling, and a percutaneous axillary vein access are valuable adjuncts in patients with obesity. Obesity may complicate the successful placement of functioning hemodialysis access, but many techniques are available to assist in the creation of successful permanent access.

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Creating Hemodialysis Access in Intravenous Drug Users: A Vascular Surgeon's Perspective

26

Nam T. Tran

Introduction

The typical hemodialysis patient has numerous associated medical comorbidities, and it can be challenging to provide these patients with reliable hemodialysis access. Even more challenging is the issue of providing hemodialysis access in patients who are intravenous drug users (IVDU). This population can be difficult as they present with multiple comorbidities, limited autologous vein for fistula creation, a limited social support system, and high rate of medical noncompliance.

While it is important to provide durable, functional access for renal replacement therapy, patients with IVDU addictions present the access surgeon with ethical challenges in addition to anatomic challenges. The delivery of optimal care to these patients requires collaboration between the access surgeon, the patient, the nephrologist, social services, and, at times, a medical ethicist [1].

The Patient

A subset of patients requiring hemodialysis access will be actively using or former users of substances of abuse. Substances of abuse can be wide ranging from marijuana to heroin, cocaine, and methamphetamines. Multiple routes of administration, including the intravenous route, are used. A recent report from the Centre for Disease and Control (CDC) suggests that despite successes in the "war on drugs," heroin abuse in the USA is still a widespread problem [2]. There are several reasons why creating hemodialysis access in these patients is challenging.

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Patients addicted to IVDU have often "burned" their superficial venous system from heroin, cocaine, or other injected substances due to the toxic impurities that are injected. As a result, not only are superficial veins as options for autogenous hemodialysis access limited, simple intravenous access is often a major problem, and these patients usually require central line placement for venous access when presenting for medical care. Hence, the possibility of central venous stenosis should be entertained in all of these patients during evaluation for hemodialysis access. Lastly, a high percentage of these individuals will have had previous incision and drainage (I and D) procedures for abscesses associated with subcutaneous drug injection. The upper extremities in these patients often have numerous scars, posing additional challenges in accessing arteries and superficial or deep veins for the creation of arteriovenous fistulas (AVF) or in tunneling arteriovenous grafts (AVG).

Finally, these patients often have lack of an adequate social support system, have underlying psychiatric disorders such as schizophrenia, and have not had routine medical care. They are often noncompliant: clinic and surgical appointments are missed; they do not follow postoperative care plans, etc. Resources that are needed to ensure that the substance abuse patient can be supported and receive adequate psychiatric evaluation are limited due to lack of funding, personnel, and the general stigma associated with this patient population.

General Approach

In order to provide optimal and consistent care of the IVDU patient with renal failure, each access surgeon must have clear policies in place. These should include collaborative efforts between the surgeon, the patient, the nephrologist, the patient's primary-care physician, and likely a social worker.

In our practice, individuals actively using intravenous drugs – as documented by a positive drug screen – will be refused surgery for hemodialysis access. We have developed

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this policy due to multiple complications associated with active drug users, who usually lack superficial veins and often inject into their dialysis access. The access then not surprisingly becomes infected and requires urgent removal. Additionally, we have had experiences with patients who present with exsanguinating hemorrhage either due to disruption of the vascular anastomosis from infection or in the graft from access. In this urgent or emergent setting, we needed to reconstruct the arterial site, ligate the venous site, and remove the entire infected graft. In the worst-case scenario, the infected graft can lead to an arterial "blow out" due to infection at the site of arterial repair and also to distal hand ischemia.

For patients with a history of drug use, our practice requires repeated evaluation to ensure that the patients can be in compliance with general medical care and also to ensure that they do not relapse. At each monthly visit, the patient is asked to provide a sample for drug screen. If the patient can demonstrate compliance and a drug-free history for three months, then we proceed with evaluation for hemodialysis access placement. Unfortunately, many patients cannot comply with this policy. These patients unfortunately require a tunneled catheter as a way to receive hemodialysis and are at high risk of catheter infection and catheter-associated bacteremia. These difficult cases are appropriate for discussion and planning at a monthly multidisciplinary committee meeting between access surgeons, nephrologists, social workers, and dialysis nurses.

Operative Considerations

As mentioned previously, central venous stenosis is a common finding in those with a history of IVDU. A high index of suspicion, careful history to determine whether or not the patient has had previous central catheterization, and liberal policy regarding central venogram at time of AV access creation are used to ensure that one does not miss occult central venous abnormalities. In our practice, all patients undergo preoperative vein mapping as well as arterial duplex evaluation of the upper extremity. Based on the results of these exams, the access surgeon can pick the optimal site and type of access for both functional success and long-term durability.

In the majority of cases, we find that there are no superficial veins available for autologous arteriovenous (AV) fistula creation in the IVDU population. Polytetrafluoroethylene (PTFE) is our preferred conduit for AVG creation. In these cases of prosthetic vascular implant, it is important to ensure that the patient has no risk factors for seeding the graft with bacteria and increasing the risk of infection. The patient should be examined to ensure that there are no open wounds, dental infection, or active catheter-related infection. The risk of bacteremia and bacterial seeding of a newly placed graft is high, and surgery should be deferred until the active infection has been completely treated.

Ethical Consideration

Without durable hemodialysis access, the renal patient cannot survive. Over time, the use of tunneled central venous catheters can result in bacteremia with associated high morbidities as well as central vein thrombosis or stenosis. As such, most dialysis centers will try to transition patients to an AVF or AVG with catheter removal as soon as possible. At the same time, the access surgeon is faced with the dilemma of placing an access that potentially can get infected and results in anastomotic disruption and exsanguination, limb ischemia, or other potential devastating complications.

This raises important ethical questions:

1. Is it medically ethical for the surgeon to refuse to place access, or, by doing so, is the access surgeon withholding potentially life-saving treatment?
2. What are the rights and responsibilities of the access surgeon when performing a procedure in a patient who will likely inject into the access with potentially lethal consequences?

These are the questions that should be asked, debated, and discussed within a multidisciplinary panel or committee on a patient-by-patient basis to optimize care for these patients. While there is no clear answer, one should be guided by the oaths we take as physicians of beneficence and nonmaleficence toward our patients.

In this regard, a good social support and outreach program is of paramount importance. This is often a challenge and, due to a lack of resources, is not always possible. Placing AV access in patients with active IVDU will likely fail and can potentially have devastating consequences. Additionally, these patients are not compliant, and maintaining three times per week dialysis can be a challenge for them. On the other hand, a patient with a tunneled catheter can have significant issues with repeated bouts of catheter-related infection and the development of central vein stenosis.

The solution to this dilemma is complex but often attainable. The primary goal is to get the patient to understand and acknowledge the problem by involving their family members as well as important care providers such as their primary-care doctor. A reliable support system with social

workers, drug rehabilitation counselors, psychologists, and case workers is critically important to ensure success. In the right setting and situation, the patient will be able to enter a rehabilitation program, be successful, and fully participate in a dialysis program with reliable hemodialysis access. While ideal, this scenario is dependent upon the significant funding and support required in organizing and maintaining a dedicated multidisciplinary access program.

Conclusion

Access creation in a patient with IVDU can be one of the most challenging problems facing the access surgeon. Not only are there anatomic and surgical barriers, but also there are ethical challenges that the surgeon will need to deal with, as well as issues of medical noncompliance, psychiatric illness, and a general lack of medical care. A multidisciplinary approach with a strong support system will be critical to ensure that one can deliver the best possible care to this difficult patient population.

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Part VI

Hemodialysis Access Dysfunction and Advanced Techniques

The Immature Arteriovenous Fistula

27

Dean Klinger

Overview

According to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, AVF maturation is considered clinically successful if 6 weeks after surgery, the fistula supports a flow of 600 ml/min, is located at a maximum of 6 mm from the skin surface, and has a diameter of at least 6 mm [1]. The ultimate goal of a mature AVF is one that can provide adequate vascular access for adequate hemodialysis. To define success by this clinical end point alone is markedly simplified but takes into consideration a whole host of factors. Factors include vein size, depth, length, tortuosity, and frailty, as well as flow in the AVF and patient size. The characteristics of the vein take into consideration the ability to successfully cannulate the AVF. Sizes as small as 4 mm or depths greater than 6 mm have both been reported as adequate; however these dimensions push the limits of cannulation. Adequate AVF flow rates are patient and dialyzer dependent, with flow rates as low as 400 ml per minute sometimes reported as adequate. This may be true if the patient is small without much muscle mass. Obviously, higher flow rates in the AVF and flows to the dialyzer will give better clearance in a shorter period of time. This may be needed particularly in a patient that is large and has much more muscle mass. Hence, to clinically define a mature AVF as one that can provide adequate hemodialysis is very simple and tailored to the patient.

Multiple studies have reported an AVF maturation failure rate range from 20 to 60 % [2–7]. A well-functioning AVF is clearly a superior conduit for hemodialysis. It achieves higher patency rates, has fewer complications, and has lower risk of infection than synthetic arteriovenous (AV) grafts and central lines [8–12]. The Fistula First Initiative and Dialysis Outcome Quality Initiative guidelines were created to help guide and direct vascular access surgeons to create AVFs. KDOQI guidelines suggest starting with forearm veins and then progressing more proximal in the extremity as the need arises [1]. This being said, approximately 20 % of patients expire in the first year after initiating hemodialysis [11]. Obviously, we cannot predict which patients are in the 20 %, but if a patient looks weak and unhealthy, consideration should be given to start where there is the greatest likelihood of successful maturation of an AVF. KDOQI guidelines suggest that arteries 2 mm and a vein 2.5 mm in diameter can be used [1]; however arteries and veins that are larger have a higher likelihood to mature. Given the clinical scenario, it may be prudent to create the best fistula with greatest likelihood of success at the first operation using the best artery and vein available.

A newly created AVF is expected to be useable within 6–8 weeks. Postoperatively, the potential for an AVF to mature can be determined by as early as 4 weeks and most often by 8 weeks. Waiting an extended length of time very rarely results in further maturation. The time-honored tradition of giving patients balls to squeeze or exercise to do in the hopes to aide in the maturation process of an AVF is founded on minimal evidence. There are two studies that looked at a total of 23 and 14 patients [13, 14]. There were noted enlargement of the radial artery and some dilation of the vein, but these results have not been validated by larger or more recent studies. Having the patient do these exercises may have the benefit of engaging the patient in taking care of their fistula and assisting in the aide of its monitoring.

Evaluation

Various postoperative algorithms can be used to assess AVF maturation (Fig. 27.1). One example will be presented here. If 7–10 days postoperatively, the AVF is robust, it will likely mature nicely; the patient returns in 4–5 weeks with the expectation that the AVF will be used. If at the first visit, the AVF is suspected of not maturing, evaluate it with physical exam and ultrasound. Make an assessment as to why it may

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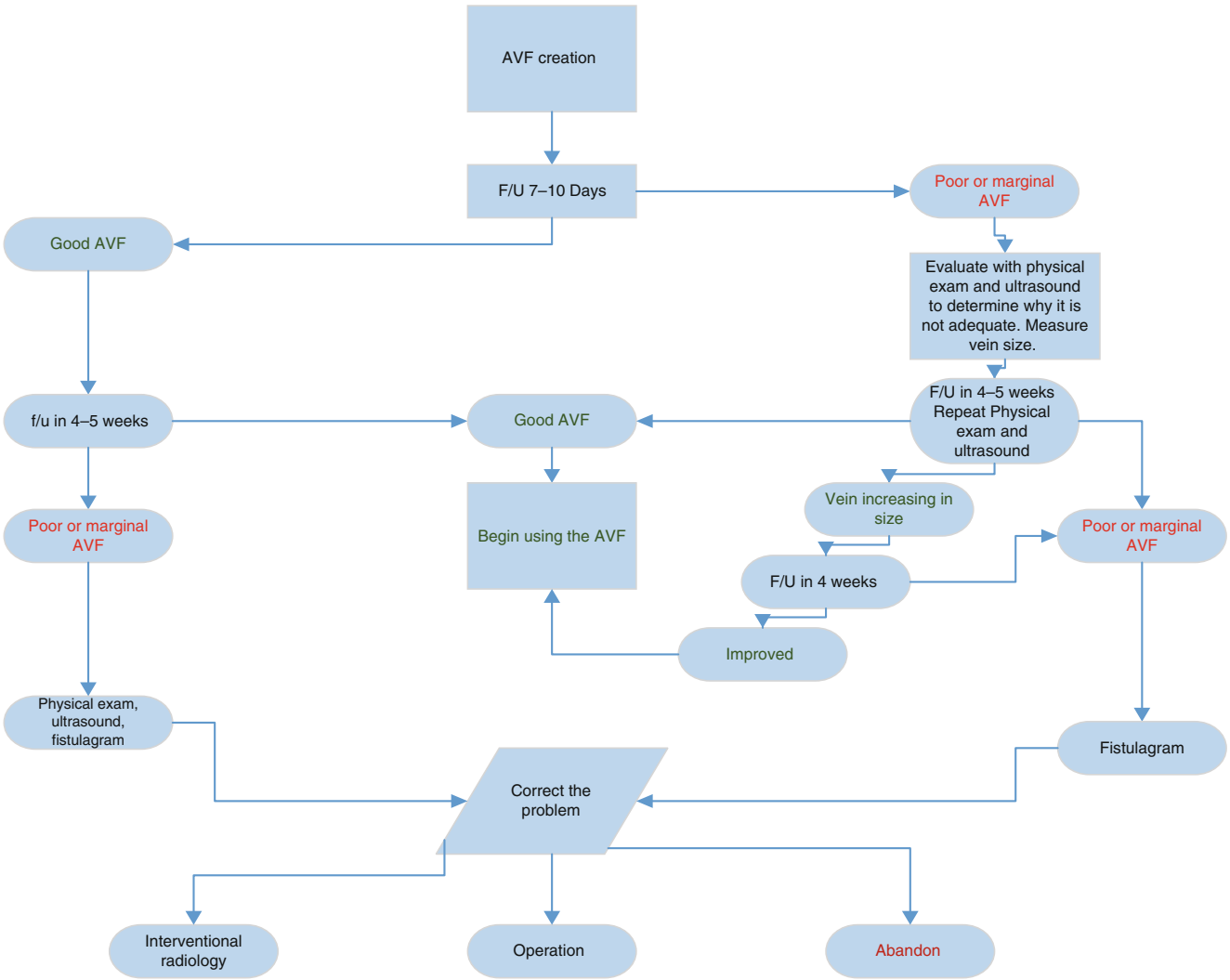


Fig. 27.1 A proposed algorithm for evaluating a fistula postoperatively

not develop. In addition, measure the diameter of the outflow vein with ultrasound and document the results. Have the patient return in 4–5 weeks. An assessment with physical exam and ultrasound is repeated and hopefully the AVF has matured and is ready for use. During the assessment with repeat ultrasound, the vein diameter is again measured and documented. Measuring the vein diameter gives objective criteria to help in decision-making. If the vein has dilated, have the patient return in about 4 weeks with the expectation that the AVF can be used if it has matured. If the vein has not dilated, then consider a fistulagram with the intention of intervening.

Most often the etiology as to why the fistula is not maturing can be categorized into three basic categories. There may be problems with arterial inflow, the anastomosis, venous outflow, or a combination of the three. Through physical exam, ultrasound, and fistulagram, the etiology can most likely be delineated [15, 16].

Inflow issues may be due to a diseased artery. On physical exam, feel the artery and note if the artery feels soft and pliable as compared to calcified and hard. Take note if the artery feels small. The same things are evaluated on ultrasound, noting the size of the artery and any calcification. Look for areas of stenosis whether they are over a short segment or extended segment. Then compare the physical exam and ultrasound with the fistulagram. Imaging the arterial inflow in addition to the AVF may help differentiate possible etiologies.

Next, evaluate the anastomotic site. This can be difficult in the early postoperative period due to the swelling and wound healing. Tissues do not always lend themselves to a good physical exam or ultrasound. Obviously, if there is an excellent thrill and bruit, it is a nonissue. If there is a weak thrill and bruit, suspect an anastomotic stricture. When the patient comes for the next visit, there is a great likelihood that the anastomotic site can be evaluated more thoroughly with physical exam and ultrasound.

Table 27.1 Frequency of the etiology as to why fistulas do not mature

AVF	Artery	Anastomosis	Swing point	Outflow vein	Central vein	Accessory vein	Multiple
453	21	106	214	203	69	88	202
	4.6 %	23.4 %	47.2 %	49.8 %	15.2 %	19.4 %	44.6 %

The outflow vein is then evaluated. On physical exam, examine if the fistula has a good thrill and bruit. If the vein is pulsatile and there is decreased flow during diastole on auscultation, then suspect an outflow stenosis or occlusion. Consider assessing whether you yourself are able to cannulate the AVF. The vein needs to be large, superficial, not tortuous, and have enough length where two needles can be placed. If access needles cannot be placed, then the AVF is inadequate or immature. Ultrasound is again used to evaluate this portion of the AVF and may show an area of stenosis or occlusion. A fistulagram is obtained to confirm findings. Venous problems include failure to dilate, intimal hyperplasia at the juxta-anastomotic area or at valves, branching of the vein, torturous veins, multiple collaterals, and stenotic and occluded segments. A vein that is too deep is not necessarily a failure of maturity, but rather merely an inadequate AVF. Many times this has been anticipated and there is a plan for correction.

Table 27.1 was created by reviewing a number of studies and tabulating the frequency as to the etiology why an AVF was felt not to be maturing [2, 3, 15, 17, 18].

Treatment

Arterial Inflow Problems

Treatment

A. Angioplasty
B. Bypass

Arterial inflow problems are not very common. It has been reported to be seen between 4 and 11 % of the time in immature AV fistulas [2, 3, 15, 17, 18]. When the problem is a focal stenosis, it can easily be treated with angioplasty with expected good outcomes.

Turmel–Rodrigues et al. presented good results in treating patients with radial artery stenosis. Some of their patients even had stenosis greater than 5 cm long. They used balloon angioplasty as their means of treatment. Primary patency at 1 and 2 years was 64 % and 61 %, respectively, with a secondary patency of 96 % and 94 % at 1 and 2 years, respectively [19].

When the artery is diffusely diseased over a long segment, bypass procedures can be considered. An example is an AVF that has been created at the wrist, and the radial artery is not deemed suitable to provide adequate flow into an otherwise good outflow vein. A bypass using polytetrafluoroethylene (PTFE) from the brachial artery to the vein can be performed. This maintains the use of a good vein that can still be used for cannulation. Obviously, this requires that the vein is optimal. If the vein is suspect or there are other good options for the creation of a new AVF, then the bypass may not be a good choice.

Arteriovenous Anastomotic and Juxta-Anastomotic Segment

Treatment

A. Angioplasty
B. Surgery:
   1. Redo the anastomosis.
   2. Patch angioplasty.
   3. Interposition graft.

When treating a stenosis at the arteriovenous anastomosis, it appears that both operative intervention and balloon angioplasty are very successful.

Asif et al. reported on their success on treating 73 patients with an anastomotic stricture. A total of 112 percutaneous angioplasty procedures were performed with an early success rate of 97 %. Primary patency at 6 and 12 months was 75 % and 51 %, respectively. The secondary patency at 6 and 12 months was 94 % and 90 %, respectively [20].

Beathard et al. reported a 100 % success rate in the angioplasty of anastomotic stenosis [15].

The surgical approach to correction of a problem at the anastomosis includes redoing the anastomosis more proximal, patch angioplasty, or rarely placing an interposition bypass using vein or synthetic graft. Lee and colleagues looked at interventions on arteriovenous fistulas (AVFs) that were failing to mature and found that surgical interventions had better results than those treated with angioplasty. One-year primary patency for treatment of an immature fistula was 83 % for those treated operatively compared to 40 % of those treated with angioplasty [21]. Long and others similarly looked at surgical revision compared to angioplasty in the treatment of stenosis at anastomotic sites. They also found that surgical revision had better results. Primary patency at 1 year was 71 % with an operation verse 41 % with angioplasty [22].

In the review of these studies and others, both methods do work well with treating a stenosis at the anastomotic

site [2, 3, 23, 24]. This leaves the treatment option to the discretion of the vascular access surgeon, along with the team of physicians caring for the patient, as to how they feel the patient should best be cared for.

Venous Outflow

A. Surgical:
   1. Ligate accessory or competing veins.
   2. Patch angioplasty.
   3. Provide new outflow.

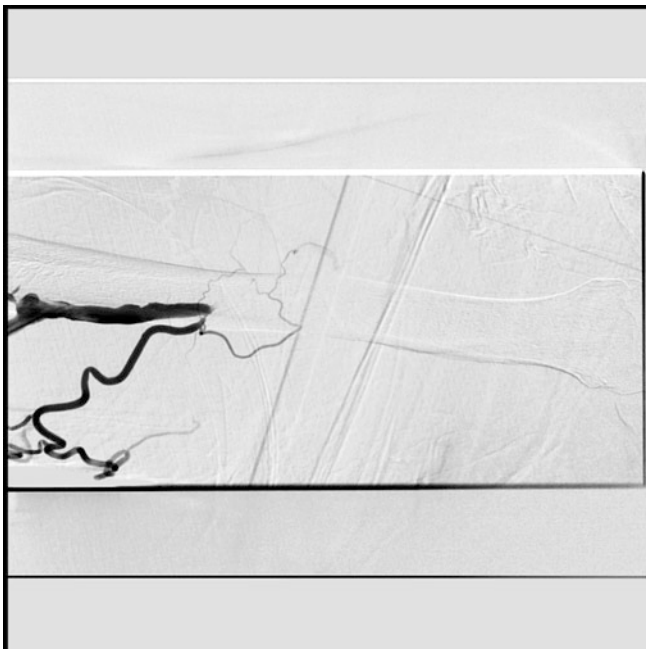
B. Percutaneous interventional approach:
   1. Coil embolization of accessory or competing veins
   2. Balloon-assisted maturation:
      (a) Innovated idea, but does it work?
   3. Stenosis
   4. Treat multiple areas

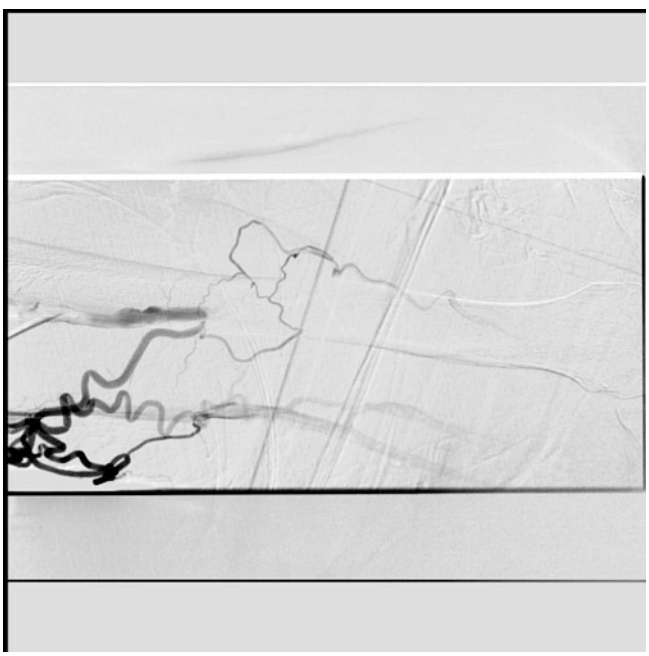
There are a number of issues that are lumped into the category of having venous outflow problems. There are issues of accessory or competing veins, poor dilation of the main outflow vein, and poor outflow due to stenosis or occlusions. Accessory or competing veins to the main outflow vein have been described as reasons for fistulas not maturing. The incidence has been reported as high as 46 % [15]. In most studies it is not reported as a common problem, and the degree to which they contribute to poor maturation is hard to say. They are rarely an isolated reason for an arteriovenous fistula to not mature. Most often they are related to a significant stenosis or occlusion in the primary outflow vein more distal. When they are present, they can easily be treated with surgical ligation or percutaneous coil embolization.

On occasion, the outflow vein will not dilate. Miller and colleagues evaluated and treated 75 patients with an outflow vein measuring 2–5 mm in diameter. Their goal was to obtain dilation of the vein up to 6 mm. Repeat dilations every 3 weeks were performed until their goal of a 6 mm vein was met by ultrasound evaluation. The mean number of procedures to maturation was 2.6, and the mean time to maturation was 7 weeks. Primary patency at 6 months was 39 % with secondary patency of 77 % at 12 months, 61% at 24 months, and 32 % at 36 months [25]. Samett et al. also had success with balloon-assisted maturation of an AVF [26]. This is an innovative way of trying to get an arteriovenous fistula to mature. Additional studies are needed before it becomes a more routine means of assisting small veins to mature. If the outflow vein is truly small over its entire length, the traditional approach would be to consider abandoning the arteriovenous fistula.

Stenosis and/or occlusion of the outflow vein can again be treated both surgically and with angioplasty. There are some obvious situations where one is preferred over the other. In the case of short isolated areas of stenosis, especially if the areas of stenosis are located where it is difficult to access operatively, it makes sense to do balloon angioplasties. Very good success has been reported [1, 3, 15].

However, there are instances where operative intervention is the preferred method. Examples include a long segment of severe stenosis or occlusion. A stenosis or occlusion in the distal outflow of a basilic vein transposition AVF or of a brachiocephalic AVF could be treated by anastomosing to the brachial vein to provide new outflow. The brachial vein can be mobilized up to the basilic of cephalic vein.





Another example includes a long stenotic or occluded cephalic arch lesion, which can be treated by swinging the cephalic vein in the upper shoulder area down medially to the basilic or brachial vein to provide new outflow. Of course there is always the option of inserting an interposition graft to a new outflow vein.

Table 27.2 is a summary of the data collected by Voormolen and colleagues [27]. They did a meta-analysis on 12 studies looking at the treatment of nonmaturing AVFs. A variety of surgical and percutaneous interventions were used in the care of 745 fistulas. A salvage rate of 86 % was obtained in creating a functional AVF. At 1 year the primary patency, after one intervention, was 51 %, and the secondary patency, after two or more interventions, was 76 % [27].

With the results as shown, it makes good sense to diligently search for the etiology as to why an AVF does not mature. Through good physical exam, ultrasound, and fistulagrams, a good majority of these AVFs can be converted to mature fistulas.

Prognosis of Immature AV Fistula's Following Attempts at Salvage

Lee et al. evaluated AVFs that required intervention to get them to mature and become functional [28]. They followed up on the patency of the AVF and the number of interventions required to maintain their function. Table 27.3 shows their results.

Table 27.2 Salvage and patency rates after intervention of an immature arteriovenous fistula

Fistulas	Interventions	Salvage rate	1-year patency
745	Surgery/IR	86 %	Primary 51 % Secondary 76 %

Compared with an AVF that matures without interventions, AVFs that require interventions have decreased cumulative survival. The more interventions required to get the AVF to mature, the more likely they will require multiple and frequent interventions to maintain patency and function. The failure of an AVF to mature is complicated and a costly problem. The solutions are not simple and do not always have great results. Abandoning a failing and likely futile AVF may sometimes be the best option.

The Future

Following surgical fistula creation, there are hemodynamic, cellular, and humoral processes that lead to vascular remodeling and adaption over time [29]. The strength and integrity of the vein wall are largely related to elastin and collagen. After the creation of an arteriovenous fistula, the desired outcome is dilation of the vein and not the development of intimal hyperplasia. The delicate balance and mechanisms involved that result in dilation of the vein compared to the development of intimal hyperplasia are not well understood. Considerations in how the anastomosis is configured and the hemodynamic stress forces involved have been studied [30, 31]. These and other factors alter the cellular and humoral processes that determine the remodeling of the arteriovenous fistula wall. A number of mediators have been investigated including a variety of growth factors, such as VEGF, platelet-derived growth factor, fibroblast growth factor, transforming growth factor beta, and stem cell factor along with its receptor C-KIT, elastin, and others [29, 32–38]. Hopefully the future will hold the powerful ability for the vascular surgeon to manipulate the cellular and humoral factors involved in the maturation of an arteriovenous fistula.

Table 27.3 Natural history of an immature arteriovenous fistulas that required intervention to make it functional

Interventions to a mature AVF	1 year % of AVFs still functioning	2 years % of AVFs still functioning	3 years % of AVFs still functioning	After the vein is considered mature, the number of interventions needed to maintain patency per year
Two or more	68	57	42	3.51 ± 2.2
One	78	71	57	1.37 ± 1.37
Zero	92	85	75	0.7 ± 0.1

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Understanding Intimal Hyperplasia Biology in Hemodialysis Access

28

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Introduction

The blood vessel wall is made up of three layers: the intima, the media, and the adventitia. Endothelial cells lying on a layer of connective tissue known as the internal elastic lamina make up the intima, the innermost layer. The internal elastic lamina contains collagen type IV, heparin sulfate proteoglycans, and laminin. Vascular smooth muscle cells (SMC) and extracellular matrix (ECM) make up the medial layer, which is supported by the external elastic lamina. Arteries are thicker than veins due to the increased number of SMCs present and due to elastic fibers in the media. The adventitia is comprised of fibroblasts, ECM, and nerves [1]. Thickening of the blood vessel wall, termed intimal hyperplasia, is due to the migration of SMCs from the media to the intimal layer and their subsequent deposition of extracellular matrix into the zone of injury. Endothelial cell activation, platelet aggregation, leukocyte recruitment, and activation of the coagulation cascade prompt SMC migration and proliferation and lead to intimal hyperplasia [1].

Endothelial cells in the intima form a layer and maintain the integrity and proper function of the vessel walls. A healthy endothelium produces nitric oxide (NO) and secretes prostacyclin (PGI2), both of which help inhibit platelet activation, adhesion, and aggregation. NO also has an anti-inflammatory effect, which inhibits cytokine production and expression of adhesion molecules [1]. Endothelial cells play a key role in activating the cascade of events responsible for intimal hyperplasia. Activated or injured endothelial cells release inflammatory mediators that trigger platelet aggregation and recruitment of leukocytes to the area of injury. These cells also now exhibit increased gene and protein level expression of growth factors such as platelet-derived growth factor (PDGF-2), which promote SMC migration and proliferation [2]. SMCs in the media are usually maintained in a quiescent state by the ECM, transforming growth factor-beta (TGFβ), heparin, and heparin-like molecules, which inhibit cell proliferation and migration. Heparin binds fibroblast growth factor and neutralizes its mitogenic effect on SMCs. TGFβ stabilizes the ECM, limiting SMC movement [1]. In response to stimuli from cytokines and mediators released by endothelial cells, SMCs in the media undergo a phenotypic transformation from a quiescent contractile state to a synthetic and motile state [1]. This prompts their migration from the medial layer to the intimal layer. Numerous stimuli and pathways are thought to be involved in this process. Once migrated, SMCs proliferate to form intimal hyperplasia lesions. Mitogens such as PDGF, insulin-like growth factor (IGF-1), thrombin, basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), TGFβ, and cytokines IL-1 and IL-6 all play a role in encouraging SMC proliferation [1, 3]. The alpha smooth muscle actin positive cells that comprise intimal lesions are mostly vimentin-positive, desmin-negative myofibroblasts, with additional fibroblasts and other contractile SMCs [4]. Increase in ECM also adds to the mass of the proliferative lesion. Migration and proliferation of SMC result in encroachment into the blood vessel lumen, causing stenosis.

In current surgical practice, there are two main forms of hemodialysis vascular access, the native arteriovenous fistula (AVF) and the polytetrafluoroethylene graft (PTFE). In the most common configuration of an AVF, a surgical anastomosis of the radial or brachial artery to the cephalic vein is performed [5]. The two major complications include an initial failure to mature and a later venous stenosis followed by access thrombosis. Rates of AVF failure to mature of up to 50 % have been reported, lowering the fistula patency rate from 85 % at 1 year and 75 % at 2 years to as low as 43 % [5].

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Arteriovenous PTFE grafts are easy to place and ready to use without a maturation period necessary but have extremely high rates of stenosis, thrombosis, and infection [5]. Patency rates are reported to be at 50 % at 1 year, but rates as low as 23 % at 1 year and 4 % at 2 years have also been reported [5]. The pathogenesis of intimal hyperplasia in AVGs is mostly similar to that in AVFs but with a few minor differences. AVFs stenosis is highly influenced by the vasodilator capacity of the vein and the surgical technique used. Also, AVG stenosis includes a layer of macrophages lining the perigraft region, a finding usually not present in AVF [4].

A series of events, including upstream activities responsible for causing vascular injury and downstream measures consisting of the response to the injury, contribute to the pathogenesis of intimal hyperplasia.

Upstream Events in the Pathogenesis of Intimal Hyperplasia

Upstream events in intimal hyperplasia development are the processes responsible for SMC and endothelial cell activation. These include a spectrum of physical injuries as well as milieu which fosters the inflammatory state needed to perpetuate hyperplasia development. One possible etiology neointimal of hyperplasia is trauma to the vessels at the time of surgery. It has been suggested that this may be significant in the case of the AVF, where the vein may be frequently stretched or manipulated [5]. The trauma from needle holes and the presence of the suture itself may also be an impetus for endothelial cell activation.

Hemodynamic shear stress has also been implicated in intimal hyperplasia. The change from laminar flow with its accompanying high shear stress (tangential force of flowing blood) to turbulent flow with low shear stress promotes endothelial cell activation [6]. At baseline the endothelial cell is able to regulate the coagulation cascade; however, with this change in shear stress, angiotensin-converting enzyme activity and angiotensin II levels significantly decrease [7]. The endothelial cell also secretes less NO and TGFβ, both of which are inhibitors of SMC proliferation. Changes in shear stress influence monocyte and leukocyte adhesion and migration to the surfaces of endothelial cells as well as the expression of adhesion molecules by the endothelial cells themselves [8, 9]. The change in compliance between the artery and the vein utilized in the fistula also contributes to shear stress at the site of the fistula. In the case of AVG, the presence of PTFE has been shown to be an attractant of macrophages [10]. These macrophages in turn form a cell layer that covers the surface of the PTFE. They then express PDGF, basic fibroblast growth factor (bFGF), and VEGF. These factors are known instigators of the migration and proliferation of SMCs and endothelial cells, respectively, which then play their biologic parts in the formation of neointimal hyperplasia.

Just as trauma at the time of fistula creation may be an impetus for intimal hyperplasia development, injury to the vessels from repeated dialysis needle punctures may also play a role in beginning the cascade of neointimal hyperplasia development. Accessing the fistula also affects the shear stress for the duration of the session. Additionally, the presence of the access needles could also initiate a foreign body reaction similar to that caused by PTFE [10].

The uremic milieu fostered by renal failure contributes to the inflammatory processes at play in neointimal hyperplasia development. Renal failure has been shown to produce a systemic inflammatory response which increases oxidative stress, coagulation activation, and endothelial dysfunction [11]. This cause of endothelial dysfunction is likely responsible for neointimal hyperplasia development in vessels of chronic kidney disease (CKD) patients. Neointimal hyperplasia has been shown to preexist in patients with stage 4 and 5 CKD up to 1 year prior to AVF creation, although no direct correlation has been made between preexisting hyperplasia and failure of fistula maturation [12].

Another upstream event (or perhaps midstream in this case) which perpetuates the cycle of intimal hyperplasia development is treatment of stenosis which has already developed. Balloon angioplasty, which results in aggressive vasodilation while rupturing the intima-media junction in the blood vessel, initiates the inflammatory cascade by signaling the migration of monocytes and SMCs [4]. Significant endothelial and medial smooth muscle damage from the procedure increases cellular proliferation, which in turn results in further, more aggressive intimal hyperplasia.

Downstream Events in the Pathogenesis of Intimal Hyperplasia

Vascular injury triggers three main downstream events that precipitate intimal hyperplasia: oxidative stress, inflammation, and endothelial dysfunction [4]. First, in the process of oxidative stress, there is an increase in the production of free radicals and their products, such as nitrotyrosine and peroxynitrate [4]. The latter is an upregulator of matrix metalloproteinases (MMPs), which are enzymes that cause breakdown of extracellular matrix components such as collagen and elastin [4]. The breakdown promotes vasodilation and facilitates SMC and inflammatory cell proliferation and migration, resulting in the formation of intimal lesions.

Second, inflammation is another downstream biological event that results in intimal hyperplasia. Monocyte chemoattractant protein-1 (MCP-1) is a chemokine that prompts the chemotaxis of macrophages and monocytes, activation and

migration of endothelial cells, proliferation and migration of SMCs, and induction of procoagulant mediators [13]. AVF/AVG results in increased MCP-1 expression that is localized within the endothelium, SMC, and leukocytes [14]. Experimental studies have shown a decrease in intimal hyperplasia after inhibition of MCP-1 [14]. Therefore, MCP-1 is a potent mediator for AVF/AVG failure.

Third, endothelial dysfunction and NO production issues prompt the development of intimal hyperplasia. Hemodialysis patients with CKD accumulate asymmetric dimethylarginine, an endogenous inhibitor of nitric oxide synthase (NOS) [14]. High levels of this inhibitor have been associated with aggressive restenosis in endovascular repair [4]. Recent studies have shown that the levels of intimal hyperplasia and MCP-1 were increased in patients with NOS inhibition [15]. Therapies targeted at inducing NOS expression could play a beneficial role in preventing stenosis.

A unifying pathway for downstream vascular biology involves heme oxygenase-1 inhibiting oxidative stress and inflammation and NO inhibiting endothelial dysfunction by regulating mediators such as MCP-1 and MMPs [16]. An important regulator of MMPs is heme oxygenase-1 (HO-1), an enzyme that catalyzes degradation of heme and is upregulated by vascular injury [17]. It also protects against inflammation, oxidant stress, and vascular proliferation. Preliminary studies have shown that the absence of the HO-1 enzyme causes increased expression of pro-inflammatory mediators such as monocyte chemoattractant protein-1 (MCP-1) and MMPs, which increase cell proliferation characteristic of intimal hyperplasia [13]. HO-1 prevents vascular access dysfunction by controlling MMPs, MCP-1, and peroxynitrite, which play an important role in intimal hyperplasia development [16]. Endothelial NOS also regulates MCP-1 expression [16]. Inadequate regulation of inflammatory and oxidative stress mediators results in a cascade of events leading to activation and proliferation of myofibroblasts, fibroblasts, and SMCs and subsequent production of intimal hyperplasia.

Genetic Factors and the Development of Intimal Hyperplasia

Intimal hyperplasia is characterized by an increased expression of mediators and cytokines. Genes that code for these inflammatory cytokines have single nucleotide polymorphisms (SNPs) in their promoter regions that influence the rate and magnitude of cytokine production, which determine the rate and magnitude of stenosis in the blood vessel [18]. A better understanding of the role of genetics on the development of intimal hyperplasia is warranted to yield more targeted novel therapies.

First, polymorphisms in mediators of inflammation lead to the development of intimal hyperplasia. TNF-α gene polymorphisms (G to A, position 308) have been associated with increased AVG thrombosis [18].SNPs in the gene sequence of TGFβ result in high-producing, intermediate-producing, and low-producing genotypes of the cytokine [18]. AVF patency rate is strongly correlated with the genotype of TGFβ.

Second, polymorphisms in mediators of endothelial function also can precipitate increased stenosis. Methylene tetrahydrofolate reductase is an enzyme that catalyzes the remethylation of homocysteine to methionine [19]. Studies show that patients with a TT versus CC genotype in the polymorphism of the gene were more likely to develop AVF thrombosis [19].A correlation between the endothelial NOS gene intron 4 and thrombosis in AVG has been proven (patients with aa genotype rather than the bb and ab genotype had significantly lower graft patency rates) [19].

Lastly, genetic variations in mediators of oxidative stress can determine the amount and rate of growth of intimal hyperplasia. For example, transcription of the HO-1 gene is regulated by the length of a polymorphism (L = long, S = short) of a dinucleotide GT repeat in the promoter region of the HO-1 gene [20]. Significant associations were found between AVF failure and the L/L and L/S genotype (compared to S/S genotype) [20]. Also, specific genotypes of MMPs have been found to be associated with higher frequencies of AVF failures [20].

Genetic factors may play an important role in vascular access stenosis and development of neointimal hyperplasia by affecting pathways that lead to inflammation, endothelial function, and oxidative stress. Knowledge of the crucial genes and gene variants will not only provide novel insights into the mechanisms (i.e., oxidative stress, inflammation, endothelial dysfunction, etc.) and pathophysiology of neointimal hyperplasia development in dialysis access stenosis but will also allow for generation of genomic patient phenotypes that will provide the detail necessary for improving diagnosis and prognosis of dialysis access dysfunction and how individual patients will respond to interventions and future therapies [20].

Conclusions

Hemodialysis vascular access dysfunction is a major cause of morbidity and mortality in hemodialysis patients, costing over $1 billion dollars annually [4]. Aggressive intimal hyperplasia lowering patency rates in both grafts and fistulas and few effective therapeutic interventions comprise the root of the issue. At the present time, our understanding of the pathophysiology and mechanisms of neointimal hyperplasia formation is still limited. Increased understanding of intimal hyperplasia biology in the context of hemodialysis access will only encourage the discovery of innovative therapies that might potentially provide a solution to this process.

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Arterial Inflow Stenosis

29

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Introduction

Native arteriovenous fistulae (AVF) are the best form of hemodialysis access. Every effort should be made to preserve and maintain these valuable access sites. Good arterial inflow is important for adequate flow for dialysis, as well as preventing AVF thrombosis. Since fistulas are created from native tissue, they are inherently non-thrombogenic. Therefore a single venous outflow stenosis will usually not cause thrombosis. Typically, a combination of venous stenosis and arterial inflow stenosis are present when AVF thrombosis occurs. Thus, to restore good flow and ensure adequate long-term function, the arterial inflow needs to be crossed, dilated, and thoroughly evaluated [1–3].

Because inflow is important, it is good to know the surgical methods and challenges in the creation of the AVF both in general and for that particular patient. Although it is beyond the scope of this chapter, it is important to mention that during the creation of AVF, there may be stretching of the vessels which in itself can lead to subsequent stenosis. Also the different ways in which the anastomosis is created can have bearings on the ease of intervention later. Briefly the anastomosis can be either artery side to vein side, artery side to vein end, or very infrequently an end-to-end anastomosis [4].

In AVF, the arteriovenous anastomosis is a typical location for stenotic lesions, whereas a majority of stenoses in arteriovenous grafts (AVG) develop at or near the venous anastomosis [5, 6]. Arterial stenoses are less frequently discussed in literature but are likely to cause dysfunction (low flow) and may be responsible for the development of limb ischemia secondary to a steal phenomenon [7]. A number of recent studies reported that arterial inflow lesions are frequently encountered in dysfunctional AVF and AVG which are not surprising as several major risk factors for atherosclerotic disease, such as older age, diabetes mellitus, and hypertension, have a high prevalence in the population of patients undergoing hemodialysis [8, 9].

Radiocephalic AVF has a higher failure rate (i.e., non-maturation) after placement than synthetic loop grafts [4]. In cases in which an AVF is not maturing adequately for dialysis, the patients need to be referred for a fistulagram, ideally, within 2 months of placement. Every poorly functioning AVF requires an evaluation [10]. An aggressive approach is needed in these instances because patient care is improved by having as many native AVF as possible vs. AVG and central lines. Typically, an immature AVF is poorly palpable. If a venous puncture cannot be performed, a transbrachial approach should be used for access and an arteriogram should be performed. Turmel-Rodrigues et al. [10] reported that a stenosis existed in every case of fistula malfunction. It is incumbent to find this stenosis and treat it. Often, the inflow can be sufficiently improved to allow the fistula to mature. However, even if the fistula cannot be salvaged, venous mapping and evaluation of the arterial inflow will help guide surgical revision.

In AVG, angioplasty or stenting of inflow stenosis is usually straightforward due to anatomy of the access and the absence of acute anastomotic angles. However, few studies address the depiction and treatment of inflow stenoses in case of AVF. Guerra et al. used a combination of arterial puncture and retrograde venous access puncture for the treatment of inflow lesions, whereas Asif et al. described angioplasty of a small number of forearm inflow stenoses after retrograde venous access puncture [8, 11].

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Assessing the Inflow

Initial noninvasive imaging of all malfunctioning dialysis accesses is usually done by color Doppler ultrasonography (CDUS) and includes evaluation of the complete arterial inflow, access site, and entire venous outflow as described in Chap. 23. A stenosis at the arteriovenous anastomosis or venous outflow is considered hemodynamically significant if the peak systolic velocity at a stenosis is greater than 375 cm/s or in case a luminal diameter narrowing of 50 % or more is found at gray-scale imaging [12]. Criteria for significant arterial inflow stenoses include diameter narrowing >50 % at gray-scale imaging and/or a peak systolic velocity ratio of three or more [5, 13]. In some institutions, a contrast-enhanced MRA or a CTA may be obtained but that depends on the clinical scenario and where the lesion is expected to be present. This may be more useful when the lesion is suspected more proximally rather than near the anastomosis (Figs. 29.1 and 29.2) [5, 14].

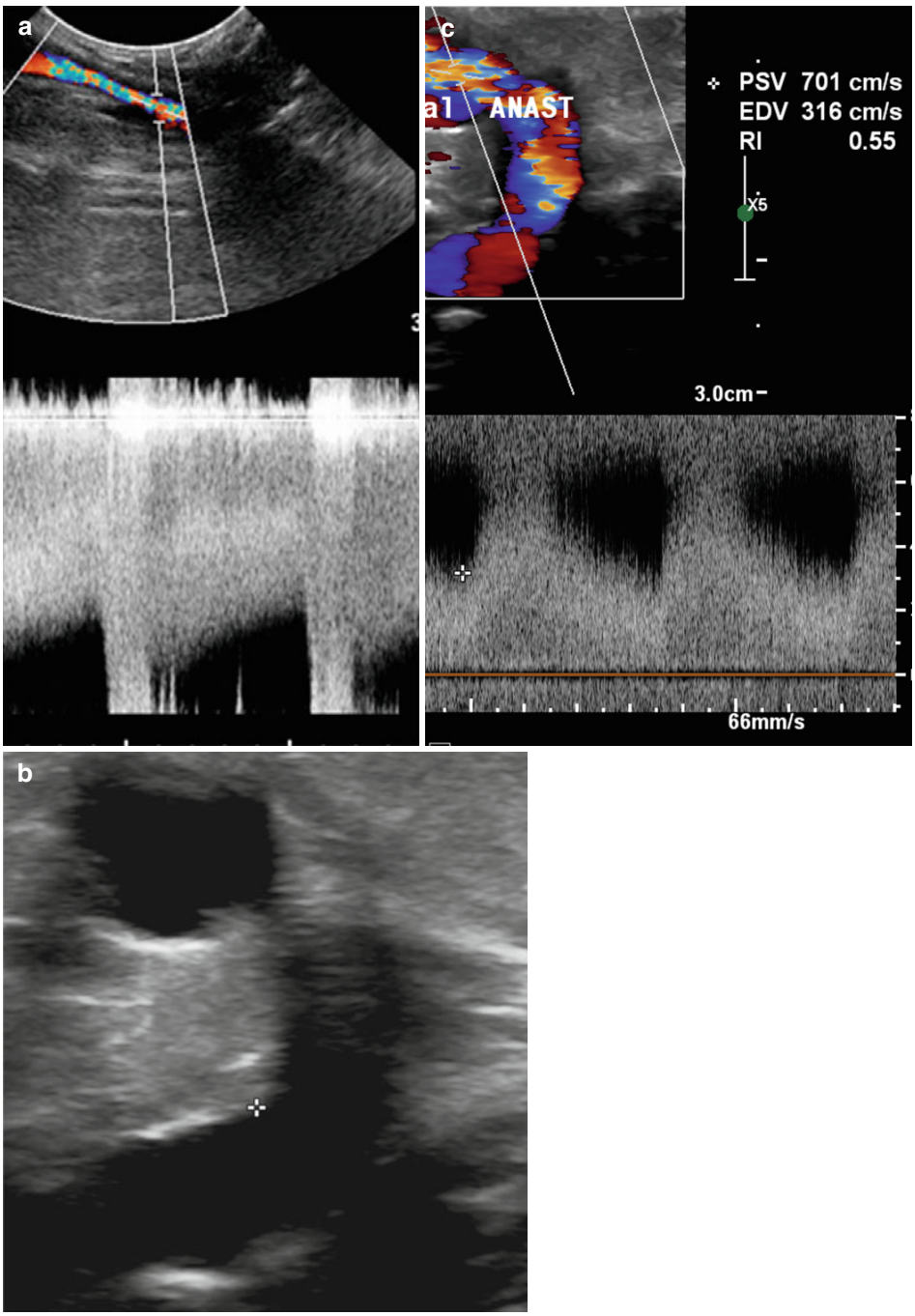

Fig. 29.1 (**a**) Doppler US shows the presence of a stenosis of the brachial artery in a patient with a poorly functioning fistula. (**b**) Gray-scale US of the anastomosis shows the presence of a significant narrowing. (**c**) Color Doppler confirms the presence of a stenosis

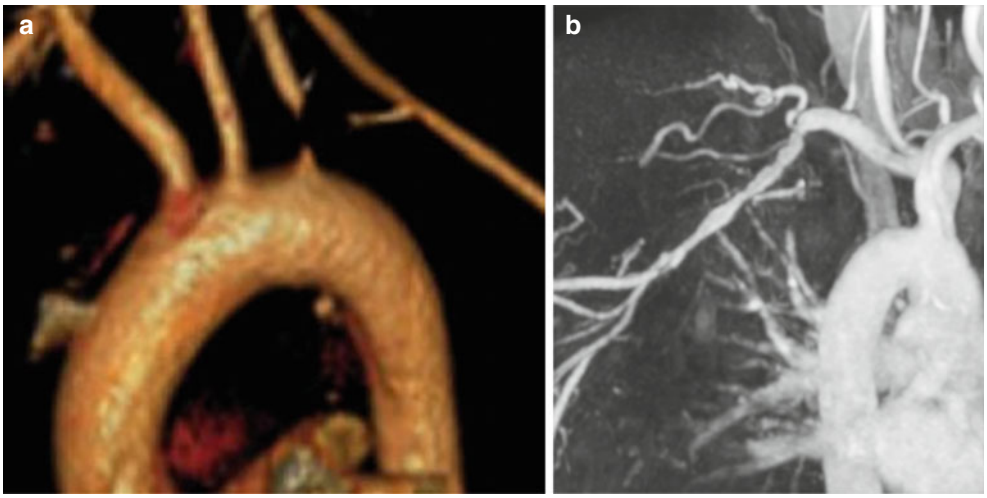

Fig. 29.2 (**a**) CTA shows the presence of a stenosis of the subclavian artery origin in a patient with upper extremity symptoms with a poorly functioning AVF. (**b**) MRA in a patient with an AVF with underlying vasculitis shows axillary artery stenosis

Assessment at digital subtraction imaging is comprised of visualization of the anastomotic region and adjacent portion of the feeding artery, by use of flow interruption of the outflow through a cuff or through manual compression [15]. Additional assessment of the entire arterial inflow is reserved for cases with arterial stenosis suspected at noninvasive imaging [9, 16]. This can be done by advancing the catheter centrally as needed even up to the aortic arch if indicated. Some interventionalists may use a brachial access when the stenosis is known to be in the forearm [10].

The arterial inflow includes the feeding artery from its origin at the aortic arch as far as 1 cm cranial to the arteriovenous anastomosis. The arteriovenous anastomosis is comprised of 1 cm of vessel length on both sides of the anastomosis, whereas the venous outflow starts 1 cm distal to the anastomosis up to the right atrium [16]. Stenoses are considered significant if there is >50 % reduction in luminal diameter. Guerra et al. proposed a classification system for the stenosis based on position with five subtypes [11].

Endovascular Management of the Arterial Anastomosis and Inflow

All interventions are done as outpatient procedures. Apart from local infection, a contraindication to dilation of an area of stenosis is an AVF that is less than 6 weeks old due to the risk of disruption of the anastomosis. Once stenosis is diagnosed, dilation is performed by cannulation of the fistula itself. For stenoses located in the artery or at the anastomosis, a retrograde approach is used. If this retrograde approach is not feasible, an antegrade cannulation may be undertaken [10].

Catheterization of the arterial inflow is initially done with an angled glide wire and angled catheter. This is usually done with the sheath directed toward the arteriovenous anastomosis. After the catheter is placed in the arterial inflow and advanced to at least the mid-forearm or across the stenotic area if the narrowing is more proximal, the glide wire is exchanged for a stiffer guide wire.

Crossing and manipulating the wire across the anastomosis and centrally can be challenging at time, and various external manipulation and endovascular maneuvers may be needed. External manipulation is usually in the form of physically straightening out the angulations with pressure on the soft tissues. In terms of endovascular maneuvers, one can use microwires with shapeable tips. Rarely, a transbrachial or radial artery puncture is needed. An arterial puncture should be used as a last resort because the patient will be anticoagulated during the procedure [1, 17, 18]. Heparinization is required with ACT control to avoid iatrogenic thromboembolic phenomena.

Balloon size is dependent on the artery in question. In the event of a more central stenosis, the angioplasty balloon sizing is matched with the size of the artery, for example, if the subclavian artery needed treatment, the angioplasty balloon would be around 8 mm. In the case of treating the subclavian artery, a femoral approach usually provides better orientation. A long sheath or guide catheter is used to provide stability. Crossing usually is straightforward with a 0.035 glide wire (Fig. 29.3). On occasion when the narrowing is critical, then using a 0.014 or 0.018 wire can be useful to cross the lesion.

Balloon angioplasty of the inflow artery to a minimum of 4 mm is performed (occasionally to 3 mm in an immature AVF). There is a school of thought that the angioplasty for a juxta-anastomotic arterial lesion should be done with the angioplasty balloon directed centrally rather than peripherally so as to avoid steal phenomenon (Fig. 29.4). In the majority of the cases, a simple angioplasty suffices to treat the inflow stenosis (Fig. 29.5). Arterial lesions are more likely to respond than the traditional venous outflow stenosis

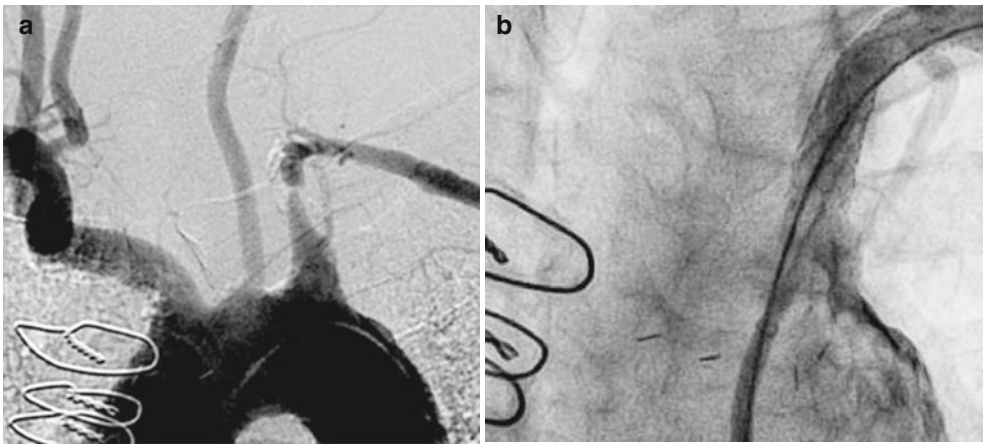

Fig. 29.3 Digital subtraction imaging of the aortic arch in the patient in Fig. 29.2a confirming the presence of a subclavian artery stenosis (**a**). The subclavian artery stenosis treated with balloon-expandable stent (b). A balloon-mounted stent is suitable here as this area is not superficial or exposed and the stent can be landed very precisely

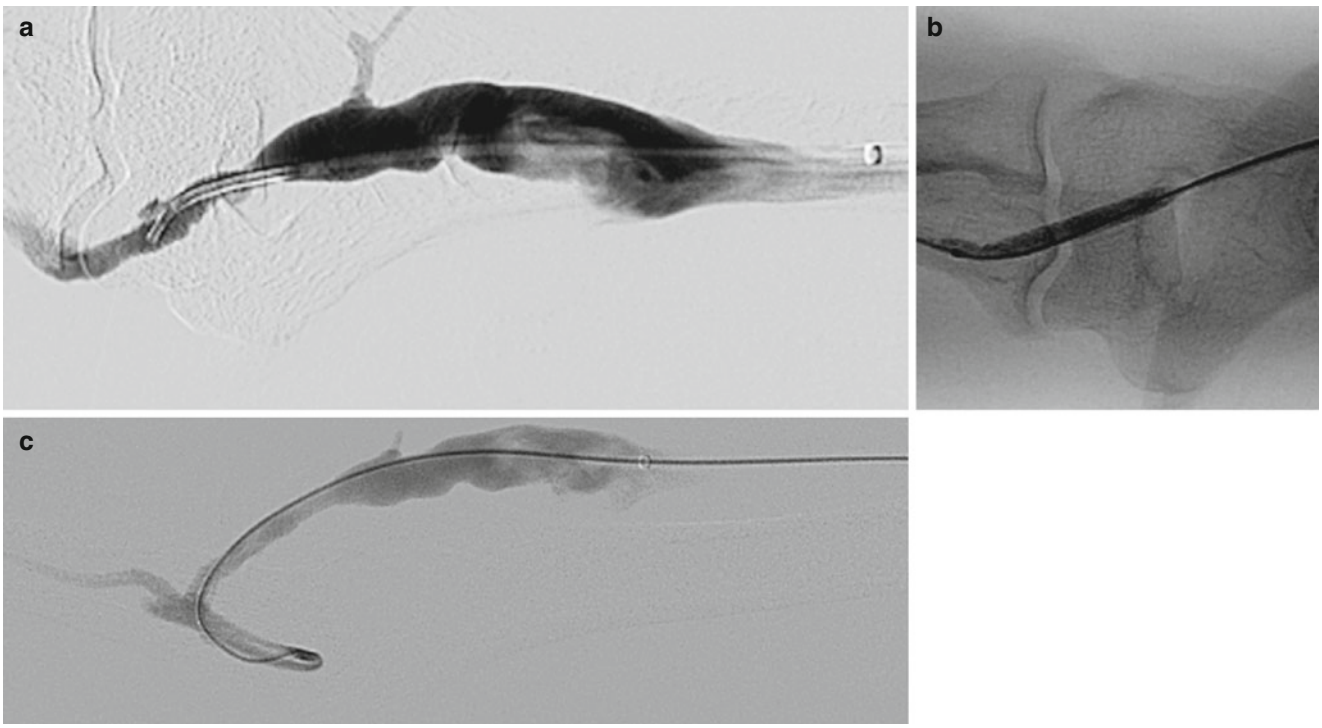

Fig. 29.4 Digital subtraction imaging obtained during a fistulagram showing the presence of the anastomotic stenosis in the patient in Fig. 29.1b (**a**). This was traversed from the retrograde approach and balloon angioplasty performed (**b**) with a good result (**c**)

in AVF which are resistant to balloon dilation and need high-pressure angioplasty balloons. In the event that there is non-resolution of the stenosis, a larger angioplasty balloon can be tried, but one has to be careful about the sizing. Too large angioplasty balloon can lead to dissection and rupture. Usually the angioplasty balloon size can be increased incrementally by about 1 mm.

In the event of nonresponse of a stenosis, a stent can be used if the flow is still compromised. In the upper extremity, preference will be given to self-expanding stents over balloon-mounted stents as they can resist deformation by external forces which is an important consideration in the arm and forearm (Fig. 29.6). In the case of central arterial lesions such as subclavian artery or near the arch, an angioplasty balloon-mounted stent can be used. The actual brand of stent used varies by institution.

If an arterial dissection were to occur, the first course of action would be to have a prolonged inflation of an angioplasty balloon but at lower than nominal pressures with the goal of tacking up the intima to the wall. If after a couple of

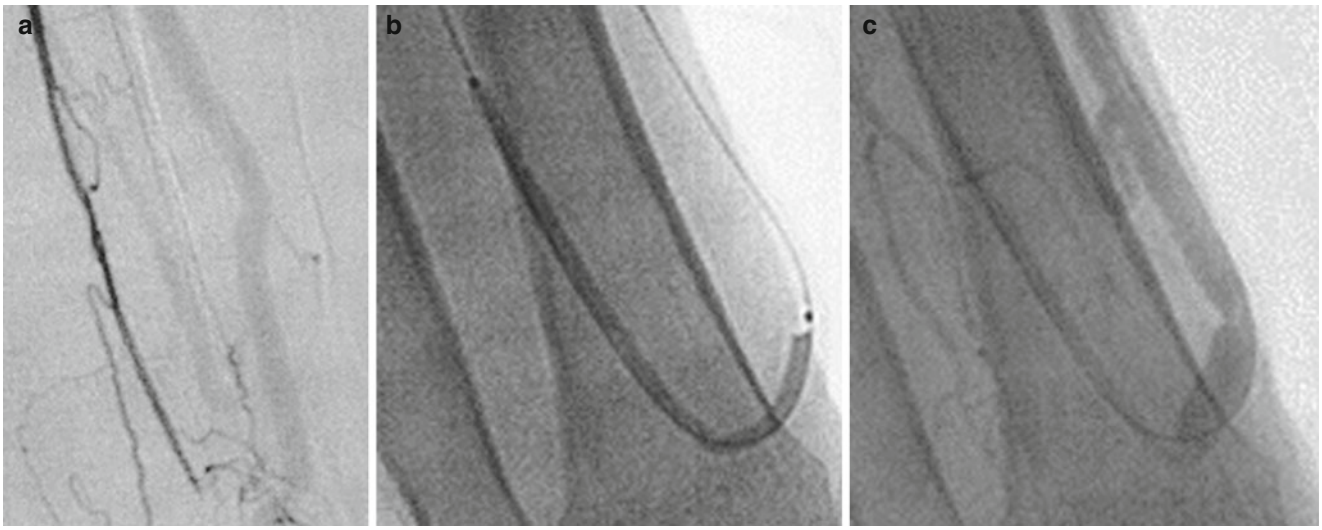

Fig. 29.5 Digital subtraction imaging obtained during a fistulagram showing patent venous outflow but a severely stenotic and nearly occluded radial artery at the anastomosis (**a**). Retrograde access was not possible so an antegrade access with angioplasty was done (**b**). Final image shows restitution of flow across the anastomosis (**c**)

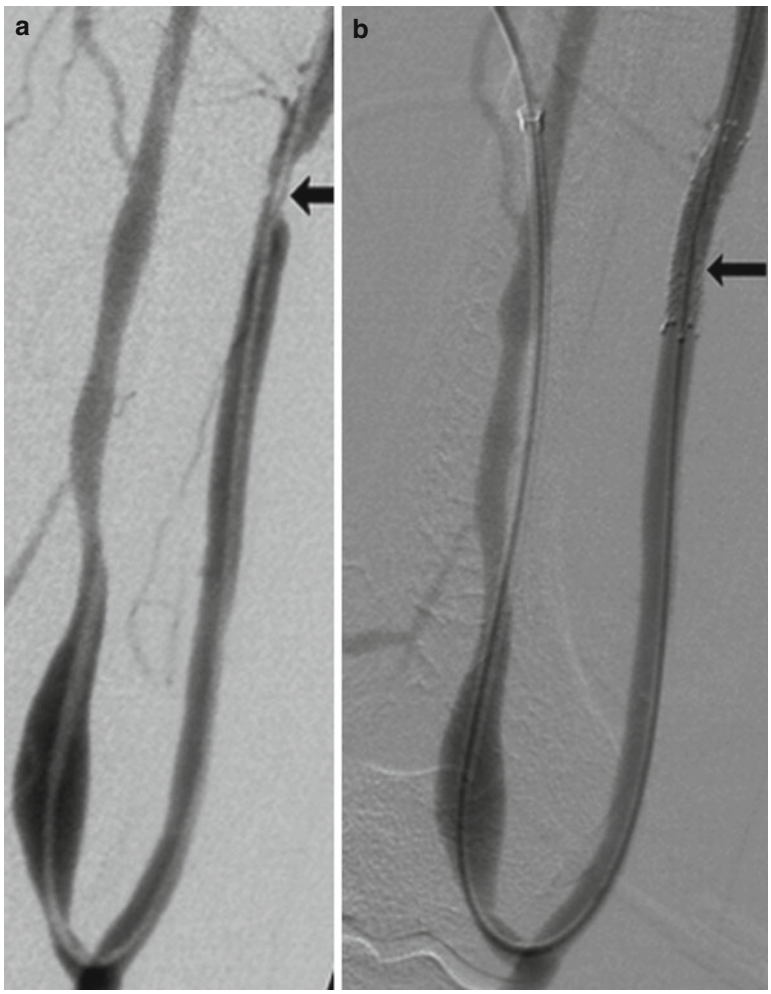

Fig. 29.6 Digital subtraction imaging obtained during a fistulagram showing (**a**) the presence of a stenosis in the brachial artery (*arrow*). (**b**) Non-resolution post-angioplasty requiring stent placement with good results (*arrow*)

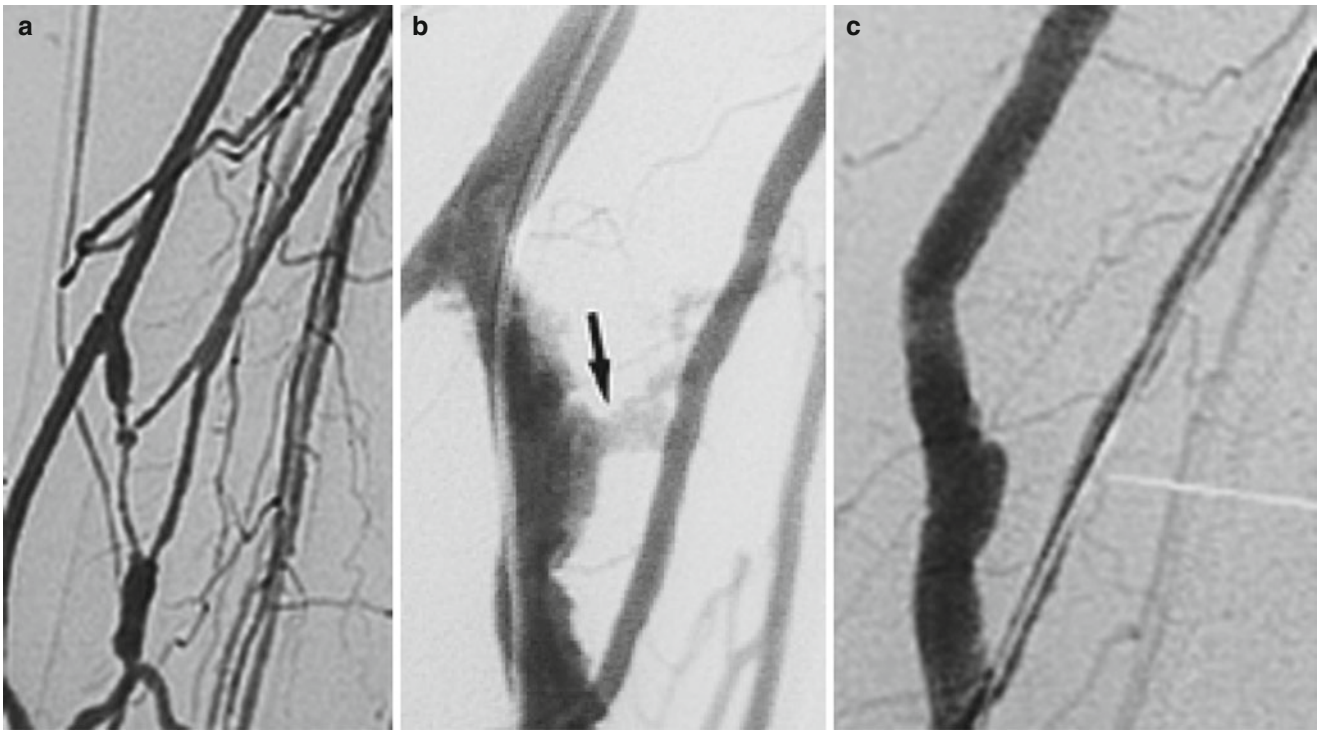

Fig. 29.7 Digital subtraction imaging obtained during a fistulagram showing (**a**) juxta-anastomotic stenosis in a failing AVF. (**b**) Contrast extravasation post-balloon angioplasty. (**c**) Good results after balloon tamponade. However, a covered stent can be used if this fails

attempts at this it is unsuccessful, then a stent may be required. Similar approach needs to be taken if there is a rupture (Fig. 29.7), but usually this situation may require surgical correction. Balloon tamponade would be employed in that situation. If that is not an option, then a covered stent can be used although at the sizes involved, they have their own long-term issues in terms of patency and need for anticoagulation and/or antiplatelet therapy.

Complications

Depending on the access, a complication rate of up to 12 % has been described with the higher rates associated with direct brachial artery access for angioplasty and/or stenting. Complications include pseudoaneurysm formation and hematomas, which may require surgical repair. The relatively high risk of complications with brachial access leads experts to argue that the routine brachial artery approach for the treatment of access stenoses is not the first choice [18, 19].

Other complications not related to the site of arterial access are similar to arterial interventions in other areas. Immediate and early re-thrombosis, flow-limiting dissection, vessel rupture, and anastomotic dehiscence do happen and have serious implications. Heparinization and correct sizing of the balloon for angioplasty is critical to avoid these complications.

Delayed pseudoaneurysm formation due to a contained rupture can also be seen on subsequent follow-up. Depending on the location and the morphology, they can be treated either surgically or with covered stents (Fig. 29.8).

Conclusion

Reduction in hemodialysis access blood flow rates due to inflow stenosis can compromise the delivery of adequate dialysis, complicate the ability to properly access the AVF, and may cause acute thrombosis. It is difficult to evaluate the exact significance of arterial stenosis in the development of access thromboses. Logically, as intra-access blood flow decreases, the risk of thrombosis increases proportionally, as would be the case in the presence of stenoses in feeding arteries, as shown in several studies describing the relationship between access flow and clotting [20, 21]. Ischemia related to the presence of a dialysis access is a relatively infrequent but potentially catastrophic complication. It can be due to venous hypertension due to venous stenosis. More relevant to this chapter is steal syn-

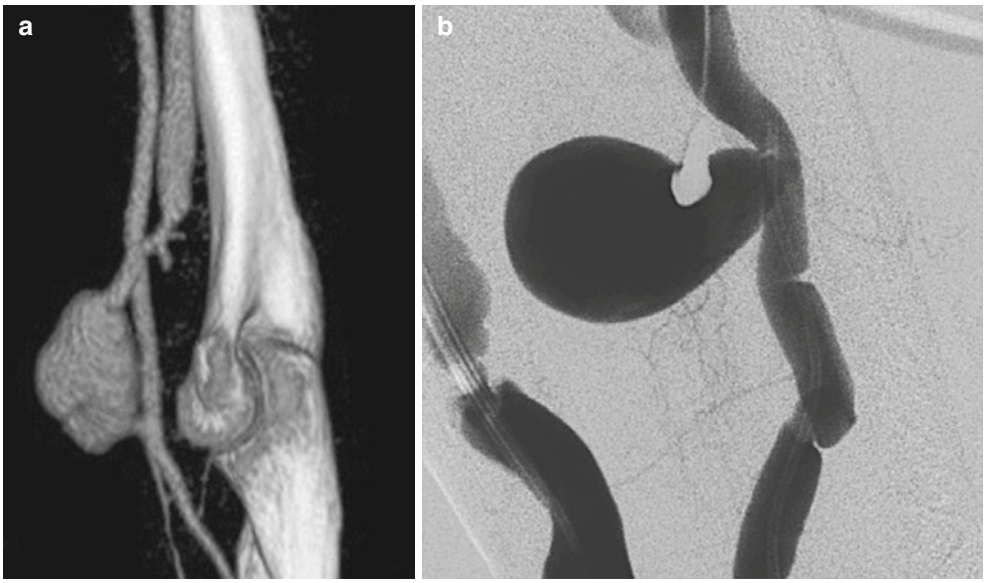

Fig. 29.8 CTA (**a**) and digital subtraction imaging obtained during a fistulagram (**b**) showing the presence of a pseudoaneurysm at the radial artery. Patient had undergone a prior balloon angioplasty for a stenosis during a fistulagram. This was repaired surgically. Placement of a covered stent is another option if needed

drome (flow reversal in the portion of the artery distal to the AVF due to a lower pressure system on the outflow side of the anastomosis) and arterial lesions, which often occur together. However, arterial lesions are relatively independent factors and should always be corrected, as shown by the clinical success of angioplasty. Successful angioplasty is durable with restenosis rates of 0 % at 1 month, 4.5 % at 6 months, 9.1 % at 12 months, 18.2 % at 24 months, and 27.3 % at 36 months [11].

As such the low morbidity and mortality of a percutaneous approach to treat inflow lesions makes it a very viable and important tool in the maintenance of hemodialysis access. It also plays an important role in augmenting an AVF with delayed maturation. All of this is highly significant in a population where dialysis is a lifeline, and it is of prime importance to salvage these as much as possible since preserving possible access sites is paramount. The advantages of having a functioning fistula are so great that it would be a great disservice to patients to not try and salvage each fistula.

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Hemodialysis Outflow Vein Stenosis

30

Eduardo Rodriguez and Karl A. Illig

Introduction

Every year, there are approximately 100,000 new patients beginning hemodialysis, and the current prevalence of patients in the United States on chronic hemodialysis is near 450,000 [1]. Most of these patients are dialyzed through an autogenous arteriovenous fistula (AVF) or prosthetic graft (AVG). The durability of any type of surgical access is relatively short, with the half-life for AVGs being approximately 1 year and those of AVFs only marginally better. Maintaining patent dialysis access for end-stage renal disease (ESRD) patients is a critical aspect to decrease morbidity and mortality for this population. Thus, understanding the mechanisms of failure and specific treatments based on the anatomic location can have an enormous positive impact on controlling access complications and improving outcomes.

The mechanisms of failure of any hemodialysis access are the result of changes, usually stenosis, at the different levels of the arteriovenous circuit and can be categorized based on the anatomic location of the stenotic area. The most common problem involves the development of a stenosis at the venous anastomosis of an AVG or in the venous outflow of any access. Some studies have shown central vein stenosis in up to 15–20 % of all patients undergoing dialysis and in up to 30 % in those with a history of prior catheter placement [2, 3].

Hemodialysis access failures affect the quality of life of ESRD patients due to the increased morbidity associated with higher numbers of hospital readmissions, invasive diagnostic studies, and open and endovascular reinterventions. The goal of this chapter is to understand the pathophysiology and management of stenosis within the hemodialysis circuit in order to better preserve functional arteriovenous access.

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Pathophysiology

Neointimal hyperplasia is the eventual cause of essentially all stenosis. Several studies have shown that neointimal hyperplasia is strongly influenced by the turbulent flow associated with the creation of an arteriovenous anastomosis. The development of neointimal hyperplasia varies in location based on the type of conduit. The majority of AVGs fail due to stenosis at the venous anastomosis, but also local tissue ingrowth in prosthetic accesses simulates neointimal hyperplasia. On the other hand, AVFs tend to present with neointimal hyperplasia throughout the entire length of the autogenous conduit as a result of repetitive puncture for cannulation.

A very common location for stenosis is within the central venous outflow tract (e.g., subclavian vein), especially in the setting of previous prolonged or repeated central venous catheterization [3–5]. The underlying pathophysiology of central venous stenosis in dialysis patients is multifactorial, and complex central venous stenosis can be present even without a previous history of indwelling central catheters [6]. Approximately 60–80 % of patients are dialyzed at some point through a central venous catheter [2]. These catheters cause intraluminal trauma which induces endothelial denudation, subsequent endothelial pericyte proliferation, increased levels of tissue factor, and, ultimately, upregulation of cytokines and growth factors that favor neointimal hyperplasia [7, 8]. In addition to the intrinsic problem (i.e., venous neointimal hyperplasia), there is an extrinsic compression involved in the pathophysiology of stenosis at the costoclavicular junction (CCJ) due to anatomic factors similar to those involved in venous thoracic outlet syndrome (VTOS) [6, 9]. The subclavian vein crosses the costoclavicular junction extending from the lateral border of the first rib to the medial end of the clavicle. This segment of vein suffers external compression by excessive bulk of the anterior scalene muscle (which lies behind the subclavian vein) as well as by tethering by the subclavius muscle underlying the clavicle and the costoclavicular ligament. All these structures

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reduce the space surrounding the central veins at the CCJ in the anterior portion of the thoracic outlet (Figs. 30.1 and 30.2). The combination of high venous flow and associated turbulence resulting from the arteriovenous access most likely exacerbates the chronic inflammatory reaction at this anatomic segment of the subclavian vein leading to stenosis and eventual occlusion [9].

Clinical Presentation

The hemodynamic result of chronic venous outflow stenosis at any level is increased pressure within the AVG or AVF, which translates clinically into venous hypertension. This presents with increasing extremity edema and extensive prominent collateral veins, pain, prolonged bleeding both during and after decannulation, and/or inability to complete efficient dialysis sessions secondary to excessive recirculation (i.e., endless loop of treatment of the same blood already filtered through the dialysis machine with little net clearance effect).

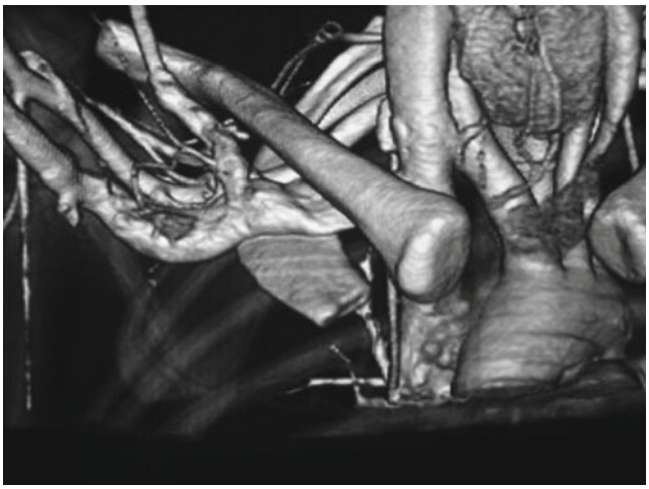

Fig. 30.2 Computed tomography scan of the right shoulder, viewed from an anterior projection, with soft tissues such as the subclavius muscle subtracted out. The right arm is elevated. Note compression of the subclavian vein as it passes between the clavicle and the first rib (Courtesy: Wallace Foster, MD, Brisbane, Australia; Reprinted from Glass et al. [25], with permission)

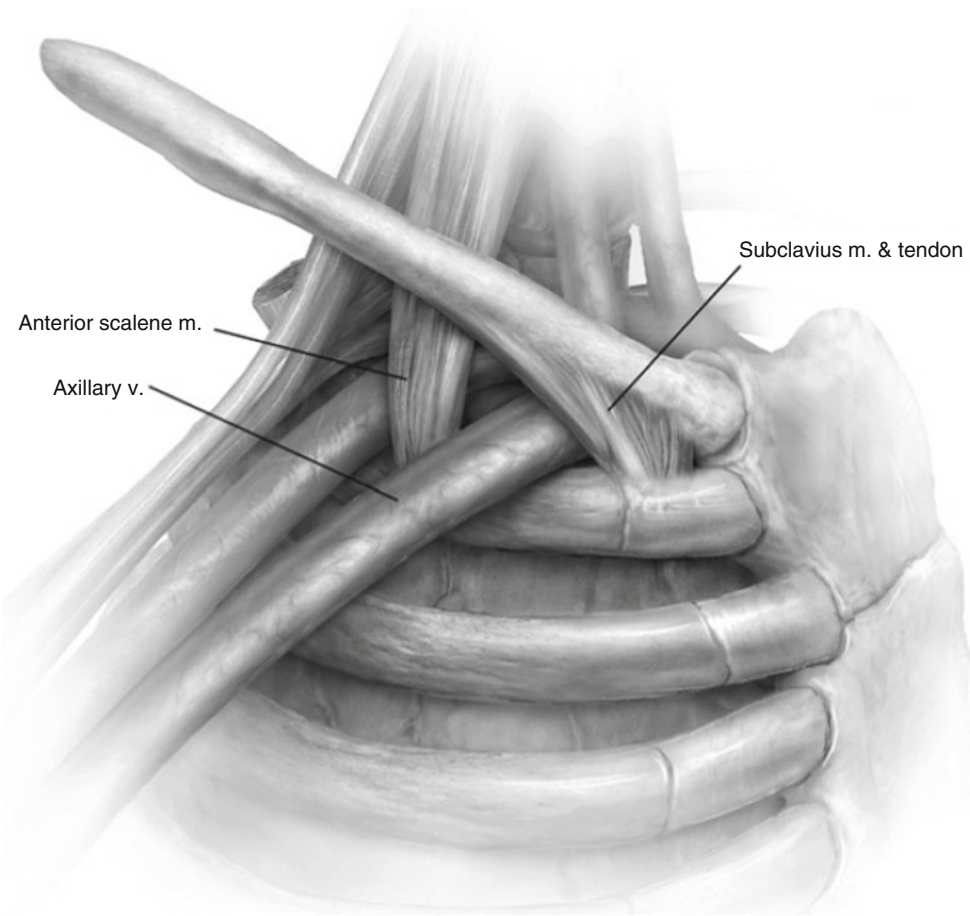

Fig. 30.1 Basic anatomy of the thoracic outlet. The axillosubclavian vein passes anteriorly, passing by the junction of the first rib and clavicle. This "space" is open superiorly, but the vein is tethered in this location by surrounding tissue. The two bones and the subclavius muscle and tendon chronically and repetitively exert pressure on it. In patients with high flow (i.e., with an ipsilateral arteriovenous fistula), this area can quickly become stenotic (Reprinted from Illig and Doyle [27], with permission)

Diagnosis

Digital subtraction fistulagraphy is the critical step in the diagnosis of patients with suspected outflow stenosis. Although invasive, a fistulagram allows identification of the anatomic location of the problem and offers the opportunity to perform therapeutic intervention in the same setting. Imaging can very easily identify stenosis in the body of the vein, the venous anastomosis of an AVG, and anywhere along the outflow tract into the atrium. Imaging of the arterial anastomosis requires occlusion of the fistula central to the injection site or injection via a catheter placed within the inflow artery itself, often with the tube angled properly to "unfold" the anastomosis. Although contrast venography is sufficient to diagnose costoclavicular junction lesions in the majority of patients, a central lesion that is present might not be identified with venography in up to 10% of cases. Intravascular ultrasound can be used in patients with classic clinical presentation without evidence of focal lesions on the fistulagram, especially in the setting of extensive collaterals on venography. Some studies suggest intravascular ultrasound should be used as standard adjunct in the diagnosis of central lesions in dialysis access patients due to its increased sensitivity [9].

Duplex ultrasound could help to confirm physical exam findings by detecting abnormalities in access flow at the level of the extremity, but the presence of the clavicle and ribs limits its utility to assess the full extent of the venous outflow tract. In terms of surveillance, studies have failed to prove any benefits of the use of duplex ultrasound to improve graft survival [10].

Management: Anatomic-Based Approach

The ultimate goal when treating a venous outflow stenosis is resolution of access function. Some signs and symptoms, such as pain and swelling, may take hours to days to resolve following the intervention. However, most problems should be expected to improve immediately following a successful procedure, including conversion of pulsatile flow to a palpable thrill in the vascular access, increased flow volumes on duplex imaging, decreased pressure gradient across the site of stenosis, and decrease filling of collateral veins on venography [6].

The options available to manage vascular access outflow stenosis or occlusion are based on the location and nature of the lesion. Once the anatomic problem is identified on the fistulagram, a definite treatment plan can be delineated. For treatment planning, it is useful to divide therapy into three separate anatomic areas where problems are commonly encountered: first, peripheral to the CCJ, which includes the arterial anastomosis, the body of the access, the venous anastomosis for an AVG, and the peripheral outflow veins (basilic and brachial veins and the cephalic arch) (Fig. 30.3); second, the veins central to the CCJ (the innominate veins and the superior vena cava (SVC)) (Fig. 30.4); and third, the subclavian vein at the CCJ (Fig. 30.5) [9].

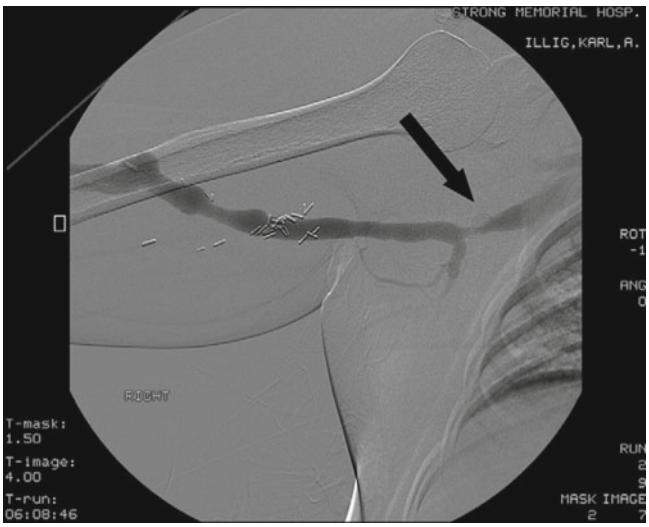

Fig. 30.3 Stenosis affecting the anatomic region proximal to the costoclavicular junction (CCJ): fistulagram showing smooth stenosis in the axillary vein in the axilla (*arrow*). This responded well to balloon angioplasty (Reprinted from Illig [9], with permission)

Outflow Stenosis/Occlusion Peripheral to the Costoclavicular Junction

The areas affected obviously differ somewhat according to whether an AVG or AVF is present. All of these lesions, however, are similar in the sense that they are only surrounded by soft tissue, making endovascular intervention attractive. Lesion location in failing AVGs can be classified into four categories: the arterial anastomosis, within the graft, the venous anastomosis, and the venous outflow tract (from the arteriovenous anastomosis to the cephalic arch). In AVFs, there are only the arterial anastomosis, body of the vein (loosely defined as the accessible segment), and outflow tract to the CCJ.

Surgical techniques were originally used to manage venous anastomotic stenosis, including placement of an interposition graft or enlargement of the anastomosis by means of patch angioplasty. Both techniques have been shown to be equivalent in terms of outcomes [11]. The main

disadvantage of using an interposition graft is the increased risk of infection (and perhaps decreased patency) due to substitution of autogenous vein with a prosthetic graft [12], although obviously autologous vein can in theory solve this problem. A patch angioplasty simply enlarges the area of stenosis without addressing the fundamental issue (i.e., neointimal hyperplasia), increasing the risk of restenosis, although this may then occur at a different and less critical location within the anastomosis.

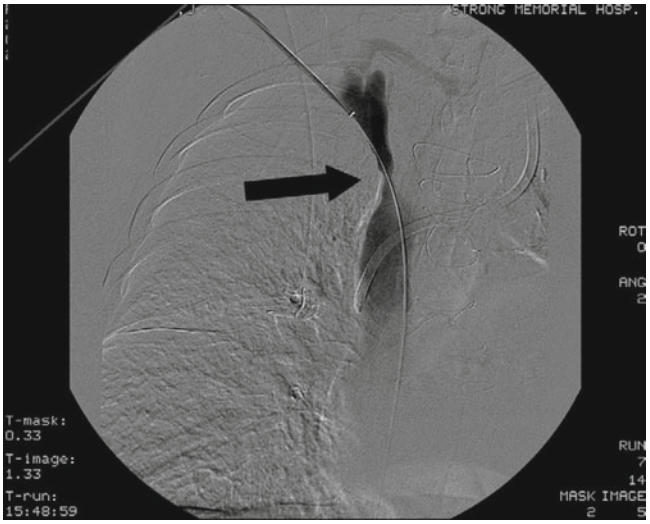

Fig. 30.4 Stenosis affecting central veins distal to costoclavicular junction (CCJ). Fistulagram of a patient with smooth stenosis of the superior vena cava (*arrow*). Note that this dialysis catheter, inserted from the left, does not seem to be involved with this lesion in any way. This responded well to placement of a 14-mm self-expanding stent that was angioplastied with a 12-mm balloon (Reprinted from Illig [9], with permission)

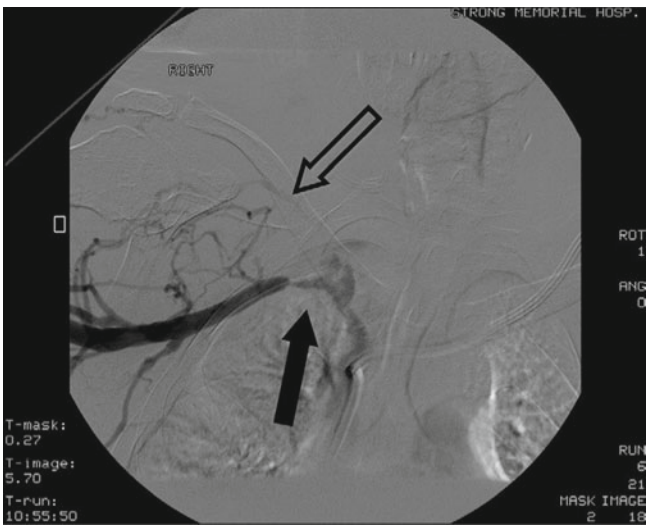

Fig. 30.5 Stenosis affecting central veins at the costoclavicular junction (CCJ). Fistulogram showing a high-grade stenosis at the CCJ with relatively normal vessels proximally and distally. Note the rather long, complex stenosis beginning at the CCJ with fairly normal vein peripherally (*solid arrow*) and extensive collateralization that is pathognomonic for this lesion (*open arrow*) (Reprinted from Illig [9], with permission)

Fully occluded outflow veins in this region require individualized treatment. Endovascular options are usually limited due to the chronicity of these lesions and the inability to cross them with a wire. In this situation, open surgical repair is usually required, with the goal being to establish adequate venous outflow. The open surgical approach depends on the extent and location of the occlusion and the status of the superficial and central veins. The most commonly used options include extensive mobilization and reimplantation of the distal segment of the AVF to a vein with patent outflow (e.g., distal cephalic vein-axillary vein), basilic or brachial vein translocation (e.g., distal cephalic vein-basilic vein), or the use of an interposition graft (autogenous or prosthetic) to bypass the lesion [9]. The patent outflow vein (i.e., cephalic) does not always need to be brought down to reach the deep system; the deep vein itself can be transected without significant clinical sequelae and brought up to meet the cephalic vein "halfway," thus preserving length for cannulation.

Most stenoses involving this anatomic segment respond well to endovascular techniques. In order of intervention, balloon angioplasty, cutting balloons for resistant lesions, or bare metal stents can all be used. Any percutaneous intervention should begin with imaging of the complete circuit to include the entire conduit from the arterial anastomosis to the central venous outflow. Endovascular percutaneous transluminal angioplasty (PTA) is the most common endovascular intervention for stenosis in this region. It is important to consider the pathophysiologic importance of neointimal hyperplasia as a cause of failure in this anatomic segment. The time and pressure required to treat the areas of stenosis can be increased due to neointimal hyperplasia. The result of these higher pressures is uncontrolled trauma to the vein, which can restimulate the neointimal hyperplasia process, leading to recurrent stenosis. Based on that assumption, multiple studies suggest that the best option may be initial use of a cutting balloon followed by PTA performed at a lower pressure [13–16]. Another important factor is the increased risk of extravasation following PTA as a result of tearing of the fibrotic neointimal hyperplasia, as opposed to the tendency to dissect in the setting of an atherosclerotic plaque.

Even though PTA has replaced surgical revision for hemodialysis access-related venous stenoses and occlusions [18], primary patency rates remain poor as a result of restenosis due to neointimal hyperplasia [17]. Even after placement of a bare metal stent, neointimal hyperplasia is still the major reason for restenosis [18]. However, when compared to angioplasty alone, stenting exhibits similar or improved patency rates. Stents are also useful for salvaging failed angioplasty procedures and thereby maintaining

patency of the hemodialysis graft. Some studies have suggested that primary patency following stenting was significantly better than the primary patency of the entire vascular access [19].

The type of stent used has been a subject of study. Covered stents have been used to prevent recurrent stenosis, probably by preventing the ingrowth of hyperplastic tissue, and thus, avoid the early failures seen with bare metal stents. This is particularly true for treating stenoses at the venous anastomosis of prosthetic AV accesses, where covered stents have been shown to have a patency advantage over bare metal stents [20].

The terminal portion of the cephalic vein, where it dives perpendicularly in the deltopectoral groove to join the axillary or subclavian vein, is labeled the cephalic arch. For unknown reasons, this is a segment particularly prone to stenosis. It is usually treated with conventional angioplasty, although high rates of restenosis are seen, and thus in and of itself is an area of research interest [17, 20]. The cephalic arch represents the outflow for any cephalic-based access (although radiocephalic AVFs usually include the deep system as outflow). Most recent studies have shown that management with bare metal stents results in unsatisfactory patency rates due to the rapid development of in-stent stenosis [21]. Some recent data support the use of covered stent grafts as an alternative to bare metal stents in recurrent cephalic arch stenosis after conventional PTA [20]. It should be strongly emphasized that any stent, whether covered or not, should protrude only minimally (or not at all) into the deep system, as this increases the risk of thrombosis of the deep as well as cephalic veins, which can lead to significant superior vena cava syndrome.

A significant clinical clue that such intervention has been hemodynamically successful is the elimination of previously present collateral veins. Such veins indicate obstruction somewhere between their origin and endpoint, no matter what is seen on the venogram. Intravascular ultrasound can be used as an adjunct in this setting to better characterize a poorly visualized stenosis, as well as to assess residual luminal diameter if collaterals are still present post-intervention. Most interventions will accomplish a relatively good result in the short term. Restenosis is common and an aggressive surveillance protocol is likely justified, although data are sparse [9].

Outflow Stenosis/Occlusion Affecting Central Veins Distal to the Costoclavicular Junction

This anatomic group includes the innominate veins and the SVC and is also usually treated with endovascular intervention (see Chap. 31, Central Venous Stenosis and Occlusion, for a full discussion).

Outflow Stenosis/Occlusion at the Costoclavicular Junction

Endovascular procedures, mainly PTA with or without stent placement, have been the most common method to manage central venous stenosis in dialysis patients with reasonable short-term results [22, 23]. Stenosis in this area seems to be much more common than would be expected. It was previously thought that the presence of subclavian dialysis catheters was the culprit, but the incidence does not seem to have decreased in the era when these are no longer used. We hypothesize that because this area is somewhat stressed in all patients, the addition of high flow after access placement causes localized turbulence in this area especially. This turbulence acts as a potent stimulus for neointimal hyperplasia, which creates an increasing fixed stenosis, worsening the turbulence and hence neointimal hyperplasia, and so on.

Recent data as well as decades' worth of experience with venous thoracic outlet syndrome suggest that, when treated with endoluminal interventions, lesions at the CCJ have poor outcomes compared to lesions surrounded by soft tissue only because of this bony impingement. Furthermore, the use of stents for treatment of lesions at the CCJ increases the risk of stent fracture and subsequent venous occlusion due to the "nutcracker" effect of the clavicle and first rib [24–27] (Figs. 30.2 and 30.6). These observations have led to changes in the management of access-related venous stenosis at the CCJ: surgical decompression by means of first rib resection or claviculectomy, with concomitant endovascular intervention, if needed [25].

The recommended algorithm starts with the diagnosis of a stenosis at the CCJ via venography/fistulogram (staged or intraoperative) (Figs. 30.5 and 30.7), followed by surgical decompression by means of infraclavicular first rib excision (i.e., removal of the anterior half of the first rib from posterior to the anterior scalene insertion site all the way to the

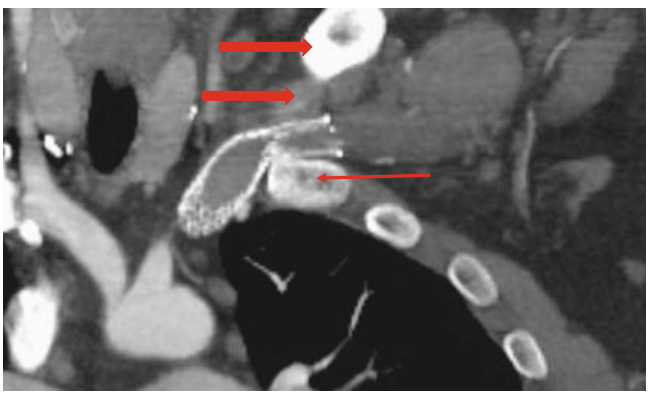

Fig. 30.6 Example of a stent crushed by the first rib (*thin arrow*) and clavicle/subclavius muscle (*thick arrows*). The CT was obtained 1 year following stenting (Courtesy Sherene Shalhub, MD)

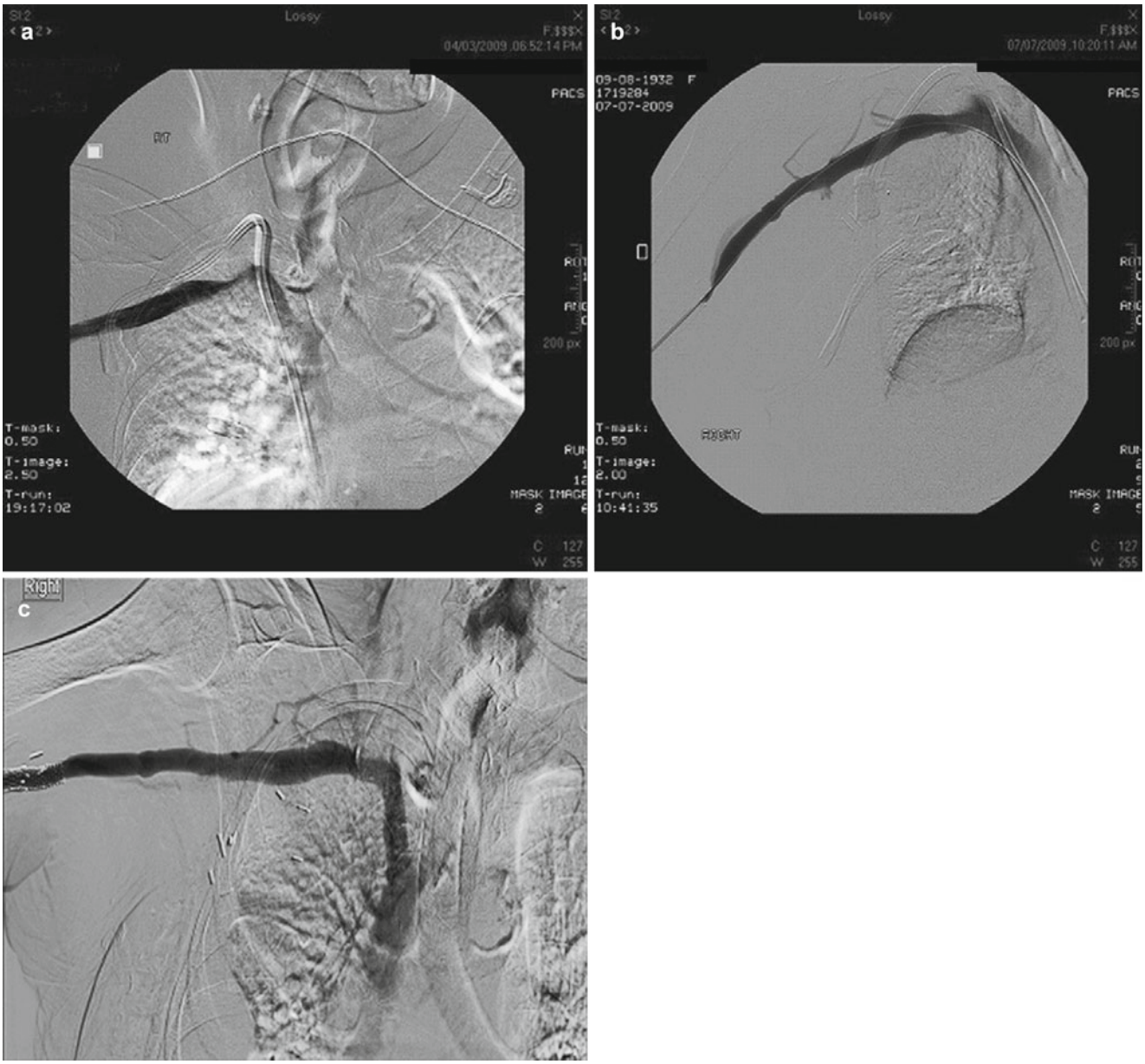

Fig. 30.7 Venography demonstrating right subclavian vein stenosis at the costoclavicular junction (**a**) before surgical decompression, (**b**) intraoperative immediately after surgical decompression with first rib resection, (**c**) demonstrating patent right subclavian vein 5 months after decompression with first rib resection (Reprinted from Glass et al. [25], with permission)

sternum), extensive mobilization of the vein, and thorough external venolysis to resect the dense cicatrix surrounding the vein. In order to ensure complete venous decompression, the tendino-cartilaginous tissue comprising the subclavius tendon and costoclavicular ligament must be completely removed and the vein completely dissected free from the overlying tissues. Claviculectomy is rarely required except for cases where extensive central outflow reconstruction extending to the innominate or SVC is expected [25].

Following rib resection, completion venography is performed to determine the degree of residual stenosis and choose endovascular vs. open repair before wound closure. The preferred option, if able to cross the lesion with a wire, would be venoplasty with or without stent placement (Fig. 30.7). An acceptable open surgical option to enhance the vessel diameter in this region after failed endovascular intervention is vein patch angioplasty (ideally using greater saphenous vein). Care should be taken to ensure that the patch extends beyond the site of the stricture both proximally and distally into the normal innominate vein medially, as well as into the normal axillary vein distally [28, 29]. Longer stenotic segments or

subclavian venous occlusions at the CCJ generally require direct reconstruction of the vein, jugular transposition, or other open surgical alternatives including extra-anatomic bypass to the internal jugular vein, subclavian vein to right atrial bypass [30, 31], and superior vena cava or innominate reconstruction using a vein or prosthetic graft for more proximal obstructions [32]. Finally, a rarely used approach in this setting includes extra-anatomic bypass from the axillary/subclavian vein to the ipsilateral internal jugular or contralateral axillary, assuming both axillary and jugular veins are patent [9].

We have used this approach since approximately 2009. In a series of cases performed at the University of South Florida, 24 patients with either failing access or need for access in the setting of CCJ lesions were so treated. Mortality was zero and morbidity low, and at 1 year 85 % of fistulas were still being used [24]. Our overall experience now includes approximately 60 patients. We have extended our indications to include the presence of a stent in situ (based on the venous TOS experience) (Fig. 30.6) and have experienced fistula salvage in approximately 90 % of patients.

Conclusions

Venous outflow stenosis or occlusion is the most common cause for access failure and is a multifactorial process that can be difficult to treat. Management of threatened hemodialysis access should be individualized based on the nature and location of the lesion. Venous lesions in the arm or chest (where the veins are surrounded by soft tissue only) can usually be treated very effectively with conventional endovascular approaches, and surgical options are excellent in the arm due to the ease of exposure. Lesions at the costoclavicular junction, however, must be addressed differently. The subclavian vein at this location is prone to injury by the bony and ligamentous structures that surround it, and for the same reason endovascular intervention, even stenting, is unusually prone to failure. Unless surgical decompression of the vein with first rib resection and venolysis is added to the algorithm, these patients very often undergo early ligation of their access, removing this arm from future consideration and likely shortening their lifespan.

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Central Venous Stenosis and Occlusion

31

Andrew E. Leake and Ellen D. Dillavou

Introduction

Etiology and Presentation

Central venous stenosis or occlusion is a common phenomenon that plagues patients on hemodialysis. The incidence of symptomatic central venous stenosis is estimated to be up to 20% of hemodialysis patients [1]. The inciting event, in almost all cases, is result of central venous stenosis can be catheters and cardiac pacemakers. The end result is venous hypertension and diminished outflow of the draining extremity. This may be asymptomatic or lead to significant morbidity, from arm swelling to life-threatening superior vena cava syndrome.

Risk factors for the development of central venous stenosis are directly related to the number of central venous catheters and their dwell time [2, 3]. Central venous catheters, tunneled and non-tunneled, cause endothelial trauma that leads to intimal hyperplasia. This appears to be further exacerbated by increased flow, turbulence, and vibrations from distal arteriovenous (AV) fistula and grafts [4, 5].

An additional, under-recognized phenomenon in patients with central venous stenosis and occlusions is the relevant subclavian vein anatomy as it traverses the thoracic outlet. The thoracic outlet is an anatomic space bounded superiorly by the clavicle and inferiorly by the first rib. Both the subclavian vein and artery pass through this space, and it is a well-recognized anatomic cause of thrombotic venous and arterial pathologies. Angiographically, this space can be recognized as the junction of the clavicle and the first rib. Stents have notoriously poor results in the subclavian vein at the costoclavicular junction, and some authors recommend outlet decompression by resection of the first rib as detailed in Chap. 33 (hemodialysis outflow vein stenosis) [6]. We find that first rib decompression is often unnecessary and is quite morbid in a compromised population. Patient selection for this procedure is paramount. However, practitioners should have a high index of suspicion for venous compression patients with a focal subclavian stenosis at the costoclavicular junction, and stenting should always be avoided in this location..

The presentation of patients with central venous stenosis varies widely. Prior to a functional access in the affected arm, most are asymptomatic due to the development of venous collaterals. When an AV access is placed on the side of occlusion, patients may develop acute onset of venous hypertension symptoms. The onset of symptoms is somewhat gradual with AV fistulas and generally increase as the fistula matures. AV grafts typically cause more immediate symptoms. Proximal AV access (brachial inflow) also is more likely to create more severe symptoms compared to distal AV access (radial). Patients with long-standing permanent accesses typically present in an indolent fashion with the development of symptoms over months to years. Symptoms include arm and facial swelling with or without pain in the extremity, neck fullness or pain and occasionally posterior cranial headache. All of these are usually exacerbated while on dialysis. Severe symptoms of massive edema and venous ulceration are rare but can occur. AV access in the extremity increases venous flow and in the presence of a central obstruction leads to venous hypertension. Venous hypertension increases transcapillary pressure, driving fluid into extracellular spaces of the extremity. Arm swelling can limit the mobility of fingers and joints with associated arm pain. Arm edema may also make palpation and cannulation of the AV access difficult and leads to increased access complications, such as pseudoaneurysms and hematomas. The increased venous pressure limits the efficiency and filtration of the dialysis requiring longer runs of hemodialysis and causes prolonged bleeding after needle decannulation.

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Diagnosis and Evaluation

After new access creation, symptoms of arm swelling and pain can be normal and generally resolve in 1–2 weeks. Persistent swelling beyond this warrants evaluation to rule out common causes of postoperative swelling such as hematomas, surgical site infections, deep venous thrombosis (DVT) and central venous stenosis, and occlusions. Physical exam gives several clues that a central venous stenosis or occlusion may be present. These include:

- Ipsilateral extremity swelling involving the entire arm and not localized to the access or the distal extremity.
- Dilated, tortuous venous collaterals across the chest (Fig. 31.1).
- Access will have a pulsatile quality from the outflow obstruction.
- Increased venous pressures during dialysis.
- Decreased flow during hemodialysis.
- Prolonged bleeding after access decannulation.

Venous duplex ultrasound of the access and the effected extremity can rule out DVT, postoperative hematoma, and any non-central venous stenosis within the access. Central venous stenosis and occlusions are difficult to diagnose by duplex, although central obstruction is suggested by diminished respiratory variation. The diagnostic study of choice to assess central vasculature is a venogram or fistulagram. This allows delineation of the entire venous outflow, central and peripheral. Stenosis and occlusion are easily identified, with the added benefit of a potential therapeutic treatment with endovascular techniques.

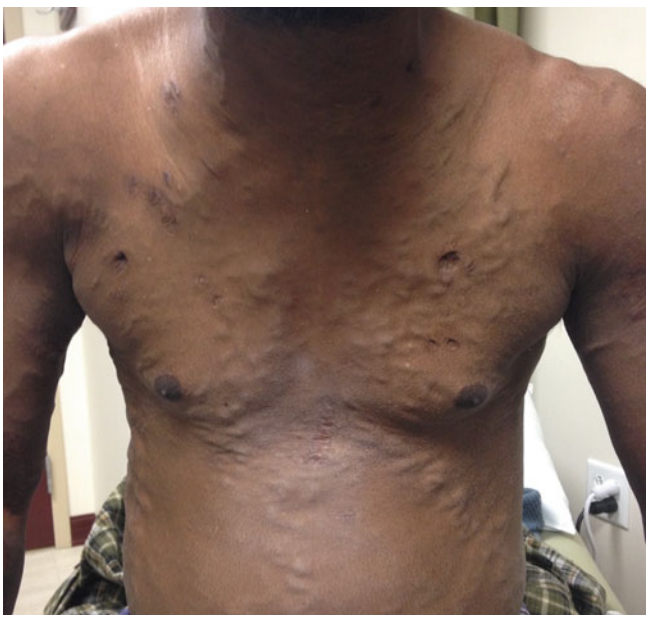

Fig. 31.1 Physical exam findings of chest collaterals in a patient with complete bilateral central venous occlusion. Note the numerous central venous catheter scars on the chest wall

The severity of venous hypertension is classically as follows [7]:

Grade 0: None
Grade 1: Mild symptoms such as mild swelling
Grade 2: Intermittent discomfort with severe swelling
Grade 3: Constant discomfort with late changes such as venous ulceration

Grade 1 can be managed with conservative therapy, while surgical treatment is reserved for patients with grades 2 and 3.

Treatment: General Considerations

The goal of treatment in patients with central venous stenosis and occlusion is improvement in symptoms (i.e., swelling) to a point that is tolerable to the patient with maintenance of the AV access. Patient education about the disease process and conservative measures to decrease arm swelling is the first step. This includes arm elevation and gentle compression of the affected extremity to decrease the symptoms of venous hypertension. Discussion should include an assessment of the patient's activity level and the use of the arm and the fact that arm swelling is not dangerous. Compression garments can be used to reduce the swelling from severe to moderate, which may be adequate in the less-active patients. The decision whether to compress the area of the fistula must be individualized, as sometimes large, high-flow fistulas may be able to tolerate compression. Aggressive fluid removal during dialysis can also help alleviate symptoms on dialysis days. Large, high-flow fistulas can be plicated near the anastomosis to decrease flow volumes while still remaining functional.

Should these conservative measures fail, there are generally three options to address the effects of central venous stenosis: endovascular treatment, open surgical treatment, and access ligation if there are other possible means of dialysis. The next several pages will highlight the different therapies in detail.

Endovascular Treatment for Central Venous Stenosis

Over the past decade, endovascular techniques have supplanted open procedures because of the large decrease in procedural morbidity, ease of use, and ability of many specialists to perform these procedures. Today, endovascular interventions are the preferred method for diagnosis and

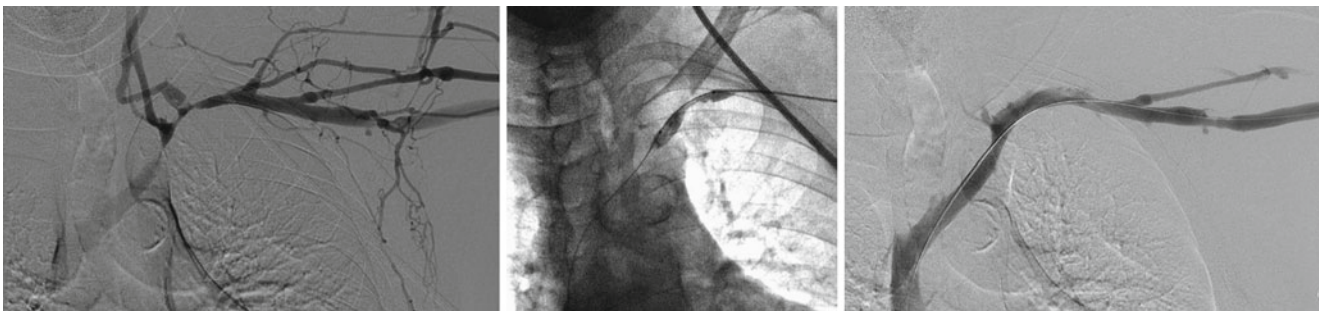

Fig. 31.2 First panel: The nearly occluded left subclavian vein with significant collaterals. Second panel: The lesion was crossed and a percutaneous angioplasty was performed with a significant waist. Third panel: Venogram after PTA shows a patent subclavian vein with no filling of the previously seen collaterals. Notice subtle irregularity of previously stenotic segment, indicating endothelial injury

treatment of central venous stenosis. The frustration with endovascular therapy is the poor durability of the repairs and need for frequent reinterventions, with some interventions compromising further surgical therapy.

Endovascular interventions can be performed in any facility with suitable fluoroscopic imaging and the ability to safely perform moderate sedation. General anesthesia is not necessary. The procedure starts through venous access, using the existing AV access. Venography is performed from the access anastomosis to the central veins draining to the right atrium. Guiding catheter placement into the central veins may be necessary to adequately visualize any significant stenosis or occlusions. Central stenosis in dialysis patients, unlike anatomic compression in other areas of the venous anatomy, is usually obvious. Confirmatory techniques such as intravascular ultrasounds or pull-through pressures are rarely needed.

Once a central stenosis is identified, the first-line treatment is percutaneous transluminal angioplasty (PTA) (Fig. 31.2). Large-size balloons (10–14 mm) are needed with inflation times of at least 2 min. Due to the fibrous nature of central venous stenosis, it often requires high-pressure, noncompliant balloons. The immediate success of initial PTA alone, without stenting, has been reported up to 70 %. Primary patency results drop down to a sobering 29 % at 1 year [8], and symptom relief at 1 year is equally poor [9]. Due to this poor durability, PTA requires frequent reinterventions to maintain patency. With frequent interventions, patency can be maintained in up to 86 % at 1 year [9].

Primary stenting also has a very poor performance, with primary patency at 1 year to be only 21 % [8]. The high failure rate of central venous stents is not fully understood, but it is clear that intimal hyperplasia is aggressive in the central veins. Stents are reserved for lesions that recur at intervals less than 3 months, perforations or residual stenosis greater than 50 %. Stents should be oversized by at least 30 % to prevent migration, and care should be taken to not cover critical venous branches (the internal jugular (IJ) or contralateral brachiocephalic vein). Stent placement should be avoided at the costoclavicular junction, where the subclavian vein enters the thoracic outlet. Technology in endovascular surgery is quickly changing, and it is important to recognize that many available studies have used first-generation stainless steel wall stents (Fig. 31.3). More recently, the use of covered stents in the central veins has gained popularity, in part, because small early studies have indicated decreases in intimal hyperplasia and stent failure [10–12]. Outcomes are promising with primary patency at 1 year of 67 % and assisted patency at 2 years of 75 % [12]. Evolving technology with drug-coated balloons and stents, targeted at halting intimal hyperplasia, may further change the endovascular management of central vein stenosis in the future.

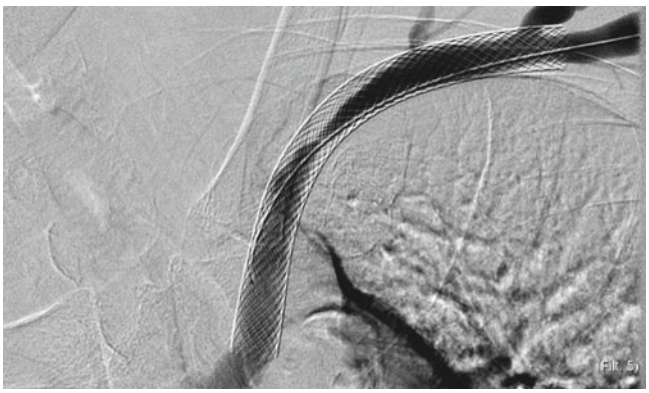

Fig. 31.3 Intimal hyperplasia seen on venogram months after a left subclavian stent with a stainless steel Wall Stent (Boston Scientific)

Endovascular Treatment for Central Venous Occlusion

Central venous occlusions are more challenging to treat than central venous stenosis. Crossing occlusions is often performed using hydrophilic wires with guiding catheters and usually requires support with long sheaths. Patience is required for these difficult lesions and establishing access from the arm, the ipsilateral neck (internal jugular), and the

contralateral IJ as well. If unable to cross from the upper extremity, attempting to cross from the lower extremity is occasionally helpful. Once the total occlusion has been crossed, some authors advocate for mechanical or catheter-directed thrombolysis to unmask the true stenotic lesion and remove any thrombus. We find this is not typically necessary as the occlusions are normally chronic and more fibrous, and so we will treat with PTA and/or stent as highlighted above and have not experienced embolic complications from this technique.

Endovascular Treatment Complications

It is important to highlight the potential complications associated with endovascular treatment. Access site complications are most common and include bleeding, cellulitis/AV access infections, and access thrombosis. Procedures should be performed under sterile conditions and the extremity adequately prepped. When accessing a prosthetic AV graft, it is our routine to give preoperative antibiotics covering common skin organisms. Complications specific to central vein stenosis/occlusion are potentially life threatening. Venous perforation, with high flow from a distal AV access, can lead to significant bleeding in the mediastinum and pleural or pericardial spaces. Early recognition is essential, and often times the bleeding can be controlled with local balloon inflation or deployment of a stent graft across the tear though open repair may be indicated and requires an emergent surgical consultation.

Open Surgical Treatment

Open surgical procedures to directly address central venous stenosis and occlusion carry a significant morbidity, usually requiring median sternotomy to access the subclavian vein and right atrium. In general, open surgical treatment is reserved for patients who have failed endovascular treatments, are young, and continue to have severe symptoms [7]. Prior to any open surgical procedure, a central venogram is necessary to fully delineate patient's venous anatomy. The goal of open surgical treatment is to provide venous outflow into the right atrium, either directly through the central veins (central reconstruction) or indirectly by way of a bypass to other open veins (extra-anatomic bypass). Below we highlight the surgical considerations for central reconstruction, extra-anatomic bypass, access ligation, and several special considerations.

The first described repair of a central vein was in 1976 using a spiral great saphenous vein graft to reconstruct the superior vena cava [13]. Central reconstruction has been reported with excellent outcomes that far exceed endovascular repair. Estimated primary patency of 88 % [14, 15] and 100 % [14, 15] secondary patency at 2 years. Central reconstruction includes either direct repair/reconstruction of the occluded central vein or bypass directly to the right atrium [16]. Reconstruction can be performed with a large prosthetic graft or a spiraled great saphenous vein (Fig. 31.4) [13]. Open venous patch angioplasty has also been described on stenotic central veins. These surgical options have excellent reported durability; however due to the associated complications with sternotomy, this is rarely performed.

Extra-anatomic bypass from the access to a peripheral vein that drains to the right atrium is another alternative to a major central reconstruction. The major advantage of this surgical option is avoidance of a sternotomy. Venous bypasses usually need general anesthesia and carry higher infectious and thrombotic risks than central reconstruction. Patients are typically maintained on anticoagulation and perhaps antiplatelet therapy for the life of the bypass. The published outcomes are also favorable to endovascular repair with a primary patency of 66–67 % [9, 17] and a secondary patency of 71 % [17]. A variety of venous bypasses have been used for access outflow, including the saphenous vein, femoral vein, ipsilateral jugular vein, and contralateral jugular vein [18, 19]. Central lesions that are medial to the internal jugular (IJ) vein require a bypass to the contralateral jugular, axillary, or lower extremity (femoral vein). The more common location, lateral to the IJ, allows utilization of the ipsilateral jugular for venous outflow. This situation allows a bypass to the internal jugular (Fig. 31.5) or transposition of the IJ vein to the distal subclavian, called an "IJ turndown" (Fig. 31.6) [19].

A relatively new tool for central stenosis is the Hemodialysis Reliable Outflow (HeRO made by Merit Medical, South Jordan, UT) graft. This can allow catheter removal and peripheral access placement without losing access to the right atrium. The HeRO graft is a composite graft composed of a central venous silicon and nitinol outflow portion placed in the right atrium that is connected to a polytetrafluoroethylene (PTFE) arteriovenous graft. The HeRO is most commonly used as a graft in the upper arm or thigh and is placed primarily in patients with known central stenosis or occlusion. This can be done using an existing tunneled catheter as a route to the right atrium or by recanalizing occluded or stenotic veins. The HeRO can also be used to "rescue" a failing fistula or swollen arm due to central venous stenosis. The failing access can be anastomosed to the PTFE cuff of the HeRO, providing outflow of the current access. The overall patency of the HeRO graft is poor with a 1-year primary patency of 15 % [20], but this is used in patients with no access options short of central reconstructions. The HeRO graft is discussed in detail in Chap. 35.

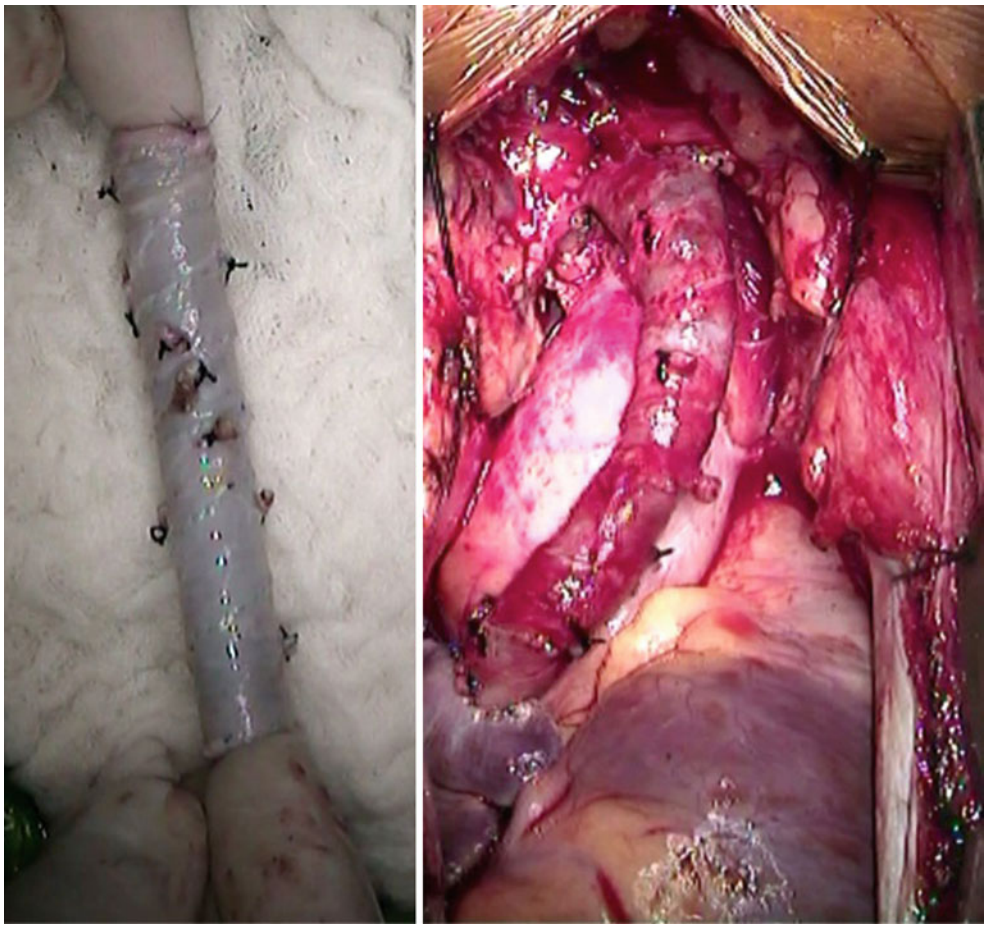

Fig. 31.4 Spiral graft: Spiral graft fashioned from the great saphenous vein (*left*). Implanted as a bypass from the left innominate vein to the right atrium (*right*) (Photos courtesy of Mitchell Cox, MD, Duke University Medical Center, Durham, NC)

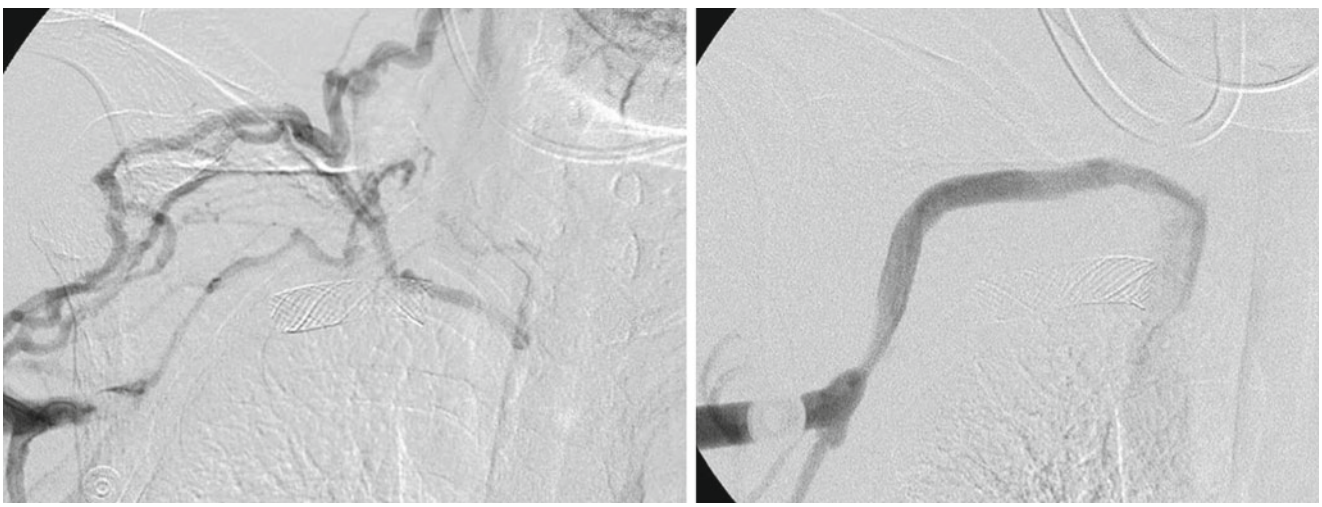

Fig. 31.5 First panel shows an occluded right subclavian stent with venous collaterals. This was treated with a right axillary artery to right IJ bypass with prosthetic shown in the second panel

Access abandonment or ligation is reserved as the last resort. It is the most definitive option for immediate resolution of patients with severe symptoms and a functioning access. This is the treatment of choice in life-threatening superior vena cava syndrome. It may not fully resolve symptoms as the central stenosis has not been addressed, but by decreasing the arterial component of venous will immediately decrease symptoms. The obvious downside is that permanent access for dialysis is now lost, necessitating another central catheter. Catheter placement in this patient

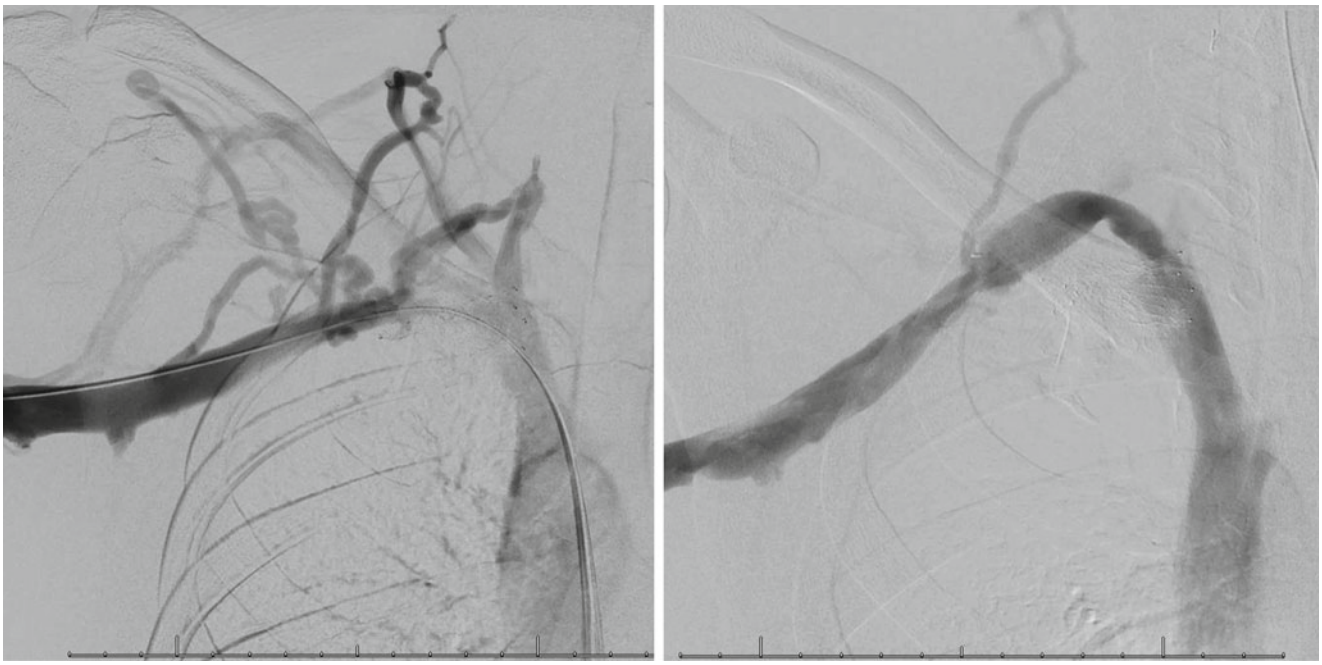

Fig. 31.6 The first panel shows an occluded right subclavian stent with significant collaterals. The second panel is after a right internal jugular turndown procedure. The right IJ is dissected in the neck then turned down and anastomosed with the right axillary vein to bypass the subclavian vein

population is particularly difficult and may mean catheter placement in suboptimal locations, such as the femoral or hepatic vein to gain access to the right atrium.

Conclusion

Central venous stenosis and occlusion are a significant source of morbidity in dialysis patients due to venous hypertension. Diagnosis is best confirmed with venography, and first-line treatment is percutaneous angioplasty. Stent placement should be reserved for patients with residual stenosis or with frequent recurrences and may mean a continued dependence on frequent fistulagrams and interventions for in-stent stenosis. Open surgical procedures are reserved for endovascular failures in good-risk patients due to their associated morbidity. Recurrence of disease after treatment is the rule, not the exception; so careful planning is necessary to maintain functioning access.

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The Hemodialysis Reliable Outflow (HeRO) Graft

32

Shawn Gage, David Ranney, and Jeffrey Lawson

Introduction

The establishment and maintenance of hemodialysis access has seen periods of challenge and stability, followed by newer and more complex challenges in the years since the dialyzer apparatus (artificial kidney) was developed by Willem Kolff in 1943. As patient longevity improves with better patient care, providers are now faced with the challenge of maintaining dialysis access for longer periods of time. An unfortunate consequence of this is an increase in encounters with the healthcare system and a growth in the number of tunneled dialysis catheters a patient requires over their arteriovenous (AV) access lifetime. This increased catheter contact time has led to an upsurge of endovascular interventions in the central venous system and an epidemic of thoracic vein pathology [1].

Since the 1970s, few technological advances have been made that truly improve upon the delivery of hemodialysis access, and, of the newer graft technologies, none have been relevant to a patient with moderate to severe central vein pathology. At the turn of the millennium, Dr. Squitieri invented a device (Graftcath) that could be used as an arteriovenous graft (AVG) but could bypass or mitigate the abnormal, stenotic, or occluded thoracic central veins that had become the cause for countless AV access complications, interventions, and failures (Figs. 32.1, 32.2, and 32.3). For those patients deemed to be "catheter dependent," Graftcath proved to be superior to tunneled dialysis catheters (TDCs) in terms of rate of infection and dialysis adequacy [2]. This technology evolved into the HeRO graft and became commercially available in July 2008. Since that time, thousands of previously catheter-dependent patients have enjoyed a catheter-free life with fewer infections, fewer interventions, and better dialysis quality [3]. In this chapter, we will discuss the patient population, selection, and strategic planning around the use of the HeRO graft, as well as the technical considerations, potential pitfalls, complications, and outcomes associated with the device.

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Patient Selection

The HeRO graft is primarily intended for use in patients with moderate to severe central venous occlusion and/or stenosis as demonstrated by upper extremity and thoracic central venous imaging [4]. Previously, the presence of central venous occlusion meant that few options remained for dialysis access and that these patients had reached the final conventional stages of dialysis. Alternatives at this juncture carried significant morbidity. The most morbid of these options was direct right atrial access via sternotomy or thoracotomy as well as the use of translumbar or hepatic catheters [3]. Central venous reconstruction was also attempted in certain cases but with poor success [3, 16–18]. The most common alternative today is the tunneled dialysis catheter (TDC); however a high incidence of infection, malfunction, poor flow rates, and mortality has incentivized the investigation of novel alternatives [5, 6]. As such, patients who have exhausted all traditional access methods and have succumbed to central venous occlusion are ideal candidates for the HeRO graft.

For patients with a preexisting AV access (arteriovenous fistula (AVF) or AVG) that is failing, the use of the HeRO device has been described as a salvage therapy. In these instances, the graft component of the HeRO device is anastomosed to the existing AV access, diverting all flow through an uninterrupted pathway to the right atrium. In some cases, this can allow for the immediate use of the access without the need for ligation or explanation. Early

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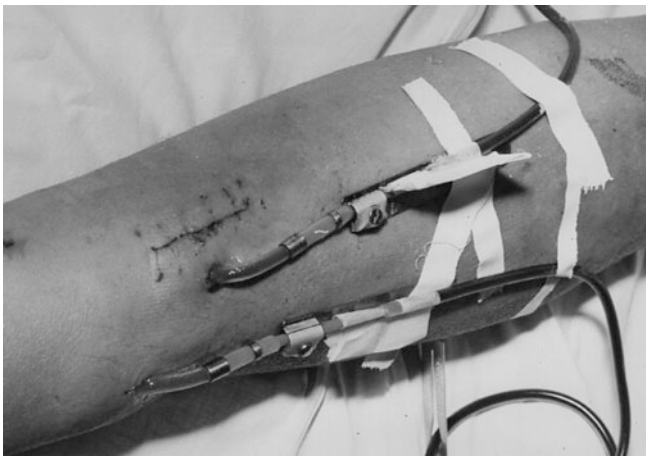

Fig. 32.1 Forearm Scribner shunt, VA Hospital, Bronx, NY 1964 (Courtesy of Dr. Lawson)

Fig. 32.2 Early Graftcath device. Note: Venous outflow component without nitinol reinforcement (generation 2) (Used with the permission of CryoLife, Inc.)

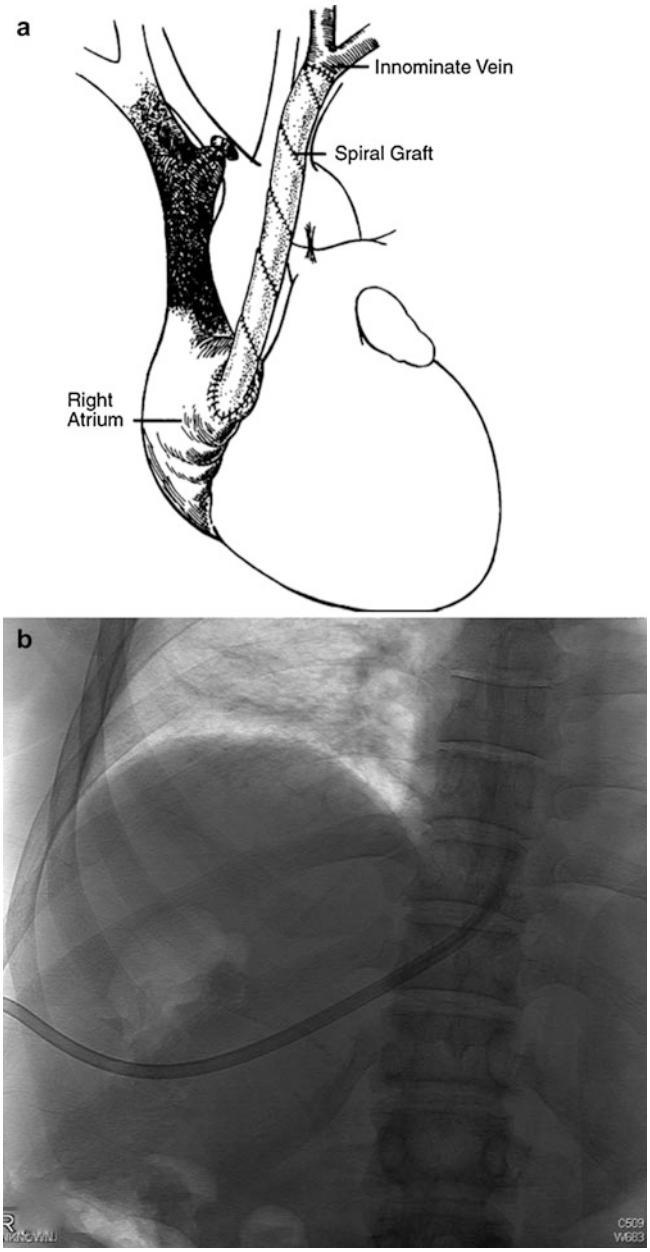

Fig. 32.3 (**a**) Reconstruction of occluded superior vena cava with spiraled vein graft to the right atrium (Reproduced with permission from Mr. Gage and Dr. Lawson) (**b**) Pre-HeRO patient with transhepatic permcath (Courtesy of Gage and Lawson, Duke University)

use also obviates the need for a bridging TDC, which carries additional clinical sequelae [5]. While balloon angioplasty or stenting can be used for short-term benefits in certain cases, the early experience would suggest that the HeRO graft provides a more durable solution to mitigating the complications associated with central venous occlusion in the dialysis population [3].

Relative contraindications for HeRO implantation include a brachial artery diameter less than 3 mm, congestive heart failure with ejection fraction less than 20%, and systolic blood pressure less than 100 mmHg [6]. However, there is no significant clinical data to support these claims. As with any intervention, particularly in this high-risk population, the risks and benefits of each alternative must be carefully evaluated prior to selection.

Technique

Pre-procedural history and physical exam should be performed prior to selection of the HeRO graft. A detailed account of prior and current dialysis access, vascular interventions, and status related to potential kidney transplantation should be noted. Imaging of the upper extremity and central veins will reveal sites of occlusion. Conventional venography provides excellent imaging of the axillary and subclavian veins, but we find that CT or magnetic reso-

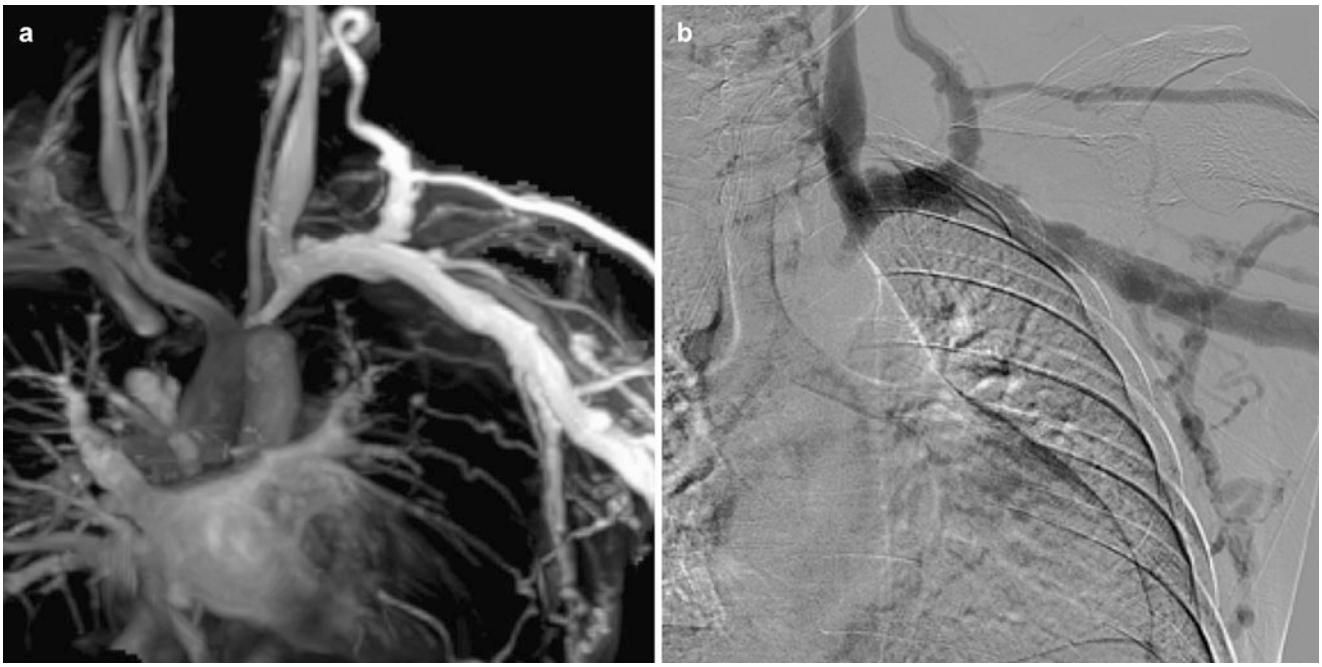

Fig. 32.4 (**a**) Magnetic resonance imaging with arterial and venous phases, using feraheme for contrasting agent. Study reveals occlusion of bilateral innominate veins and SVC and also notes relationship of arterial structures. (**b**) Conventional venography which only reveals occlusion of the left innominate vein (Courtesy of Duke University and Charles Kim)

nance (MR) angiography in the arterial and venous phases provides the most comprehensive data in cases of total central vein occlusion (Fig. 32.4). Central vein recanalization requires evaluation of the structures adjacent to the native venous anatomy and requires careful operative planning. As with any AV access surgery, there are three main principles for success: good inflow, good conduit, and good outflow. When planning for HeRO graft placement, in general, inflow is less of an obstacle. However, one must be aware of atherosclerotic disease as well as severe diabetic arterial vasculopathy. Establishment of central venous access can often be the most challenging aspect of the procedure. In the patient with moderate stenosis, percutaneous access via the most common routes (i.e., internal jugular and subclavian vein) has a high rate of success. In cases of severe central stenosis or occlusion around an indwelling tunneled dialysis catheter, central venous access can be attained with ease by exposing the catheter at its venous access point, transecting and guiding wire placement (Fig. 32.5). However, in those patients with severe stenosis or occlusion without access, preoperative central vein recanalization is recommended to ensure a successful HeRO graft implantation.

The procedure is performed in the operating room or hybrid OR under general anesthesia to facilitate the need for operative management of complications such as bleeding and intrathoracic venous rupture or vascular injury, as well as the vigorous nature of subcutaneous tunneling in the neck and chest. Preoperative antibiotics are administered per standard protocol.

A venous access site is selected first. Standard options include the internal jugular, subclavian, axillary, or femoral veins. The internal jugular vein is the most common choice, followed by the subclavian vein and then femoral vein [3]. The right or left side can be accessed interchangeably. The venous outflow component (VOC) of the device consists of a 5 mm ID silicon stent reinforced with nitinol and is inserted through the venous target and into the right atrium using the Seldinger technique. Traversing the stenotic lesion can be challenging depending on the luminal area. Once the wire traverses the lesion, balloon angioplasty of the central veins is recommended prior to delivering the HeRO VOC [6]. We recommend using an 8 × 40 mm high-pressure balloon over a stiff wire in order to create sufficient space to deliver the VOC. Using a stiff wire improves the maneuverability of large devices in tight spaces and reduces the risk of tearing or rupturing the central veins when inserting rigid dilators and peel-away sheaths. Once the VOC traverses the lesion over the wire, angiography is used to verify the radiopaque tip location at the cavoatrial junction. We find that the dome of the right hemidiaphragm is a useful initial landmark to guide placement of the VOC tip close to the middle of the right atrium. Once confirmed, the opposite end of the venous outflow is tunneled subcutaneously toward the shoulder or delto-pectoral groove and is delivered outside the body through a

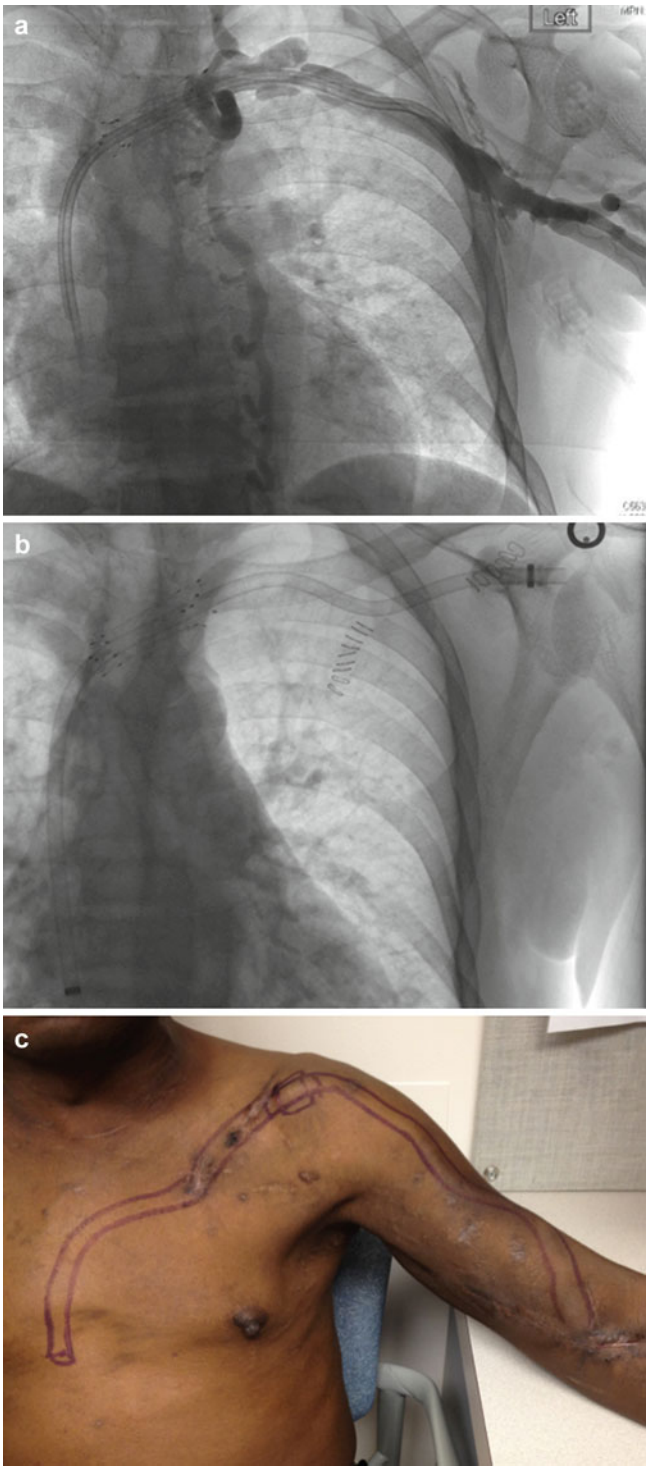

Fig. 32.5 (**a**) Patient with total central venous occlusion around left subclavian TDC. (**b**) TDC now exchanged for HeRO VOC. (**c**) Outline of completed HeRO graft noting its position on the chest, shoulder, and arm (Courtesy of the authors, Duke University)

counter incision. Care should be taken to avoid tunneling the VOC too lateral which can lead to kinking of the graft/connector interface.

Attention is then turned to the arterial side. Graft material is most commonly expanded polytetrafluoroethylene (ePTFE). This material requires time for tissue incorporation, although the use of early-access graft material such as Flixene or Acuseal has been described [7]. This early-use method requires an additional anastomosis to the most proximal aspect of the arterial end but can be used within 24–72 h, which thus obviates the need for a bridging TDC and its added risks. Next, the arterial graft is tunneled from the counter incision out toward the bicep in a generously curved tract to avoid kinking. The distal end is brought out through an incision over the expected arterial anastomosis site. The arterial and venous ends at the previous counter incision are coupled using the titanium connector by sliding the VOC over the hose-barb connection.

In late 2015, CryoLife released its new HeRO Graft Adapter in a limited launch. The development of this feature came about as a result of clinician feedback and the desire to use the surgeon's graft of choice as the cannulation segment (particularly early cannulation or low-bleed grafts). At this point, the only two grafts approved for use with the Adapter are the Gore® Acuseal (W.L. Gore & Associates, Flagstaff, AZ and Flixene® Standard Wall Atrium Medical Corp., Hudson, NH) hemodialysis grafts (Fig. 32.6). A final angiogram is performed through the entire access circuit to ensure the VOC is in the proper position and there is no kinking at the connector or within the graft tunnel. We then perform the arterial graft anastomosis to the selected artery. Incisions are fully closed and the HeRO device can be safely accessed in 3–4 weeks. While the bridging TDC is in place, we recommend administration of vancomycin with hemodialysis sessions until removed [4].

When salvaging preexisting AV access, the arterial inflow from an AVF or AVG can be anastomosed directly to the HeRO AV graft while the venous end is installed in the usual fashion (Fig. 32.7). Allan and Gage describe this method in several case reports with favorable success [8].

Complications

Complications arising from the use of the HeRO device have been well characterized in the recent literature. Thrombosis most commonly occurs in the lumen of the arterial graft and not at the interface within the connector as previously thought. Clot within the venous cannula does not vigorously adhere to the silicon surface, which provides an advantage when removing thrombus. Kim et al. describe intra-graft stenosis as the most common culprit lesion in their series of HeRO graft interventions [9] (Fig. 32.8). Thrombectomy in these instances is straight-

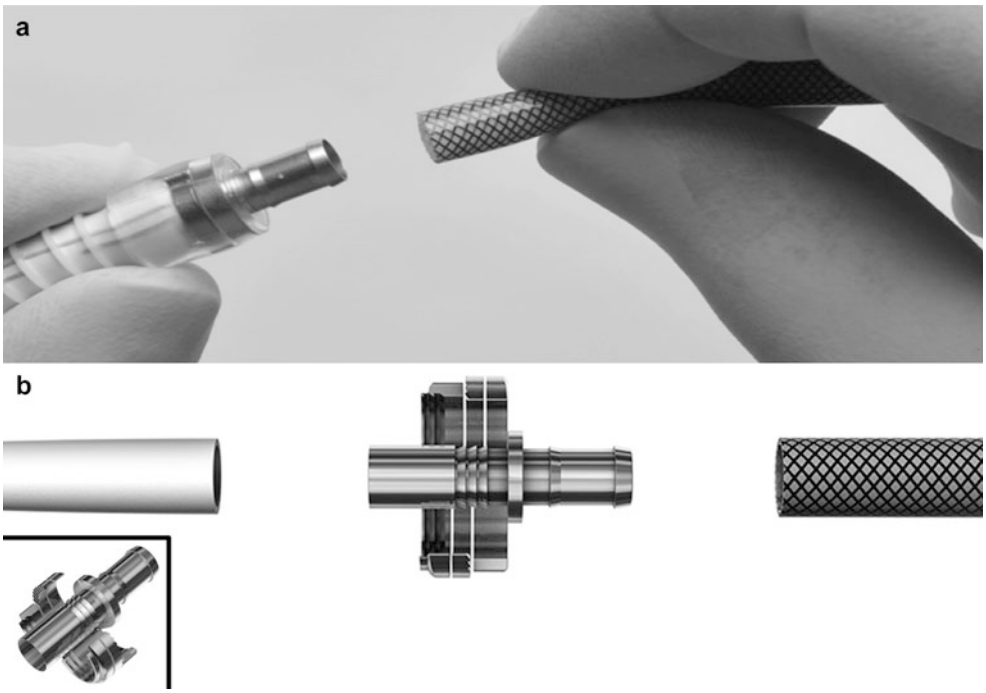

Fig. 32.6 (**a**) HeRO connector (*left*) and VOC (*right*). (**b**) HeRO Adapter (Used with the permission of CryoLife, Inc.)

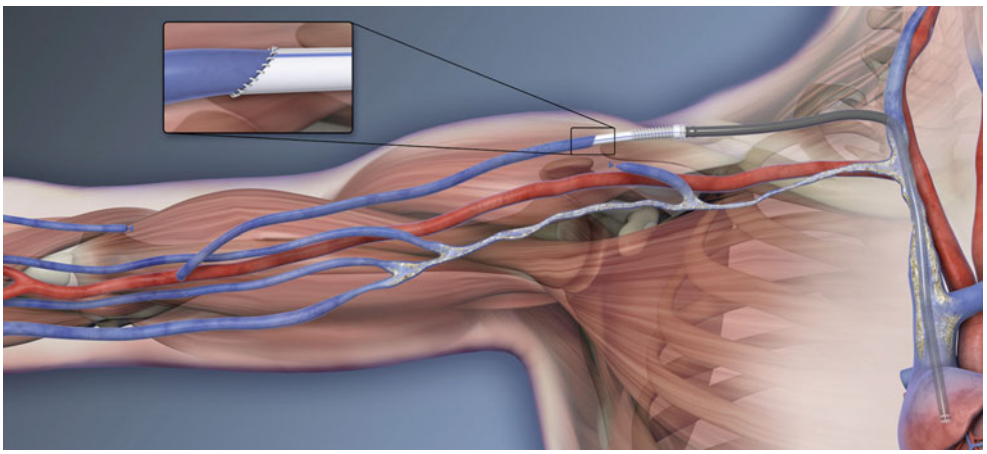

Fig. 32.7 Illustration of fistula outflow revision with HeRO graft via fistula to graft end-to-end anastomosis (Used with the permission of CryoLife, Inc.)

forward and can be performed with open or endovascular techniques [3]. Mechanical or chemical thrombectomy can be utilized; however, mechanical techniques other than Fogarty balloon thrombectomy are discouraged in some reports for fear of damage to the device [6].

Infection rates vary in the literature, although a bacteremia rate of 0.14 per 1000 implant days has been reported [3]. This is considerably lower than a rate of 2.3 per 1000 days as seen in the TDC population. A study by Katzman of 36 patients followed for 8.6 months demonstrated a bacteremia rate of 0.70 per 1000 days, with all of these occurring in the presence of a bridging TDC [1]. One systematic review documented a bacteremia rate of 0.13–0.70 per 1000 days [10]. Rates of bacteremia have been shown to be similar to those with upper and lower extremity AV grafts [11] (Table 32.1).

Steal syndrome has been reported in 1.4 % of cases in a series by Gage [3]. The absence of a venous anastomosis with the HeRO graft is thought to be responsible for this phenomenon, although the smaller diameter of the VOC and longer overall access circuit length of the HeRO often provide enough resistance to counteract the forces that lead to steal. Impingement and crushing of a HeRO graft at the costoclavicular junction when inserted into the subclavian vein have also been reported (Fig. 32.9). This complication led to outflow obstruction requiring graft explantation [13]. In these cases, moving the VOC to the supraclavicular position is ideal, but when not

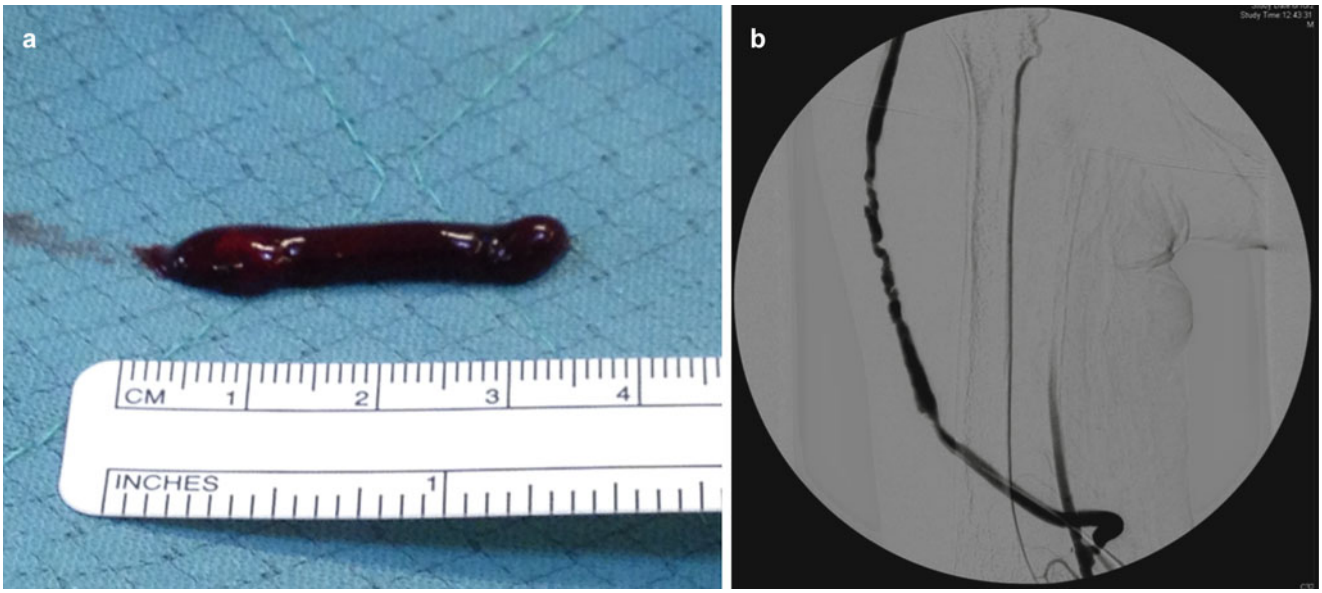

Fig. 32.8 (**a**) Small (approximately 3 cm in length), congealed, nonadherent thrombus reminiscent of the typical, minimal clot burden present within the VOC during thrombectomy. This is typically located in the proximal aspect of the VOC, adjacent to the connector. (**b**) Typical intra-graft stenosis seen within the HeRO and most ePTFE graft cannulation segments (Courtesy of the authors, Duke University)

Table 32.1 Bacteremia and intervention comparison of published HeRO data, AVG literature, and TDC literature

Study	Bacteremia rate per 1000 days	Intervention rate per year
Current HeRO multicenter	0.14	1.5
Gage et al. review May 2010 [12]	1.29	1.38
Katzman et al. study Sept 2009 [2]	0.7	2.5
AVG literature control [2]	NA[a]	1.6–2.4
TDC literature control [2]	2.3	5.8

Reproduced from Gage et al. [3]

[a]Information not available

possible, we have simply replaced the VOC in the subclavian vein and have observed acceptable patency. Placement via the subclavian vein is not a contraindication; however, the possibility of a VOC crush injury should be considered when placement into the subclavian vein is necessary.

VOC placement is critical. Placement of the tip beyond the cavoatrial junction into the IVC can lead to stenosis or lodge in the hepatic veins causing thrombosis. Inadvertent placement of the VOC into the right ventricle can lead to tricuspid valve injury, regurgitation, and HeRO thrombosis. Conversely, VOC tip placement too high can result in the VOC lodging into the origin of the azygos vein, leading to thrombosis or HeRO failure in a stenotic superior vena cava (SVC). When implanting the device in obese patients or those with large, pendulous breasts, great care should be taken to secure the breasts caudally. Doing so will mimic the effect of gravity on the skin and tissue of the chest when the patient is in the upright position and provide a more favorable position for the skin when accessing the vessels percutaneously. Failure to do so may result in significant retraction of the VOC and lead to certain HeRO thrombosis (Fig. 32.10).

Outcomes

In general, the rates of infection, patency, and need for reintervention are similar to traditional AV grafts but are an improvement over the TDC, a finding supported in several studies [4].

Gage and colleagues demonstrated primary patency rates of 60.0 %, 48.8 %, and 42.9 % at 6, 12, and 24 months, respectively. Secondary patency rates were impressive at these same time intervals, reported as 90.8, 90.8, and 86.7 % [3]. Katzman reported primary and secondary patency rates

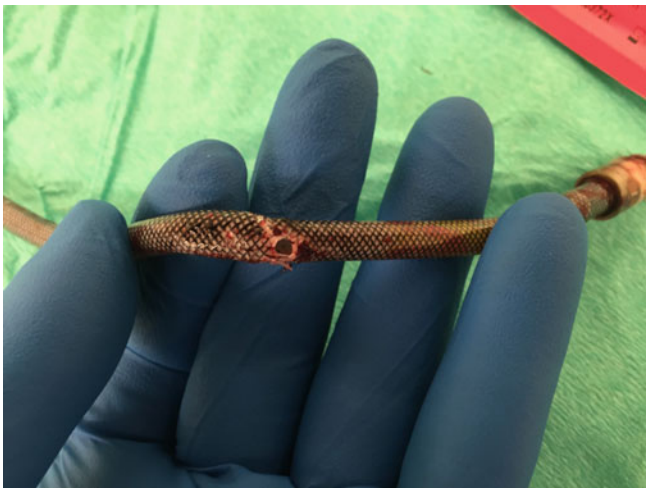

Fig. 32.9 Example of kinked and crushed VOC with visible open defect as a result of repetitive crush injury between the clavicle and first rib (Courtesy of the authors, Duke University)

of 38.9 % and 72.2 %, respectively, which is similar to that of AV grafts [1] (Table 32.2).

Shakarchi's systematic review showed primary and secondary patency rates of 21.9 % (9.6–37.2 %) and 59.4 % (39.4–78 %) in their pooled cohorts [10]. A second multi-institutional study demonstrated equivalent patency rates between HeRO (34.8 and 67.6 %) and AV grafts (30.6 and 58.4 %) at 12 months [14]. These findings have been similar in other studies as well [11, 15].

Summary/Future Direction

Since its commercial availability 7 years ago, we have continued to learn more about the HeRO graft and its role in the hemodialysis access algorithm. As we have illustrated, there have been numerous case reports reflecting both the benefits of the HeRO and the shortcomings and complications of the device. The utility of the HeRO has been well documented and has made a clear impact on the delivery of hemodialysis access care to our patients. Even with years of innovation and development in the hemodialysis access arena, HeRO remains the first and only dialysis graft technology that addresses the vexing issue of central venous occlusive pathology. Despite a growing population of patients with central vein stenosis/occlusion, this technology has not been fully adopted and remains a therapy regionalized to centers of excellence. While many dialysis access surgeons may lack the volume or expertise to include the HeRO device in their access algorithms, it is the lack of multidisciplinary clinical support and resources that often impede the ability to safely

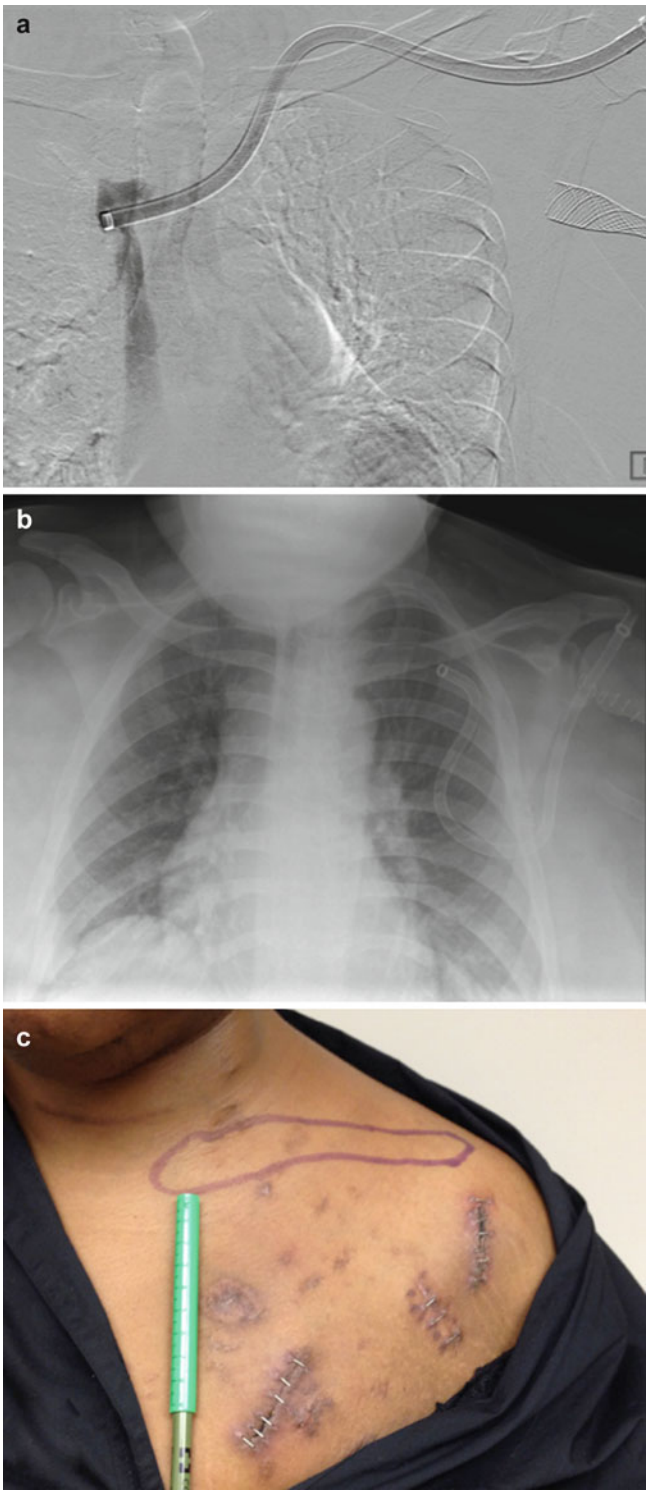

Fig. 32.10 HeRO malfunction in a patient with large, pendulous breasts that were not securely positioned prior to percutaneous access. (**a**) Post-HeRO implant #1 with retraction of the VOC from SVC and lodged into the azygos vein. (**b**) Post-HeRO implant #2 with VOC retracted out of the subclavian vein completely. (**c**) Patient in the upright position with 10 cm distance between clavicle and original access site (Courtesy of the authors, Duke University)

Table 32.2 Patency comparison of published HeRO data, AVG literature, and TDC literature

Study	Current HeRO multicenter		Gage et al. review May 2010 [12][a]	Katzman et al. study Sept 2009 [2]	AVG literature [14]		TDC literature [2]	
Months	*6 months*	*12 months*	*6 months*	*8.6 months*	*6 months*	*12 months*	*6 months*	*12 months*
Patency								
Primary, %	60	48.8	68.3	38.9	58	42	50	36
Secondary, %	90.8	90.8	87.8	72.2	76	65	55	37

Reproduced from Gage et al. [3]

[a]39 of the 41 patients in the Gage review are included in this current multicenter review

deliver the technology and care for these tremendously ill patients. The open/endovascular (hybrid) nature of the device is a significant barrier for many access surgeons (namely, transplant, general, and vascular) given the majority of them have not had formal endovascular training. The most successful practices are those that include an access surgeon with a strong endovascular background or strong collaboration with their interventional radiology colleagues. Emphasis on endovascular skills, identification of central venous pathology, and mindful access creation algorithms are essential training points to facilitate the adoption and use of the HeRO graft in order to deliver the most comprehensive care possible for our patients.

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Hemodialysis Access: Fundamentals and Advanced Management

33

April Rodriguez and Sherene Shalhub

Introduction

There is no consensus regarding the size definition for AVF aneurysms [2]. A recent proposed definition of AVF aneurysm is dilatation of all three vein layers with a minimal diameter of 18 mm which represents three times the enlargement of a vein in a maturated AVF given that Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommended a diameter of 6 mm for a usable fistula [2]. AVF aneurysms most commonly occur in the outflow vein; however aneurysmal dilation of the inflow artery has also been described [3].

Epidemiology

AVF aneurysms can occur in fistulas used for dialysis and in patients who have an access that have yet to be used. The prevalence of AVF aneurysms ranges between 6 and 51 % depending on the definition criteria and method of identification [1, 2, 4]. In a recent single-center cross-sectional study of 181 patients with AVF and on hemodialysis for more than 6 months, AVF aneurysmal degeneration was detected in 60 % of the patients. Of those, 66 % had a minimum diameter of 2 cm and 71 % had had at least a bilobed aneurysm [5]. The authors noted that AVF aneurysms prevalence was highest in patients with adult polycystic kidney disease, nondiabetic patients, and in those treated by high-flux membranes [5]. Risk of AVF aneurysmal degeneration is associated with the duration of hemodialysis with a mean time to treatment of 3.9–4.9 years from AVF creation [5–7].

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Classification

While there is no consensus on a classification system, there are two proposed classification systems, one by Valenti and colleagues [4] and the other by Balaz and colleagues [2].

The Valenti Classification System

This classification is based on a review of 344 patients with AVF. It is based on the shape of the AVF aneurysm and thus is a primarily clinical examination classification with simple duplex examination as an adjunct. The AVF aneurysms are classified as follows (Fig. 33.1):

Type 1a: The vein uniformly aneurysmal from the arterial anastomosis along most, if not all, of its length resembling a hosepipe (Fig. 33.2).

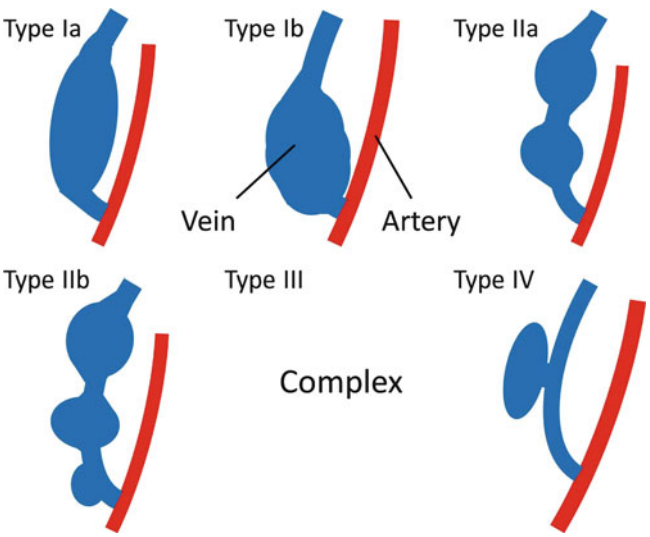

Fig. 33.1 Arteriovenous fistula aneurysms classification by Valenti and colleagues

S. Shalhub et al. (eds.), *Hemodialysis Access*, DOI 10.1007/978-3-319-40061-7_33

Type 1b: The proximal part of the vein is dilated within 5 cm of the arterial anastomosis.

Type 1 AVF aneurysms were most common in unused AVF and appeared to be associated with high-flow states.

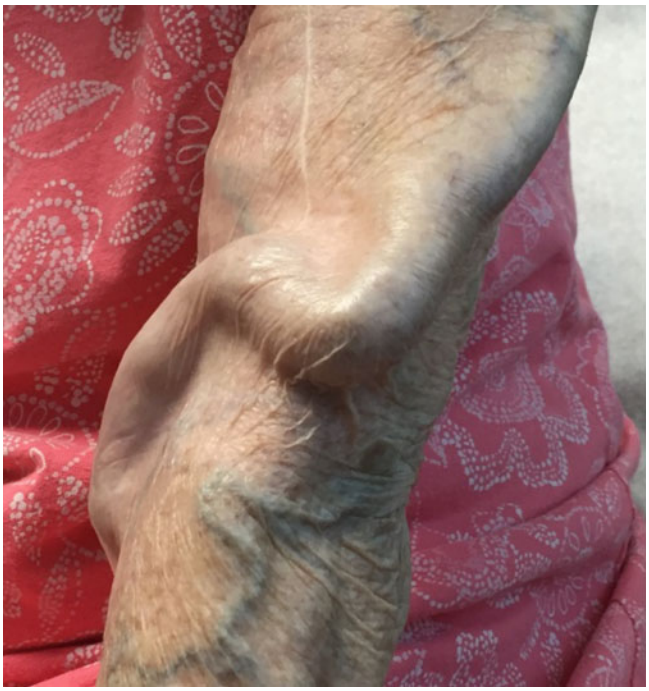

Fig. 33.2 Diffuse aneurysmal degeneration of a right brachiobasilic arteriovenous fistula. The vein is uniformly aneurysmal from the arterial anastomosis of the entire length of the arteriovenous fistula resembling a hosepipe

Type 2a: The classic "camel hump" with at least one localized area of dilation. These areas of dilation correlate with sites of access needle placement for hemodialysis. In between these localized aneurysms, the vein is of normal caliber or has stenosis (Fig. 33.3).

Type 2b: There is both a post-anastomotic aneurysm and also multiple aneurysmal segments throughout the length of the vein; thus, it is a combination of types 1b and 2a.

Type 2 AVF aneurysms are more common in AVF being used for hemodialysis.

Type 3: Complex/heterogeneous. This was the minority of AVF aneurysms (3.7 %) that did not fit into any typical pattern.

Type 4: These may appear as aneurysms, but on duplex they are found to be pseudoaneurysms and thus are indistinguishable from type 2 AVF aneurysms on clinical exam.

The Balaz Classification System

This classification is based on ultrasound or fistulagram findings as follows:

Type I: Without stenosis and thrombosis.

Type II: With hemodynamic significant stenosis (≥50 %), this is further subdivided by location of the stenosis: (A) in the inflow artery, (B) in the at arterial anastomosis, (C) along the cannulation zone, and (D) in the central vein.

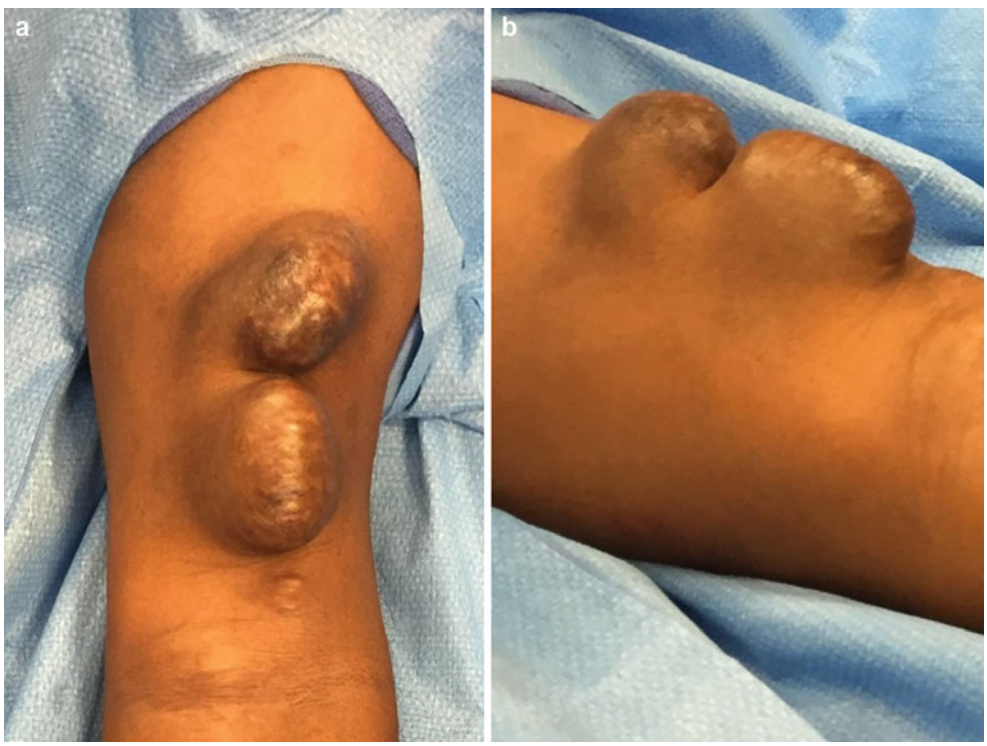

Fig. 33.3 Left brachiocephalic arteriovenous fistula with large bilobed aneurysmal degeneration creating a challenge for needle placement and complicated by progressive skin thinning. (**a**) Anterior view. (**b**) Lateral view

Type III: With partial thrombosis occluding ≥50 % of the lumen.

Type IV: With complete thrombosis of the AVF.

Pathophysiology

Formation of an AVF aneurysm starts at the time of the creation of the AVF. The combination of a low venous outflow resistance and venous wall distention leads to venous wall remodeling into an arterialized vein. The vein over time dilates and becomes tortuous because of the constant arterial pressure. As the vein dilates and the diameter enlarges, the wall tension increases, causing further vein dilation [2].

Several mechanisms have been proposed to explain the pathophysiology of AVF:

- *Central or outflow vein stenosis:* the increased venous pressure due to the central veins and outflow vein stenosis accelerates the aneurysmal degeneration (Fig. 33.4). In a detailed study of 89 patients with AVF aneurysms at a mean diameter of 2.3 cm, 78 % had an associated venous outflow stenosis. The stenoses were present most commonly in the outflow cephalic vein (57 %), followed by

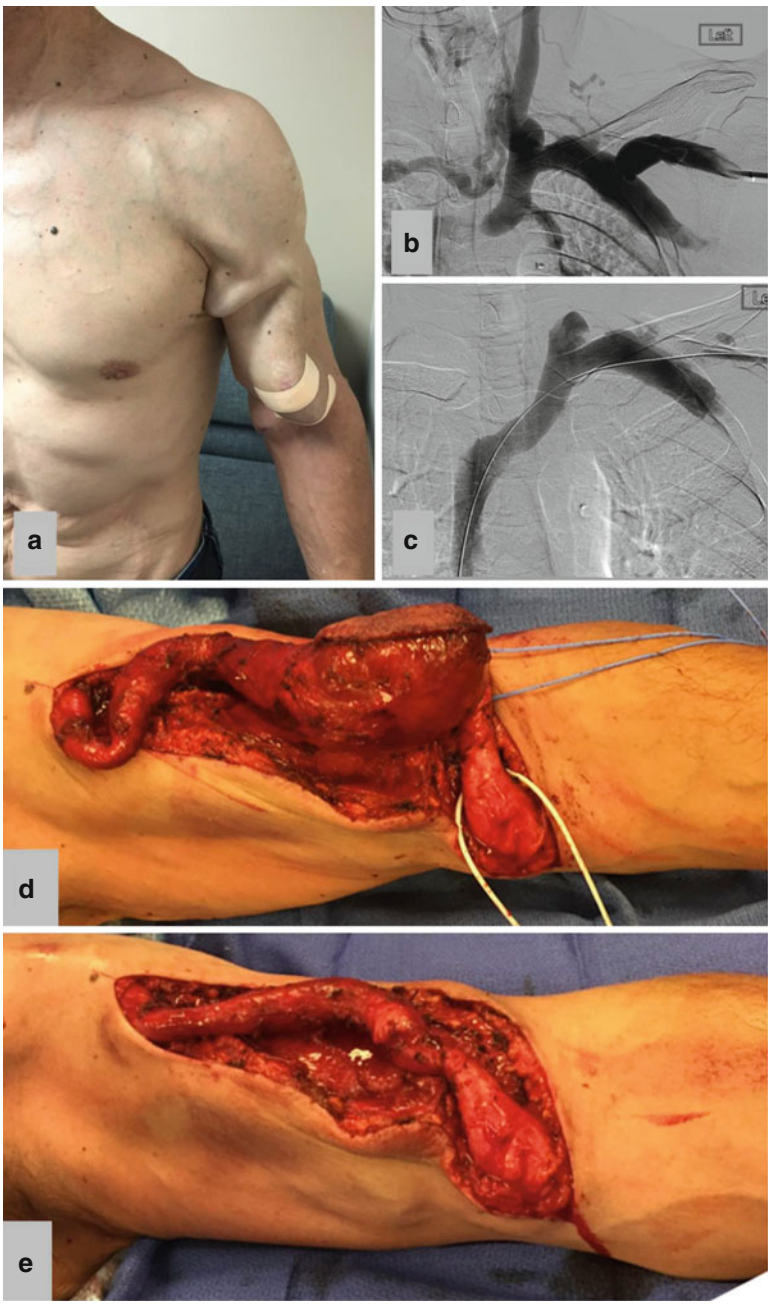

Fig. 33.4 A patient with a left brachiocephalic arteriovenous fistula with aneurysmal degeneration due to central venous stenosis. (**a**) Note the collaterals on the left side of the chest and neck. (**b**) Diagnostic fistulagram showing near occlusion of the innominate artery and reflux in the left internal jugular vein. Of note, the patient was experiencing headaches during his hemodialysis treatment. (**c**) Treatment of the stenosis by balloon angioplasty. The patient's headaches resolved after treatment. (**d**) Circumferentially dissected arteriovenous fistula with an overlying skin island. (**e**) The aneurysm treated with excision and end-to-end anastomosis of the remainder of the fistula

the cephalic arch (20%), brachiocephalic vein (10%), and subclavian vein (6%) [8]. Outflow stenoses in AVFs with aneurysmal degeneration were observed in 87% of brachiocephalic AVFs, 60% of radiocephalic AVFs, and 80% of brachiobasilic AVFs [8]. Central venous stenosis was documented in 90% of cases in two series of AVF aneurysms requiring surgical revision [9, 10].

- *Repeated punctures at clustered sites.* Repeated needling results in multiple small fibrous scars in the vessel wall, which may expand with time and result in localized aneurysmal areas (Fig. 33.5) [2]. This can occur due to two different mechanisms, repeated trauma causes thinning of the wall of the AVF and aneurysm formation or repeated trauma leads to an area of stenosis causing pre- or post-stenotic aneurysmal degeneration [4]. It can be difficult at time to distinguish the tow mechanisms and both may be at play. This distinction has been made by some in the sense that if the etiology is due to degeneration of the vein wall, from repeated cannulation trauma, then the abnormality would likely be a pseudoaneurysm while the focal dilatation of the native vein was secondary to increased intraluminal pressure, due to the presence of a distal stenosis, then the abnormality may be an aneurysm [11]. Duplex ultrasound can distinguish aneurysms and pseudoaneurysms.
- Current K/DOQI guidelines encourage a "rope-ladder technique" to avoid AVF aneurysmal degeneration unless "buttonhole technique" is being used [12]. The rope-ladder technique is one in which cannulation occurs along the whole length of the vein, thus rotating access sites. The buttonhole technique is that of cannulation in exactly the same location during every dialysis session [13–15].
- *Elevated mean flow rates.* In a large series of AVF aneurysms, mean flow rates were much higher in those without outflow vein stenosis, and these high flow rates are associated with aneurysmal degeneration [5, 6]. High flow was present in 29% of the cases in one series [7]. The underlying mechanism is thought to be due to abnormal shear stress on the vessel wall, which promotes outward remodeling and gradual dilation with grossly increased caliber of the vessel [16].
- *History of renal transplantation.* Interestingly, multiple patients with AVF aneurysmal degeneration develop diffuse aneurysmal dilation. In one series, 47% of the patients had a history of renal transplantation. There is speculation that there may be an association between immunosuppression and AVF aneurysm formation [17].

Assessment

In addition to a detailed history about the function of the AVF and any symptoms the patient is experiencing, a thorough physical exam by inspection and palpation is essential in identifying the underlying etiology of the aneurysmal degeneration. A history of prolonged bleeding from the needle access sites and a pulsatile AVF that is hard and non-compressible is suggestive of stenosis in the outflow vein or central venous stenosis (Fig. 33.4). Skin changes such as thinning of the overlying skin may herald future skin necrosis (Fig. 33.6). A history of a herald bleed is especially concerning for impending complete rupture with hemorrhage (Fig. 33.7).

Objective measurements can be obtained via duplex ultrasound evaluation, a CT angiogram or a diagnostic fistulagram. The duplex ultrasound assesses the diameter of the AVF, areas of stenosis, the presence of laminar thrombus, and flow measurements. As mentioned previously, fistulas with flows greater than 2.0 L/min should be further assessed to determine if intervention is necessary. The presence of hemodynamically significant stenosis or laminar thrombus can lead to technical or mechanical issues with access, which threaten the use of the fistula. Central venous stenosis can be diagnosed or confirmed with a CT angiogram

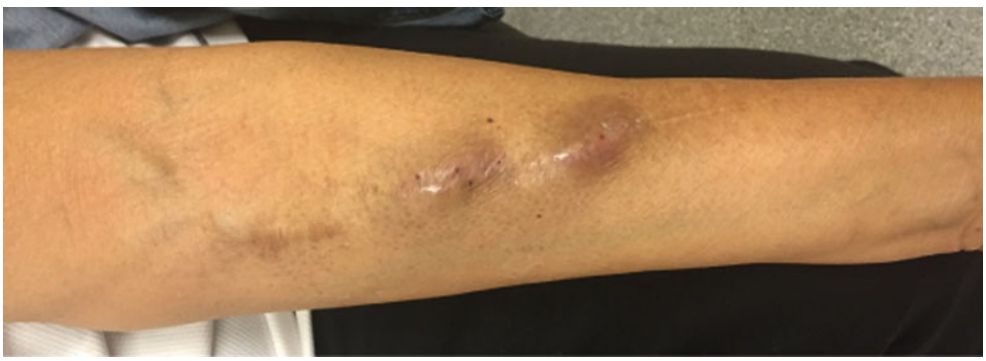

Fig. 33.5 A right radiocephalic arteriovenous fistula with early aneurysmal degeneration occurring in a bilobed configuration due to repeated needle access in the same location. Access technique needs to be changed to a rope-ladder technique or a buttonhole technique to prevent further aneurysmal degeneration

or diagnostic fistulagram. The latter allows concurrent treatment of the stenosis if found.

Management

An aneurysmal AVF may raise concern from the staff, but there is no reason to intervene as long as the AVF is functioning well for dialysis and the dilatation is not steadily and rapidly enlarging [12, 18]. While size alone is not an indication for repair, monitoring for enlargement and symptom development is essential. Current K/DOQI guidelines recommend conservative management of asymptomatic AVF aneurysms by abandoning cannulation in the aneurysmal areas [12]. Using the modified buttonhole cannulation technique has been proposed as a solution for AVF aneurysms [19]. The indications for surgical management include:

- The overlying skin condition: Skin thinning or erosion is a marker of impending skin necrosis leading to fistula exposure, subsequent risk for exsanguinating hemorrhage, and subsequent death (Fig. 33.7). In Valenti and colleagues series, type 2 AVF aneurysms had the highest risk of rupture, leading the authors to conclude that these should be carefully monitored for evidence of overlying skin thinning which if present should prompt consideration for prophylactic intervention.

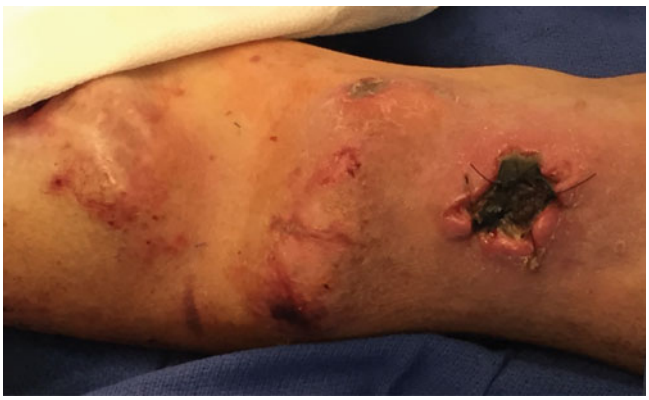

Fig. 33.7 A left brachiocephalic arteriovenous fistula with large multilobed aneurysmal degeneration. The patient presented with acute bleeding and hemorrhagic shock due to necrosis of skin overlying the aneurysmal portion in the upper arm. The aneurysm with overlying eschar through which the patient bled is clearly visible along with old repair sutures at the site of skin breakdown. The fistula was ligated emergently

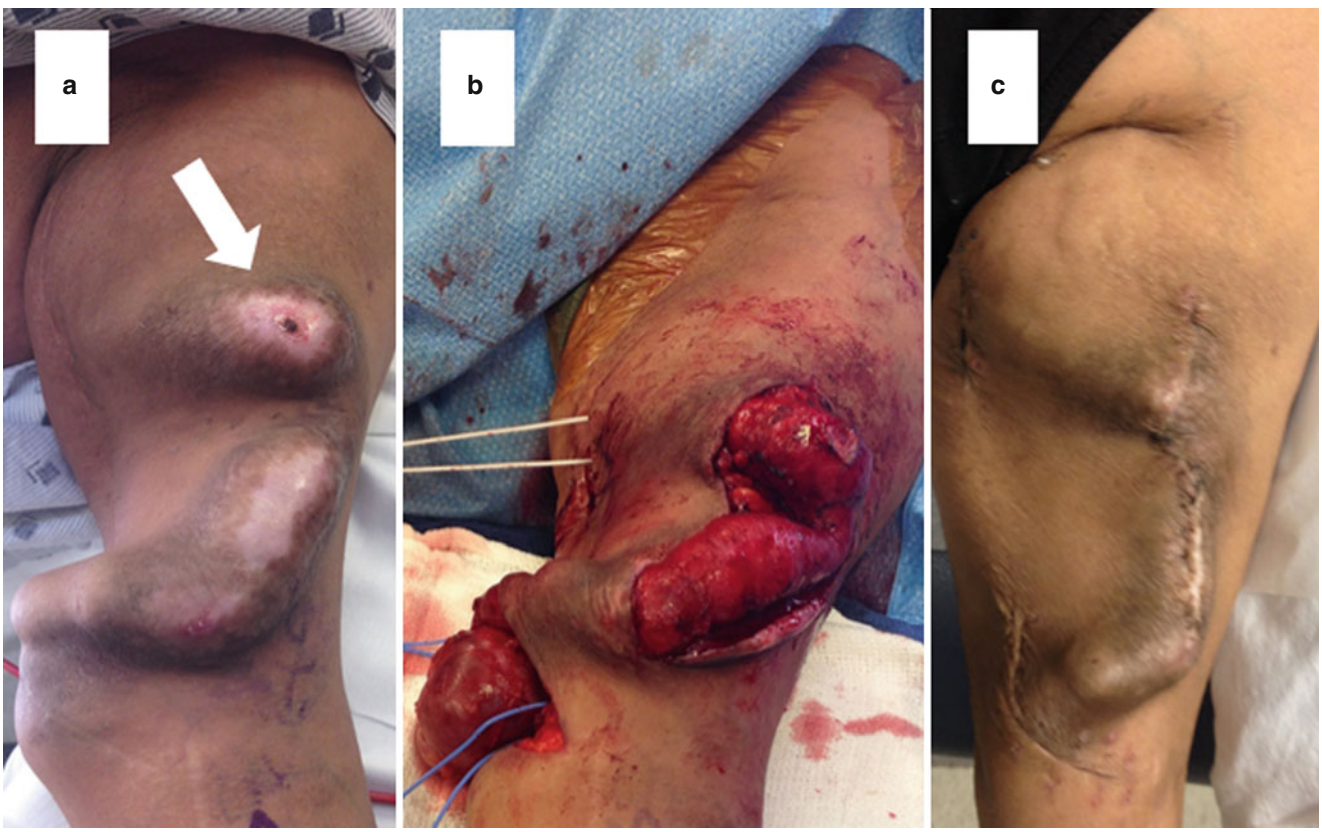

Fig. 33.6 Left brachiobasilic arteriovenous fistula with large aneurysmal degeneration. (**a**) The aneurysmal degeneration is complicated by skin thinning, depigmentation, and early breakdown (*arrow*) in addition to chronic arm pain. (**b**) Circumferentially dissected trilobed aneurysm. One of the aneurysms was treated with excision with end-to-end anastomosis and the remaining two treated with aneurysmectomy and plication. (**c**) Postoperative week three images

- Clinical signs and symptoms:
  - *High-output congestive heart failure (CHF)*: When a fistula becomes aneurysmal, it can develop flows that are markedly elevated and can result in high-output CHF. Basile and colleagues demonstrated that flows greater than 2.0 L/min are predictive of heart failure, while MacRae and colleagues suggested that the risk of high-flow access on the cardiac function should be entertained when the flow rate is >3000 ml/min [20, 21]. These observations were also confirmed by Pasklinsky and colleagues. In their series of AVF aneurysms, the mean flow in the AVF was 1288 ml/min in those without CHF compared to 2500 ml/min in those with high-output CHF [6].
  - *Cosmetic reasons:* Some patients wish to have an AVF ligated due to the unsightly appearance of the fistula and wish to have it repaired for this reason alone. The reconstruction of an aneurysmal AVF for cosmetic reasons must be carefully weighed and discussed with the patient with a focus on an explanation of the potential postoperative complications including loss of a functioning AVF.
- Ease of cannulation and functionality of the AVF. AVF aneurysmal degeneration can in multiple ways impair hemodialysis.
  - The laminar thrombus in the lumen of the aneurysm can cause flow impediment.
  - The aneurysmal degeneration can lead to a shortened area of cannulation.
  - Impaired arterial inflow or venous outflow stenosis between aneurysms can lead to inadequate dialysis.

Surgical Repair

While there are many ways to approach and treat AVF aneurysms, there is no consensus on which technique is best, and management is tailored to the individual patient. The goal of treatment is to preserve the AVF function and treatment of the underlying etiology (high flow, stenosis).

The Remodeling Technique

This technique uses the native vein in the repair, so the character of the AVF is preserved. The operative incision is usually extended from the arterial anastomosis to a non-dilated section of the vein. The aneurysmal portion is then circumferentially dissected. A skin island can be left on the aneurysm surface if densely adherent due to necrosis. After mobilization of the AVF, including the aneurysms, an assessment is made. If the vein is excessively elongated with redundancy, then the patient is heparinized with 5000 units of heparin given intravenously. Proximal and distal control of the fistula is obtained using vascular clamps, the aneurysm is excised along with any areas of stenosis the access, and continuity is reestablished with an end-to-end anastomosis (Fig. 33.4).

If the vein is not redundant to provide length that would allow aneurysm resection (Fig. 33.6), then the patient is heparinized with 5000 units of heparin given intravenously. Proximal and distal control of the fistula is obtained using vascular clamps; the aneurysmal fistula is then opened longitudinally along its entire length, followed by aneurysmectomy by sharp resection of the anterior aneurysm. This is then followed by plication with a running 6.0–4.0 Prolene (depending on wall thickness) [7, 17, 22]. Hegar probes, bougies, and a 20 F red-rubber catheter have been used in order to guide the extent of the plication and achieve an inner diameter of 6–10 mm [7, 17, 23]. Alternatively aneurysmorrhaphy by firing a longitudinal staple line (TA stapler [3.5 mm depth, Covidien, Norwalk, CT] or Endo GIA stapler [Covidien, Mansfield, MA] with a vascular load) along the axis of the venous aneurysm can be performed followed by reinforcement of the staple line with a layer of Prolene suture [7, 24–26]. Proponents of the staple aneurysmorrhaphy highlight that the AVF does not need to be opened; thus the inflow is arrested for a few minutes, obviating the need for systemic heparinization. This may facilitate hemostasis and reduce postoperative bleeding complications [25]. Some authors recommend that the aneurysmorrhaphy be combined with an external reinforcement of the reconstructed vein with a macroporous polyester tube or a porous polyethylene external prosthesis to prevent the development of new aneurysms [27–29]. It is unclear whether external reinforcement is necessary.

The excess or compromised skin overlying the fistula is then excised after the aneurysm has been remodeled. A subcutaneous skin flap is elevated followed by positioning the remodeled vein under the flap with the plicated line oriented to avoid direct needle puncture. The subcutaneous flaps then closed in two layers using absorbable sutures. A drain could be left if needed with planned removal in 24 h.

Ideally, a segment long enough for needle access should be preserved at the time of the revision to avoid the use of a dialysis catheter with its associated risk for complications. Some advocate a staged approach to achieve this aim starting with revision of the largest aneurysm first [22]. This should be considered carefully as it would predispose the patient to additional visits and multiple operations [25]. The remodeled sections can be accessed after a minimum of 3 weeks. Several series have described the remodeling technique with satisfactory outcomes and a 1-year patency between 67 and 86 % [25, 30].

AVF Aneurysm Excision with Placement of an Interposition Graft

An alternative technique includes excision of the aneurysm, and then an interposition graft (great saphenous vein (GSV) or polytetrafluoroethylene (PTFE), bovine pericardium patches) can be placed [6, 31]. This technique requires a sufficient proximal and distal vein segment free from thrombosis or aneurysm to allow the construction of end-to-end or end-to-side anastomoses. If there is evidence of skin erosion, bleeding, or local infection, bypass grafting around the lesion can be performed with local extra-anatomic bypass techniques, provided that the sections adjacent to the local infection were well incorporated and that the remaining graft canal beyond the stumps are free of fluid on a preoperative duplex [32]. The excess or compromised skin overlying the dilated fistula is excised at the conclusion of the procedure. The advantage of a prosthetic graft is earlier cannulation compared to an autogenous graft. The major drawback is the increased risk of prosthetic graft thrombosis and infection compared to an autogenous graft.

In a large series using GSV or PTFE, both conduits had a similar primary patency rates at 12 months of 46.7 % [6]. In a study evaluating the use of prosthetic conduits, the 12-month primary patency was 57 % [32].

In terms of choice between a remodeling technique and interposition graft placement, Georgiadis and colleagues observed significantly higher primary patency rates after autologous aneurysm repair when compared to graft interposition [32].

AVF Ligation Without Resection

This is the first-line therapy, the emergent setting of acute bleeding associated with hemorrhagic shock (Fig. 33.7) and the last resort measure in the elective setting. In the case of rupture and hemorrhagic shock, the new access is planned in the recovery period. In the elective setting, AVF ligation is performed when the AVF is deemed non-salvageable with an option to construct a more proximal AV access using the arterialized vein. Additionally, AVF aneurysm ligation can be performed in patients with a functioning renal transplant and wish to have the AVF aneurysm ligated for cosmetic reasons (after a thorough discussion). The disadvantage of ligation is that it subjects the patient who is still needing hemodialysis to a temporary hemodialysis access while awaiting maturation of another newly created fistula or graft. Possible complications associated with this approach include phlebitis of the aneurysmal vein which may require evacuation of the aneurysm thrombus [6]. Another complication is subclavian vein occlusion due to vein thrombosis with subsequent upper-extremity edema [6].

Use of Stent Grafts

The use of endovascular techniques has been incorporated into the management of AVF aneurysms. The first reported successful use of a covered stent to treat AVF aneurysm was reported by Allaria et al. in 2002 [33]. Recently, Shemesh and colleagues described the use of self-expanding covered stent grafts to treat 11 AVF aneurysms [9]. The technique described includes selecting stents with a diameter 1 mm larger than the normal vein adjacent to the aneurysm. Patients with steal syndrome, aneurysms close to the anastomosis, and large aneurysms lacking a stent graft sealing zone were excluded. The stent length was selected in order to exclude the aneurysm and cover at least 1 cm of the normal vein or graft on either side. Hemodialysis was resumed post-discharge using the existing access. If there was a subsequent need to use the stent site for puncture, this was performed after the aneurysm sac has remodeled. The functional patency rate was reported at 87 % at 12 months [9]. Limitations to this technique include the presence of infection and the need for an adequate "sealing zone" for the stent graft [9]. While these techniques appear promising, the presence of the stent grafts can lead to risk of infection along with difficulties in cannulation. The latest K/DOQI guidelines in 2006 advise against stent insertion along cannulation sites in AVFs [12].

Conclusions

AVF aneurysms are characterized by an enlargement of all three vein layers with a diameter of more than 18 mm. The diameter of the AVF alone is not an indication for repair. Repair is indicated by clinical parameters based on the overlying skin conditions, symptoms, and ease of cannulation. Multiple techniques for repair have been described and are tailored to the patient's presentation and needs.

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The Infected Hemodialysis Access

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Animesh Rathore and Audra A. Duncan

Introduction

Infection is a significant source of morbidity and mortality in the end-stage renal disease (ESRD) patients [1]. It is the second leading cause for access loss following graft thrombosis. Likewise, infections are the second leading cause of mortality in the dialysis patients, second only to the cardiovascular mortality. The incidence of the infection is higher with the prosthetic arteriovenous grafts (AVGs) compared to autologous arteriovenous fistulae (AVF). Because of this reason, the Society for Vascular Surgery clinical practice guidelines and the KDOQI fistula first initiatives recommend the preferential use of autologous AVFs in most cases before resorting to the use of prosthetic material [2]. Regardless of attempts to place a fistula first, approximately 20% of the 400000 US hemodialysis patients dialyze with prosthetic grafts [3].

Graft infections occur in 8–40% of patients and result in prolonged hospitalizations, systemic complications, longer catheter dependence, and death. Approximately 20–36% of deaths in dialysis patients are caused from complications of infection. The risk of death due to sepsis in dialysis patients is estimated to increase by 100- to 300-fold [4, 5]. A series from University of Alabama identified 90 graft infections over 4.5 years with 1104 graft-years of follow-up resulting in a rate of 8.2 infections/100 graft-years [6]. Majority of the graft infections occur in the first year after the graft placement, but the incidence decreases in the subsequent years [7].

For the purpose of the management of the hemodialysis access infection, it can be classified into catheter-related infections and AVG-related infections. While the infections are more common with the use of prosthetics, these can also occur with autogenous AVF access. In the systematic review and meta-analysis comparing autologous versus prosthetic access, the authors assessed a subgroup of 249 pooled patients and compared autogenous upper arm access with prosthetic lower arm access [8]. They demonstrated that the autologous access in the upper arm had a significantly lower rate of infections. However, the overall analysis with heterogeneous data yielded the conclusion that very low-quality evidence exists to confirm that autogenous access is superior to prosthetic in terms of infection risk. The treatment of the infections depends on the type of access, the location, and the extent of infection as well as the time of infection onset from the creation of the access.

Pathophysiology

ESRD patients are more prone to infections because of several factors. Uremia can interfere with T-cell and B-cell functions, macrocyte phagocytosis, and antigen presentation [9]. Multiple hospitalizations due to acute and chronic illnesses also contribute to increased infection rates. In addition, personal hygiene was found to be a significant independent risk factor for infectious complications, as patient with poor hygiene had significantly higher concentrations of *S. aureus* on the skin at the access site after application of antiseptic than patients with good hygiene [10]. In Minga et al. series, patients with graft infections had a lower serum albumin level (<3.5 g/dL) in the month preceding infection compared to a noninfected hemodialysis cohort (73 vs. 18% $p<0.001$) [6].

Multiple interventions (repeated thrombectomy, thrombolysis, fistulagrams) or even repeated graft access by an inexperienced dialysis team may predispose patients to infection by introducing bacteria. In cases when AVG pseudoaneurysms are treated percutaneously with covered stent grafts, there is a higher risk of graft infections than when covered stents are used for other indications, or bare metal stents are used [11]. Type of access has a significant impact

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on the infection and was noted to be an independent risk factor for infection in a Center for Disease Control and Prevention study [12]. The relative risk of infection with tunneled catheter is 13.6, non-tunneled catheter 32.6, and prosthetic AVG access 2.2 [13]. Other factors that affect the infection rates include repeated cannulation, increasing age, diabetes mellitus, location of access (upper versus lower extremity), and ambulatory limitations [14]. Access cannulation technique has also been reported to play an important role in the infection of the hemodialysis access. The "buttonhole technique" (cannulation at the exact same site, angle, direction, and depth, with blunt needle used after the track has developed) was described to decrease the rate of aneurysm. This technique, however, is associated with increased risk of hematoma formation and infection of the access [15]. In comparison, the "rope–ladder technique" (use of the entire length of the access, moving 2 cm from the last insertion) or the "area technique" (cannulation of only a few areas) is associated with reduced infection rates [16]. In addition, inappropriate use of sharp needle, inadequate use of disinfecting agents, and incomplete scab removal are noted to be additional factors affecting the infection rates [17, 18].

Microbiology

Dialysis-related infections are predominantly caused by gram-positive organisms, *Staphylococcus aureus* being the most common. Gram-negative and polymicrobial infections account for a minority of the infections. The infection with *S. aureus* is associated with significant complications (endocarditis, osteomyelitis, and septic arthritis) and mortality rate. Methicillin resistance is increasingly becoming a significant problem in these infections. Hemodialysis patients are at a higher risk of developing vancomycin resistance. Tunneled catheter infections as well as lower extremity AVGs are more frequently (24–45 %) due to gram-negative organisms and as more likely to have systemic complications [19, 20].

Diagnosis

History and Physical Examination

Careful history and physical examination and having a low index of suspicion are the keys to diagnosis for hemodialysis access-related infection. These are often diagnosed early because of superficial nature as well as frequent evaluation of this patient population. Erythema, tenderness, and swelling over the graft may be noted with concomitant fever or chills. Severe infections may present with hypotension from sepsis or anastomotic hemorrhage. Clinical exam may reveal an exposed graft, draining sinus tract, or a fluctuant or painful mass over the graft. These patients must be evaluated for distant complications (endocarditis, osteomyelitis, and septic arthritis) based on presentation. Laboratory studies may reveal leukocytosis; however, the lack of leukocytosis in chronically immunosuppressed renal failure patients does not eliminate the possibility of significant infection.

Imaging

Diagnosis is typically made with physical exam, but ultrasound can also be used to distinguish between a seroma, hematoma, and abscess (Fig. 34.1). In patients with fevers of

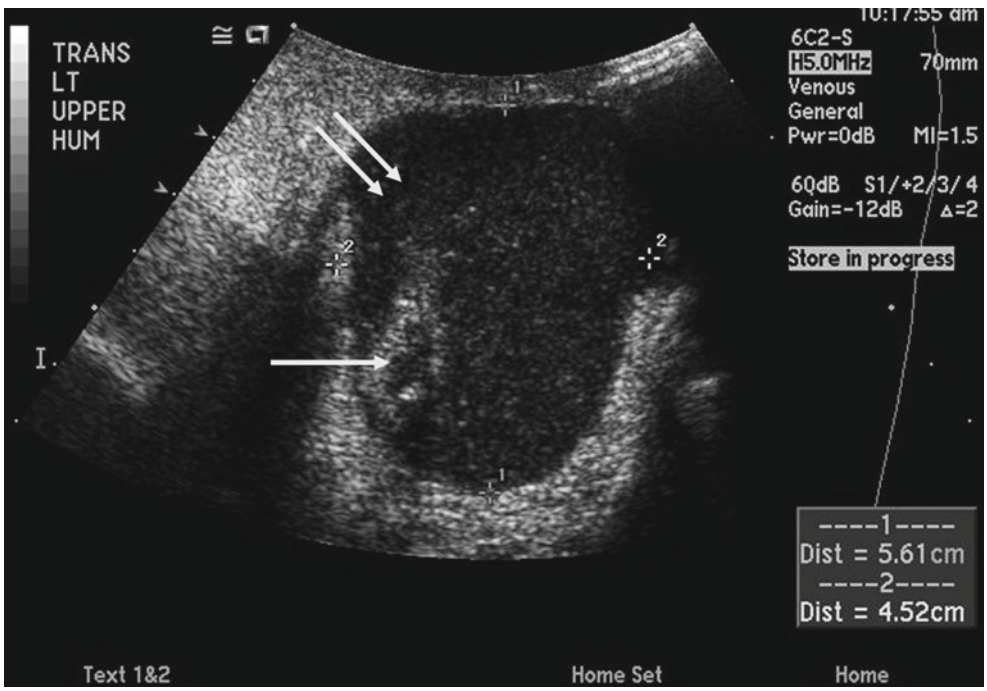

Fig. 34.1 Ultrasound of prosthetic graft identifies the graft (*single arrow*) within a large pocket of fluid with heterogeneous material (*double arrow*) indicating infection

unknown origin, radiolabeled white blood cell scans can be sensitive (95–100 %) and specific (90–93 %) for confirming a graft infection. In a series of 30 scans in 26 patients, 16 patients with normal physical exams had a positive scan results, and infection was confirmed at the time of graft removal [21]. These white blood cell scans may be particularly important to eliminate the AVG as an infectious source in a patient with an unknown infectious etiology in order to be able to keep the graft intact if it is not clinically infected. In cases of complex graft anatomy and several sinus tracts or to determine extent of the infection, computed tomography may be of use (Fig. 34.2).

Treatment

Standard of care for the treatment of hemodialysis access infection involves prompt hospitalization and systemic antibiotics followed by surgical excision of the graft and open wound packing.

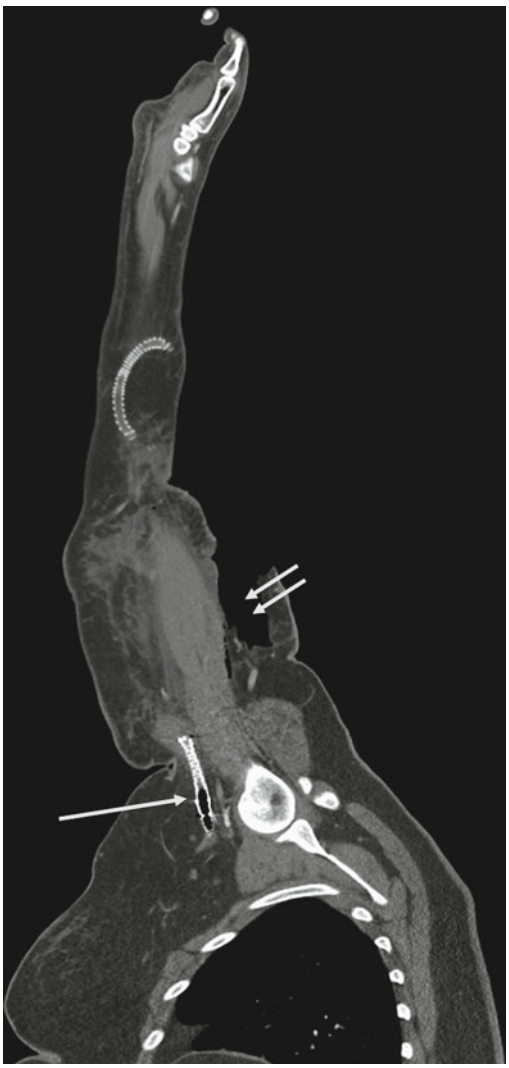

Fig. 34.2 Computed tomography of an infected upper arm loop graft demonstrates air within the graft (*single arrow*) and a large open wound adjacent to the graft (*double arrows*)

The treatment is tailored based on the type of access. Surgical decision-making involves the considerations for access salvage, vascular reconstruction, and wound management. Salvage may be attempted if only local signs of infection are seen without skin breakdown or bacteremia. This strategy allows for continued dialysis access and avoids additional catheter days. Early graft infection (<30 days) should be treated by complete graft excision and placement of new access elsewhere [22].

Infections involving *autogenous AVF* are usually related to the cannulation technique or hematoma and rarely require revision or excision of the access. Most respond to 2–4 weeks of antibiotics and abscess drainage as needed. In case of any intraluminal devices (covered or bare metal stents), a prolonged course (4–6 weeks) of parenteral antibiotics or surgical excision of access is needed. Recurrent infections may require ligation of excision of the access.

In prosthetic AVG infections, salvage may be attempted with only localized erythema or a focal sinus track. In cases of *midgraft infection*, the uninvolved segments of the prosthetic material are exposed proximally and distally, while the infected segment is covered with an impermeable dressing. A new segment of prosthetic material is tunneled through clean tissue planes, anastomosis completed, and incisions are closed. The infected portion of the segment is then excised through a separate incision followed by local care for the infected wound. Various authors have reported an access salvage rates ranging from 74 % to upwards of 90 % [22–24]. With *anastomotic infections*, a complete excision of prosthetic material is usually required along with patch repair of the artery. Partial graft excision while leaving a 2–3 mm cuff of well-incorporated prosthetic on the underlying artery to be used for a new tunneled graft is a technique for access salvage. Ryan et al. reported their experience treating 51 infected PTFE AVGs in 45 patients employing 13 successful total graft excisions, 15 subtotal graft excisions with graft cuffs left, and 23 partial graft excisions leaving a portion of usable graft. Of these 23, 6 patients ultimately required total graft excision due to nonhealing wounds with an overall success rate of 74 %. However, this approach has high reinfection rates in another study by Walz et al. [23, 25]. Brachial artery ligation has been reported in critically ill patients with grossly infected prosthetic AVGs with ischemic complications in one-third of the patients in a series by Schanzer et al. [26, 27]. Replacement of the prosthetic AVG with cryopreserved femoral vein or femoral artery has been described by Matsuura et al. with 1-year primary and secondary patency rates of 42 and 68 % and only 2.3 % recurrent infection rate [28]. A thrombosed AVG can serve as a nidus for infection. In presence of systemic signs of infection, the graft excision may be performed once the thrombosed AVG is proved to be a source of infection. Rarely, a thrombosed AVG with no obvious sign of infection may be removed in a septic patient with no otherwise identified source of sepsis.

Summary

Infections in hemodialysis access can be life-threatening but are often identified early and treated with excision and antibiotics. The extent of excision versus salvage of the access, the management of the brachial artery anastomosis, and the timing and conduit used for future access should be managed on a case-by-case basis. If temporary access is required, the patients are at further infection risk from the tunneled catheters and should be converted to permanent access as soon as it is feasible. The best management for AVG infection is prevention with good hygiene, fewer hospitalizations, good nutrition, and minimizing interventions.

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The Thrombosed Hemodialysis Access

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Edward Caldwell and George H. Meier

Vascular access is a lifeline for end-stage renal disease patients. The National Kidney Foundation-Kidney Dialysis Outcomes Quality Initiative (NKF-KDOQI) published practice guidelines that recommend all patients with stage IV or stage V chronic kidney disease to undergo fistula creation [1]. The guidelines also included an order of preference for AV access procedures in order to preserve viable access sites. The recommendations are based on autogenous fistulas having a superior patency than prosthetic grafts and tunneled catheters, as well as fewer complications and repeat interventions. Despite these recommendations, dialysis access fails and re-intervention is needed [2, 3]. While there are often signs that an access is failing, there are many options for both avoiding and treating the access failure as it occurs.

The optimal function of the patient's autogenous fistula or prosthetic graft is key to achieving desired results during hemodialysis treatments. Intimal hyperplasia is a common occurrence in both autogenous access and prosthetic grafts (Fig. 35.1), occurring anywhere in autogenous vein and at the outflow anastomosis in prosthetic grafts [4]. It is important to recognize signs of a failing AV fistula/graft to prevent thrombosis. Various open, percutaneous, and hybrid procedures are available to assist the patency of failing AV access and to salvage a thrombosed graft.

Causes of Access Failure

Thrombosis of arteriovenous access is related to the same issues that cause thrombosis and any other blood vessel: Virchow's triad. Virchow outlined three causes of thrombosis in any blood vessel: an abnormality of the blood vessel, an abnormality of flow, and an abnormality in coagulation.

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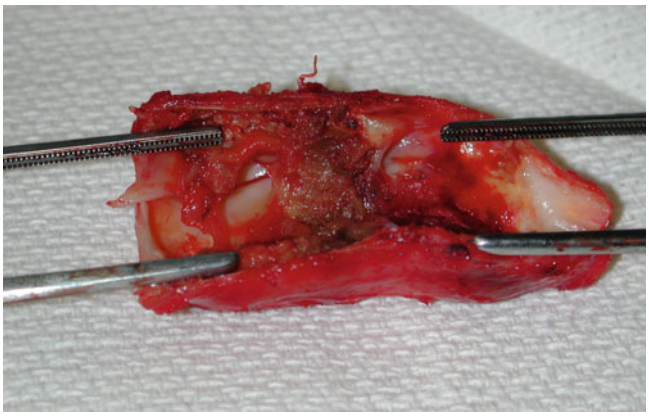

Fig. 35.1 Intimal hyperplasia at the distal anastomosis of a prosthetic graft (*left*) to a vein (*right*)

Access thrombosis is no different. Typically, as the access is used for dialysis, cannulation of the conduit generates trauma to the vessel wall. This cannulation trauma can incite thrombosis at the site of cannulation or, more commonly, lead to false aneurysm formation.

The greatest risk to an arteriovenous access is venous outflow stenosis associated with intimal hyperplasia [5]. Often this has no relationship to cannulation whatsoever. Nonetheless, the development of venous stenosis is often a precursor before access thrombosis. This is particularly true in prosthetic access since intimal hyperplasia tends to develop at the venous end of the artificial conduit. This slows flow in the prosthetic graft leading to thrombosis of the prosthetic graft from its beginning all the way to the venous end stenosis. Management is therefore focused on relieving the venous and stenosis to normalize graft blood flow.

Rarely hypercoagulability can become an issue in a mature arteriovenous access. Generally these acquired forms of hypercoagulability are not common, but when they occur, long-term arteriovenous access can be challenging [6–9]. At this point, routine screening for hypercoagulable states is not recommended [6, 10].

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Signs of Impending Thrombosis

Concerns relative to arteriovenous access thrombosis are raised by any evidence slowing the flow in the access or by venous hypertension in the access [11–13]. Typically, as venous outflow stenosis develops in the access, prolonged bleeding occurs at the time of the cannulation after dialysis, often associated with an increased pulsatility in the access. Prolonged bleeding is often the first sign of impending access failure but may be so subtle as to initially be missed. With time, the bleeding may persist for a longer period of time and may be more voluminous. Prolonged bleeding should lead to referral for access evaluation and management.

Sometimes, external bleeding is not the issue. In many cases hematoma formation may develop after decannulation, potentially resulting in false aneurysms along the course of the access (Fig. 35.2). This may threaten the access or even lead to thrombosis access. Hematoma formation should be viewed as an equivalent to decannulation bleeding, and a careful evaluation of the trends in venous pressures should be undertaken. In many cases an access ultrasound or a fistulogram is needed to help define any underlying causes for the hematoma formation.

Alternatively, slow flow in the access may lead to increased recirculation [14], resulting in poorer clearances and a need for more prolonged dialysis. This decreasing clearance should be monitored each time the patient subjected to dialysis. If there is a trend toward decreasing clearance associated with increased recirculation, this would suggest a venous outflow stenosis which may threaten the long-term use of the dialysis access.

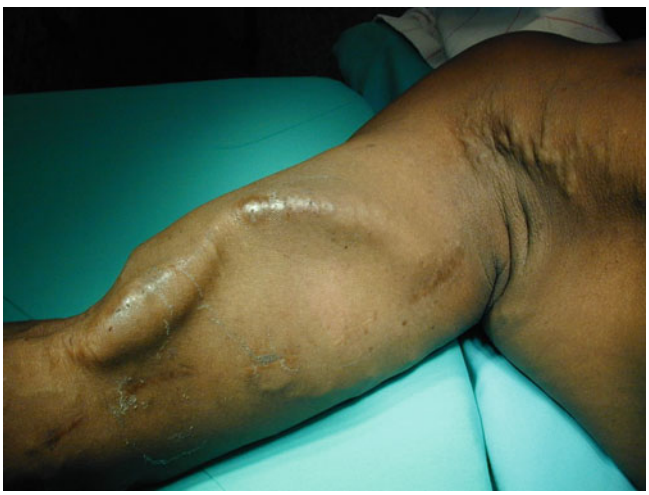

Fig. 35.2 Pseudoaneurysm associated with repetitive needle punctures and upper arm arteriovenous graft

Venous Factors

Venous stenosis in autogenous fistulas and prosthetic grafts is primarily caused by intimal hyperplasia. It is characterized by alpha-smooth muscle actin-positive cells, extracellular matrix proteins, and cytokines within the intima and media of the vein [4, 15]. This pathological lesion results in stenosis of the fistula/graft and may ultimately lead to thrombosis. In a prosthetic graft, intimal hyperplasia typically occurs at the outflow anastomosis. This is in contrast to autogenous access in which intimal hyperplasia can occur anywhere in the outflow vein.

The site of stenosis in autogenous access is dependent on the type of AV fistula performed. In radiocephalic (Cimino) fistulas, the site of stenosis is often within the perianastomotic region. More proximal fistulas, such as a brachiobasilic fistula or basilic vein transposition, typically have the site of stenosis located further from the anastomosis. Venous outflow stenosis may lead to recirculation during dialysis, with the retreatment of blood already filtered during dialysis.

Currently, a minimum vein size of 2.0 mm is recommended for fistula creation at the wrist. A wide range of data exists for prediction of fistula maturation with recommended vein sizes ranging from 2.0 to 4.0 mm [16].

Central vein stenosis is another contributor to access failure. Suspicion of possible central venous stenosis should be high in patients who have a prior history of central venous catheters, pacemakers, and peripherally inserted central catheters [17, 18]. Creation of a fistula/graft and the increase of blood flow in the upper extremity veins can suddenly elicit symptoms from a previously asymptomatic lesion. Patients may complain of face/upper extremity edema and pain, skin color changes, and venous varicosities. This leads to aneurysm formation, pulsatile flow, prolonged bleeding after dialysis, and eventual thrombosis of the access [19].

Arterial Factors

Preoperative imaging should be performed prior to fistula creation to evaluate the native arteries from the subclavian artery to the radial/ulnar arteries at the wrist. Currently, data suggests that a minimum arterial size of 2.0 mm is necessary to achieve an adequate radiocephalic fistula maturation rate. Data at other sites regarding size is limited [20, 21].

A patient with a history of peripheral vascular disease may have small, calcified distal arteries. The presence of more proximal subclavian artery stenosis may be spotted as well. A proper history and physical exam should elicit this information.

Surveillance of Dialysis Access

Physical Exam

A thorough physical exam is important in the maintenance of vascular access [22–24]. A proper examination requires the evaluation of the arterial anastomosis as well as the outflow vein. A continuous thrill should be present at the arterial anastomosis if the fistula/graft is functioning properly. If a thrill is present with only the systolic component or is reduced, further evaluation is warranted. The thrill should also be detectable at the outflow vein. If a pulse is present at the outflow vein, there is a high likelihood of a venous outflow stenosis.

Patients with central vein stenosis typically have enlarged collateral veins. These patients have elevated venous pressures, and physical exam will often reveal large collateral veins at the chest, shoulder, and upper extremity (Fig. 35.3). If a fistula/graft is placed ipsilateral to the site of central stenosis, symptoms of venous hypertension progress and the access are likely to thrombose [25].

The increase in venous pressure can lead to prolonged bleeding from access sites following removal of the cannulation needles after dialysis. This finding should warrant further interrogation with duplex ultrasound or venogram to evaluate for central vein stenosis.

Urea Clearance with Dialysis

Access function is commonly measured as urea clearance during dialysis, or Kt/*V*. *K* is the clearance of urea in mL/min over the entire period of dialysis; *t* is the duration of dialysis measured in minutes; *V* is the patient's volume of urea distribution measured in milliliters. Kt/*V* gives nephrologists an objective way to calculate the effectiveness of hemodialysis treatments. According to guidelines, Kt/*V* should be 1.2 at minimum in a patient receiving hemodialysis three times per week, with a target value of 1.4. In patients receiving peritoneal dialysis, the target is 1.7.

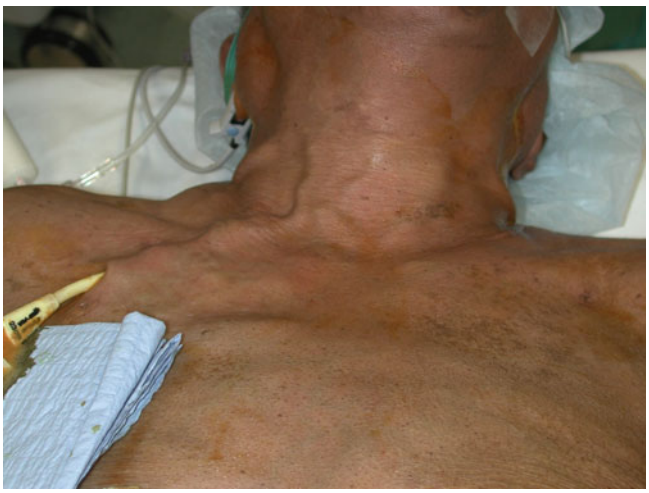

Fig. 35.3 Venous hypertension in the neck and chest secondary to a chronic indwelling tunneled dialysis catheter

Flow Surveillance

The current KDOQI guidelines recommend that autologous fistulas and AV grafts undergo routine flow and pressure surveillance. Changes in flow and pressure can alert the physician to a developing stenosis. Flow measurements can be measured using a Transonic Hemodialysis Monitor that is located within the dialysis circuit. This device works by an ultrasound dilution technique where a bolus of isotonic saline is introduced into the bloodstream and reduces the ultrasound velocity. Next, the arterial and venous sensors each register an indicator dilution curve that can be used to calculate a flow rate and monitor for recirculation. This gives the physician a direct measurement of access function and can be monitored over time to detect a developing stenosis.

KDOQI guidelines state that flow rates less than 400–500 mL/min in autogenous fistulas and less than 600–800 mL/min in prosthetic grafts are indicative of a clinically significant stenosis. Monthly assessments are warranted to monitor flow rates. A decrease in rate by more than 25 % over 4 months should warrant further investigation with a fistulogram.

Venous Pressure

Venous pressure is easily measured during dialysis and provides a ready measure of the resistance to outflow in the extremity veins. The pump of the dialysis machine is turned off, and the pressure is allowed to equilibrate, yielding a static venous pressure. A ratio of the static venous pressure to the mean arterial pressure that is greater than 0.5 is abnormal. This ratio has approximately an 80 % specificity and an 80 % sensitivity in detecting a stenosis greater than 50 % [26, 27].

Ultrasound Surveillance

Perhaps the most attractive modality for assessing dialysis access function for vascular surgeons is the use of duplex ultrasound in the vascular laboratory to assess dialysis access

anatomy, flow, and complications. While the data concerning surveillance of dialysis access with duplex ultrasound is conflicting [28–34], more and more centers are using this modality to monitor access function. While the criteria for graft stenosis can be confusing and measurement of volume flow in the access can be difficult, as additional experience has accrued, more centers are using ultrasound for access assessment. At this point the use of duplex ultrasound should probably not be used as a routine, but its value remains as a research tool to assess access function and anticipate the need for interventions. In many centers, physical examination of the access now includes grayscale ultrasound interrogation to better identify problem areas that need surveillance. In the future, ultrasound evaluation of the access will be routinely used during patient follow-up.

Is There a Best Technique for Monitoring Vascular Access?

Although some individuals would proclaim flow surveillance with ultrasound dilution technology, the "gold standard" for access surveillance during dialysis, no single technique adequately detects lesions in all locations within the arteriovenous access. For instance, a venous outflow stenosis would cause an increase in venous pressure measurements, but decreased flow velocities may not be present immediately. Flow measurements are more indicative of inflow stenosis, but the intra-access venous pressure may remain stable or decrease in the setting of inflow stenosis [35, 36]. Based on this, it is necessary to monitor patients for failing access by multiple methods rather than just a single method due to the potential presence of inflow, outflow, and various combinations of processes. At this point, no single modality fulfills the ideal for dialysis access surveillance.

Management of Failing Access

The management of failing access will ideally prevent thrombosis and the inconvenience of potentially missing a dialysis session or requiring catheter access to provide dialysis. Typically, autogenous access fails at much lower flow rates than does a graft due to the endothelial lining, which limits thrombogenicity for an arteriovenous fistula. For a dialysis access graft, the first sign of access dysfunction may actually be graft thrombosis with an inability to provide dialysis at all. For autogenous accesses, poor quality dialysis or increasing venous pressures over time may be the first sign seen.

If poor access function is seen in any dialysis access, autogenous or prosthetic, then the management is the same: diagnostic imaging of the access, followed by an intervention on the underlying issue impairing dialysis function. The initial dialysis access imaging may be duplex ultrasound or venography, often depending on the clinical setting. Medicare generally will reimburse for one diagnostic test or the other; if a second test is needed, then no reimbursement is available.

If a venogram is performed, then the invasive nature of the venogram allows endovascular intervention to be provided at the same time. If an ultrasound is performed initially, then a venogram is scheduled with the patient's intervention; the diagnostic portion of the venogram is not reimbursable. Once the diagnostic portion of the venogram is completed, the remainder of the procedure is billable as usual.

Timing of Intervention

There is no question that early intervention avoids many complications related to the dialysis access. If the access remains patent until the intervention, then often the treatment is more limited since a stenosis is generally more focal than a complete access thrombosis. Additionally, avoiding an extensive thrombectomy makes the procedure more limited and better tolerated. All efforts in dialysis access surveillance are focused on trying to find the failing access before it has actually thrombosed. While there are many clues to a failing access, thrombosis is often the first sign of a failed arteriovenous graft since failure occurs at much higher flow rates than seen in an autogenous arteriovenous fistula. Therefore, an autogenous fistula often demonstrates decreasing dialysis efficiency and increasing venous pressures prior to autogenous access thrombosis. Since grafts fail at much higher flow rates than autogenous arteriovenous accesses, detection of impending failure of the graft may be much more difficult.

Management of Failed Access

If there is no flow in an arteriovenous access, the obvious first step in remediation and revision of the access is to reestablish flow. Fundamentally, there are two techniques for reestablishing flow in an occluded access: mechanical thrombectomy to physically remove clot present within the access and thrombolysis to pharmacologically dissolve any thrombus present in the access. Occasionally, these techniques are used together, and this will be discussed further later in this chapter.

The management of the failed dialysis access can be undertaken as a percutaneous intervention, an open intervention, or a combination of open and endovascular treatment. The first issue in managing a failed access that needs revision

is to define the problem. This may be as simple as a fistulogram in the open but failing access or as complex as an extensive open procedure to revise problems with the access using open techniques. Nonetheless, establishing whether any flow across the dialysis access persists is the first level in interrogating the failing access.

Typically, this fact can be defined by a combination of physical exam and handheld duplex ultrasound with Doppler interrogation of flow as needed. If flow is seen, then a fistulogram can be performed to define the underlying etiology of poor access function. If on the other hand a thrombosed access is seen, then the clot has to be first removed prior to undertaking any treatment. Once again, removal of the clot can be undertaken with either a percutaneous endovascular technique or an open surgical technique. Which is best is controversial since thrombolysis may leave residual thrombus that may once again impair access function or may embolize to the pulmonary vasculature with what is hopefully a small, subclinical pulmonary embolus [37]. In either case, the procedure to remove thrombus can be undertaken under local anesthesia with IV sedation.

Thrombectomy

In its simplest form, thrombectomy is simply the removal of obstructing thrombus to reestablish flow. Typically, this is performed by passing a mechanical balloon thrombectomy catheter through an arteriotomy made in the arteriovenous fistula, usually after administration of systemic heparin intravenously. The catheter for removal of thrombus is passed toward the central venous end of the access first, and a clear outflow path is obtained. Once the outflow is cleared of thrombus, the catheter is passed retrograde into the arterial inflow. As inflow is reestablished, pulsatile flow is encountered, and clamp control of inflow and outflow is obtained. At this point one of two things can occur: either the arteriotomy can be closed and continuous flow reestablished or, alternatively, contrast imaging can be performed of the inflow and outflow of the thrombosed segment before repairing the arteriotomy. The advantage of performing imaging prior to reestablishing flow is that intervention can be undertaken through the arteriotomy based on the images obtained. If the arteriotomy is closed first, then secondary access may be necessary in order to intervene on the underlying cause of the thrombosis.

Thrombolysis

While open thrombectomy has been used since the late 1960s to reestablish flow after thrombosis, in the 1970s, work began on pharmacologic adjuncts to dissolve thrombus. Initially these agents were crude and difficult to use, but with time predictable thrombolysis with acceptable bleeding risk was achieved. These agents are all related to tissue plasminogen activator: by activating plasminogen to plasmin, fibrin clot can be broken down into degradation products, and flow can be reestablished without a surgical incision. In dialysis access, the classic paradigm for use of normal lysis is referred to as the "lyse and wait" technique [38, 39]; in this technique tissue plasminogen activator to a dose of 2 mg is given across the thrombosed segment as the patient is prepared for surgery. If flow is returned in the access by this, then the patient undergoes venography, and the treatment from that point forward is the same as for any stenotic access. If flow is not returned after a short period of observation, then the patient is taken to the operating room, and the treatment from that point forward is the same as for any occluded access. The lytic is simply an adjunct to assist in removal of thrombus in preparation for definitive treatment of the underlying cause of stenosis or occlusion.

Endovascular Management Techniques, Complications, and Outcomes

Endovascular management of the failing or failed dialysis access starts with contrast interrogation of the entire conduit. If the access is thrombosed, thrombectomy must be performed followed by contrast injection in an attempt to define the underlying cause that led to thrombosis. If, on the other hand, the access remains patent but poorly functioning, a fistulogram to define the underlying cause for dysfunction is the first step. The goal remains however to treat underlying defects in an effort to maintain dialysis access function for as long as possible.

After the fistulogram is performed, angiographic assessment of the entire access allows treatment of the underlying defects responsible for poor function. If the access is already failed, then thrombectomy or thrombolysis is necessary to reestablish flow in the access prior to fistulogram or access assessment. If the access is patent but malfunctioning, then necessary interventions can be performed without thrombectomy or thrombolysis. Numerous comparisons between angioplasty and surgical revision have been performed [40–44], but there is no clear preferred technique when endovascular and open techniques are compared.

Endovascular Interventions

The decision to undertake an endovascular intervention on a failing or failed access depends on the underlying etiology of the failure. Generally, endovascular treatment is best reserved for the stenotic access, which, fortunately, is the most

common mechanism of failure. Alternatively, if aneurysmal degeneration has occurred and is leading to access failure, this is somewhat more difficult to treat with endovascular techniques. Nonetheless, good results have been achieved with endovascular covered stent placement as will be discussed further later in this chapter.

Angioplasty

In its simplest form, a failing access develops a stenosis which leads to slower flow and the potential for recirculation or venous hypertension. After gaining needle access upstream to the area of pathology, a wire is passed across the stenosis through an intravascular sheath that is used for the remainder of the intervention [45–52]. Again, after performing an initial diagnostic fistulogram, a balloon angioplasty catheter is brought into the area of stenosis and inflated, usually with an 8-mm diameter high-pressure balloon (Fig. 35.4).

Typically these venous stenoses are fibrous and not atherosclerotic and therefore behave differently than the typical atherosclerotic stenosis seen in lower extremity arterial disease. The result is that it often takes a high-pressure balloon to stretch the stenosis, and there is often significant recoil associated with treatment. Nonetheless, the balloon provides a significant luminal gain to improve the blood flow in the access.

Occasionally, a stenosis can develop at the arterial anastomosis of an autogenous arteriovenous fistula (Fig. 35.5).

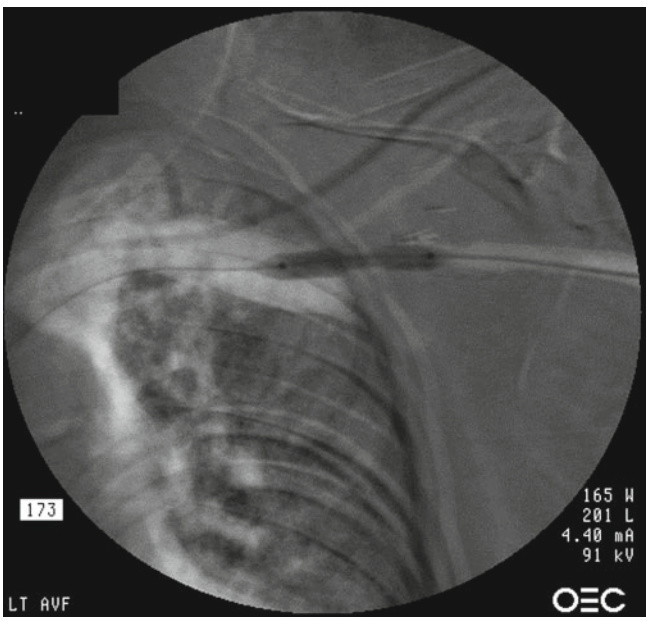

Fig. 35.4 Subclavian vein balloon angioplasty using an 8-mm high-pressure venous balloon. Note the waist on the balloon secondary to the fibrous stenosis

When this occurs, the lesion may indeed be atherosclerotic, and the treatment at that location should be undertaken much as one would treat an atherosclerotic lesion elsewhere. In this setting a smaller balloon is generally used, usually in the 4–6-mm range. If there is a significant atherosclerosis at the proximal anastomosis of an AV fistula, then great care must be taken to preserve flow to the distal upper extremity to avoid steal. The presence of atherosclerosis in an upper extremity artery greatly increases the risk of steal with arteriovenous access.

Stenting

In some cases, the elastic recoil of an arteriovenous access stenosis can be so severe as to provide minimal, if any, improvement in the lumen after angioplasty alone. In this setting a barrier to recoil is necessary using a typical

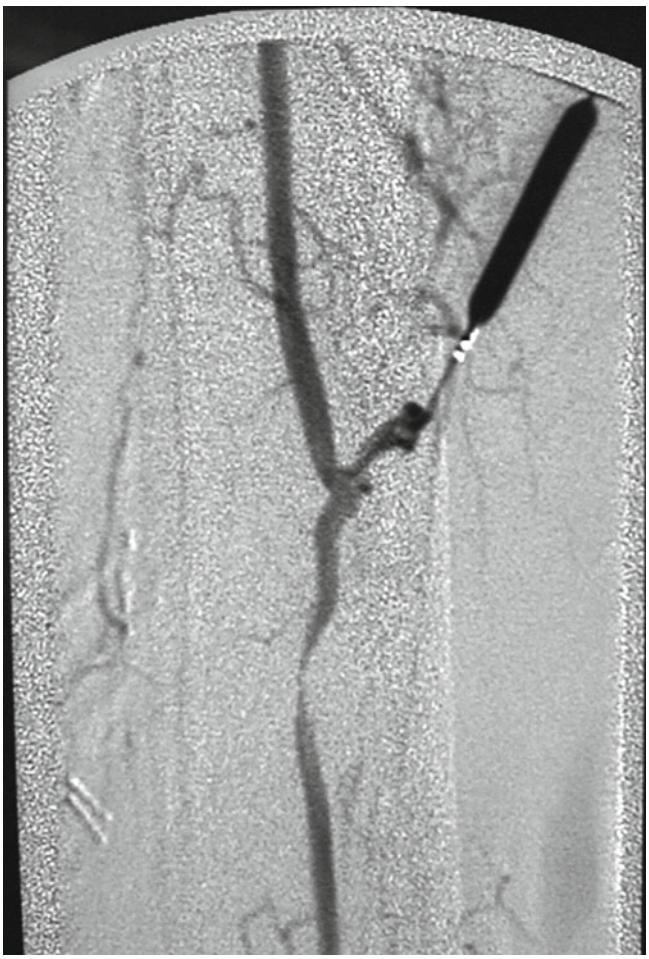

Fig. 35.5 Retrograde fistulogram from the cephalic vein showing a high-grade stenosis in the radiocephalic fistula just beyond the anastomosis to the radial artery. The balloon is used to occlude flow while injecting through the wire lumen to better visualize the anastomosis

intravascular stent, such as that used in the coronary circulation or in lower extremity arterial disease. The performance of the stents can be significantly impacted by the characteristics of the stenosis being treated: a fibrous venous lesion due to intimal hyperplasia in the venous outflow may lead to in-stent restenosis with early lesion recurrence. Nonetheless, when faced with significant lesion recoil and the potential for early failure of the treatment, a barrier to the recoil seems prudent. Generally, stenting of venous lesions is only undertaken after prior treatment with balloon angioplasty alone. If the lesion fails early, then stents may be appropriate; additionally, these self-expanding stents that are typically used need vessel preparation prior to stent placement to allow the stent to fully expand and provide full lesion expansion. Stents are typically of two varieties: self-expanding and balloon expandable.

Usually, self-expanding stents have less radial force than balloon expandable stents, but balloon expandable stents tend to exhibit metal memory and therefore are prone to stent deformation in a superficial location accessible to external pressure (Fig. 35.6). Balloon expandable stents would rarely be used over a joint or in an area easily accessible to trauma. Nonetheless, balloon expandable stents (or covered stents as will be discussed) may be necessary in certain circumstances to provide additional radial force. Balloon expandable stents also have advantage in that they can be further expanded beyond their nominal size using larger balloons and will fit a larger range of sizes than the traditional self-expanding stent. On the other hand, self-expanding stents always want to return to their nominal diameter, and therefore flexion is better tolerated since any compression of the stent will generally be accommodated by expansion back to the nominal diameter of the stent.

Both types of bare metal stents suffer from the fact that the mesh used for the stent provides no barrier to recurrent intimal hyperplasia. Patency may ultimately be limited by the return of the scarring process within the interstices of the stent. This results in recurrent stenosis at the same location as the stent was placed although the intimal hyperplastic response may extend throughout the length of the stent and even beyond.

Fig. 35.6 Newer designs for self-expanding stents improve radial force and flexibility

Covered Stents

In an effort to limit tissue in growth at the location of stent placement, covered stents have become popular for treating both peripheral and central venous stenoses (Fig. 35.7). The advantage of covered stents is preventing in growth of tissue into the area covered by the stent; while the stent provides support against elastic recoil, the covering prevents in growth of recurrent intimal hyperplasia. These have been used extensively in dialysis access [53, 54], particularly relative to arteriovenous grafts and intimal hyperplasia at the distal anastomosis.

Similarly, in the central veins, covered stents have been valuable in extending the durability of stent placement in patients with central venous stenosis or occlusion [55–57]. Although this is not a perfect solution since stenosis can recur at the ends of the covered stent, this does provide improved durability in those situations where early recurrence would be the norm.

Similarly, endovascular placement of covered stents has been used to treat aneurysmal segments [58–60], allowing continued use of the conduit for ongoing dialysis.

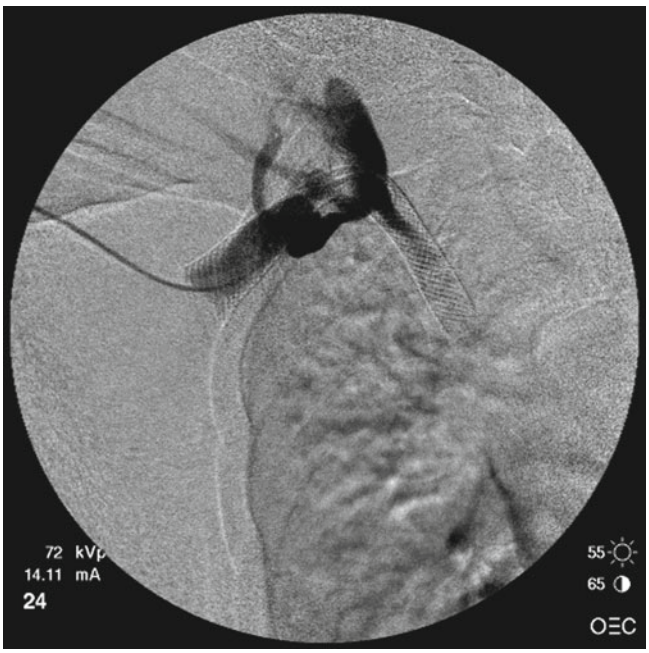

Fig. 35.7 A subclavian vein central venous stenosis showing a covered stent (lateral) inside a bare metal stent (medial). While intimal hyperplasia has caused significant in-stent restenosis in the bare metal stent, contrast can still be seen in the lumen of the covered stent

Open Repair Techniques, Complications, and Outcomes

Surgical repair of a stenosis in an outflow vein from arteriovenous access inevitably creates more scarring and the risk for recurrent intimal hyperplasia. As vascular surgeons are trained to repair blood vessels from normal proximal vein to normal distal vein, inevitably more vein is consumed with open surgery than is usually treated with endovascular techniques. Despite this surgery is more definitive, often resetting the patency after surgery back to where it was when the access was first placed. Therefore, open surgery is inevitably a compromise between consuming outflow and improving patency in the short term.

Open Treatment for Stenosis

Open surgical techniques for revision of the failing or failed access centers on the underlying cause once again. Generally, venous stenosis is the most common cause of access failure in treatment of this with open surgical technique that requires opening of the stenosis by patch angioplasty across the stenosis with a vein or prosthetic patch. This requires an incision over each area of stenosis, and, in the access with multiple stenoses, multiple incisions may be necessary. While this is often not realistic, incorporating more than one stenosis into a patch is more feasible and may be appropriate if they are located close together.

At some point venous stenosis may lead to outflow failure to such an extent that graft replacement of a segment may be necessary. Multiple stenoses may be treated by graft replacement of that segment with preservation of proximal or distal autogenous conduit. While this lowers the long-term patency of the access overall, it does provide continued use of the same dialysis access for a longer period of time, and in many cases, the durability of conduit replacement with prosthetic may be sufficient to prolong access use.

Open Treatment for Aneurysmal Degeneration

Aneurysmal degeneration of an access is very common as it is repetitively punctured over months or years. As the access wall weakens over time, diffuse aneurysmal degeneration or saccular pseudoaneurysm formation can develop. These are often associated with stenosis of the access conduit, and the combination of aneurysm and stenosis can lead to significant access dysfunction due to recirculation between the two needle access sites. While stenosis can be treated by patch angioplasty, aneurysmal degeneration is more difficult to treat since the conduit is intrinsically damaged. One option is to replace the conduit with a new prosthetic graft; again, this may decrease the patency of an autogenous access over time. A second option which is less commonly performed is endoaneurysmorrhaphy or aneurysm plication [61]. In this technique the diffuse aneurysmal enlargement is narrowed down to a more normal size by resection of aneurysm wall and repair. The advantage of this technique is that it preserves the autogenous conduit although aneurysm re-formation can occur with further conduit degeneration.

In general, replacement with a prosthetic conduit is probably more durable (Fig. 35.8).

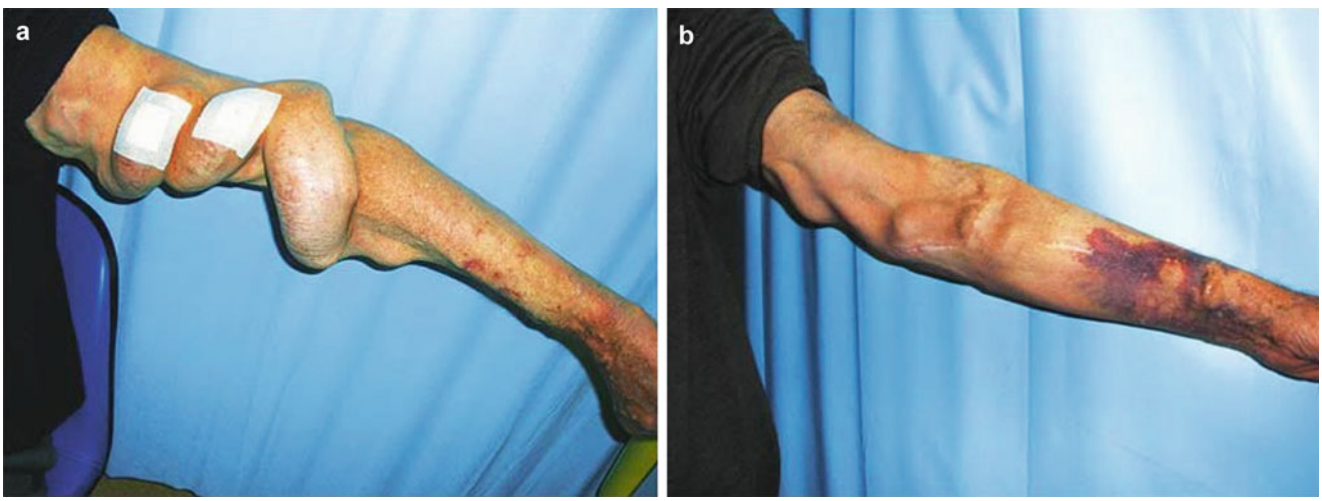

Fig. 35.8 (**a**) Aneurysmal degeneration of a brachiocephalic arteriovenous fistula with no evidence of central venous stenosis (**b**) A subsequent fistula in the opposite arm also developed aneurysmal degeneration (With permission, *New England Journal of Medicine*)

Long-Term Outcomes Post Thrombectomy and Revision

From the day the access is created, tissue biology compromises the long-term function of that access and leads to failure inevitably. While interventions can prolong the use of a given access, all accesses will fail in the long term. While some accesses fail faster than others and the reasons for this are not always clear, in general access failure is inevitable. Many attempts have been made to compare endovascular and open treatment after thrombosed arteriovenous access. While endovascular treatment potentially avoids loss of upper extremity veins, patency is less durable than after open revision. For this reason, most trials comparing open and endovascular treatment for failed or failing arteriovenous access have been unable to show any significant difference in outcomes. While short-term patencies may be better for surgical revision, this improvement is achieved at the cost of loss of venous outflow.

While surgical treatment of arteriovenous access thrombosis has been mostly unchanged for the past 30 years, endovascular treatment of the same lesions has resulted in improved outcomes at less morbidity. As progress and innovation continue in endovascular techniques, improved durability can be expected. Ultimately, the long-term success of arteriovenous access revision is going to depend on controlling intimal hyperplasia which currently appears to still be a long way off. Nonetheless, as research improves our understanding of intimal hyperplasia, drug therapy can be undertaken that may dramatically improve the outcome from thrombectomy and arteriovenous access revision.

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Understanding Hemodialysis Access Recirculation

36

Susanna H. Shin

Introduction

Hemodialysis access recirculation decreases the adequacy of dialysis delivery to the patient and is important to diagnose because inadequate dialysis can be associated with increased mortality. In some series, a high degree of access recirculation can reliably predict a hemodynamically significant stenosis [1].

Hemodialysis Access Recirculation Mechanism

Hemodialysis occurs through two cannulas, one arterial and one venous (Fig. 36.1a). The arterial cannula draws flow from the patient to the dialysis machine, and the blood returns through the venous cannula to the patient (Fig. 36.1b). Recirculation occurs when dialyzed blood returns to the extracorporeal circuit through the arterial needle, rather than returning to the systemic circulation (Fig. 36.1c). This causes the mixing of already dialyzed blood with undialyzed blood, and the urea concentration of the blood entering the circuit is reduced. This decreases the solute concentration gradient across the dialysis membrane, which decreases the rate of solute removal. This results in significantly decreased effectiveness of dialysis and may result in long-term negative effects if recirculation is not diagnosed and treated.

Causes of Recirculation

Recirculation is caused by arterial anastomosis stenosis, venous outflow stenosis, and technical issues (Table 36.1).

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Decreased Arterial Inflow: Arterial Anastomosis Stenosis

Normally the rate of blood flow through an arteriovenous (AV) access and particularly an AV graft is about 1 l per minute. During hemodialysis, the blood is pumped through the dialysis machine at rates up to 500 cc per minute leading to a flow differential. This results in the desired circumstance of only blood from the arterial side of the access entering the blood pump. However, if flow through the access is decreased significantly, such as in decreased arterial inflow, some of the blood from the venous cannula will be taken up again through the arterial cannula in order to support the set rate of flow of the blood pump, resulting in recirculation.

Decreased Venous Outflow: Venous Stenosis

Another common cause of recirculation is the presence of a high-grade venous stenosis, in which case, the outflow is restricted, and some of the blood leaving the venous cannula cycles back to the arterial cannula and results in recirculation.

Technical: Improper Needle Placement

Other causes of access circulation can result from improper technique of needle placement. In some centers, this has been found to be responsible for the great majority of recirculation in their patient population [2]. Close proximity or misdirection of arterial and venous needle placement, especially in new vascular access due to a lack of familiarity with the access anatomy will result in access recirculation. Misdirection of needle placement can be corrected by good communication with the access surgeon or establishing arterial versus venous limbs of the access. Arterial and venous limbs can be differentiated easily by occluding the access at the midpoint, and the side with a pulse is the arterial limb.

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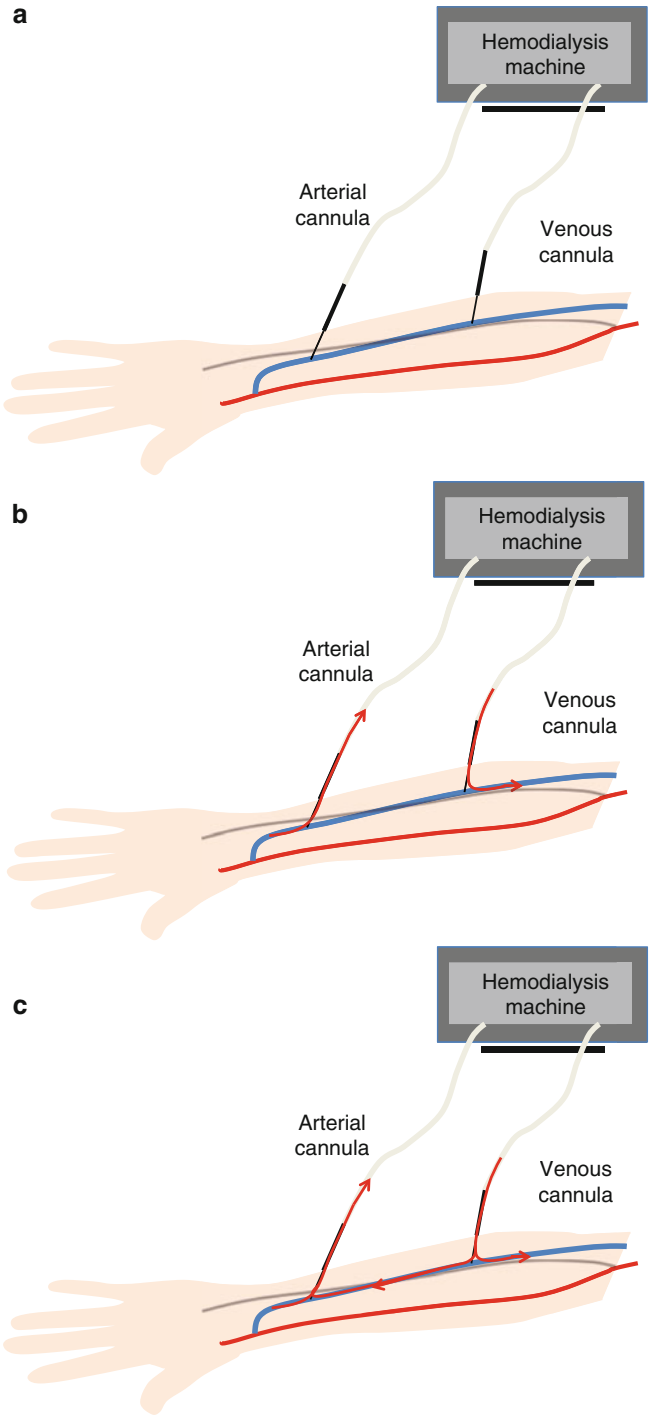

Fig. 36.1 Hemodialysis with arteriovenous fistula with arterial and venous cannulas (**a**). Normal circulation during hemodialysis (**b**). Recirculation (**c**)

Table 36.1 Causes of recirculation

Decreased arterial inflow (arterial anastomosis stenosis)
Decreased venous outflow (venous stenosis)
Technical issues

Detecting Recirculation

Screening for recirculation may be used as a surveillance technique for the early detection of fistula stenosis, the correction of which may prevent thrombosis [3]. However, some authors suggest that measurement of recirculation may have a large analytical error, and therefore the measurement of recirculation and the use of recirculation measurements as a surveillance tool vary widely without consensus on universally accepted guidelines. Tonelli et al. found that measuring recirculation did not improve utility of ultrasound dilution techniques in detecting problems with dialysis access but is time-consuming and is not appropriate for screening of autogenous access [4].

There are various methods for assessing for access recirculation (1–13). There is variability in the accuracy of the measurement depending on the method, and when in the dialysis session, the test is performed. The presence of high degrees of access recirculation should be suspected when there is an inadequate reduction in the blood urea nitrogen (BUN) as monitored by a patient's nephrologist and/or reported by the dialysis unit to the nephrologist.

One method measures the BUN level from the arterial and venous cannulas at different time points during dialysis. The degree of recirculation is calculated by comparing the arterial and venous BUN levels using the following formula, where P is the BUN level in the peripheral blood (or from circuit prior to initiating hemodialysis), A is the BUN level entering the arterial cannula (after initiation of dialysis), and V is the BUN level in the post-dialyzer venous circuit (after initiation of dialysis).

$$\text{Percent recirculation} = \frac{P - A}{P - V} \times 100$$

In the situation of 0 % recirculation, the systemic BUN level will be the same as that of the blood entering the arterial cannula after initiation of dialysis. However, if the BUN level of the blood entering the arterial cannula after initiation of dialysis is lower than that of the systemic circulation, this indicates that there is recirculation and will result in a nonzero value in the above calculation. Other methods utilize the measurement of a tracer, such as hypertonic saline, which is injected into the venous cannula, and the recirculated hypertonic saline is detected that returns through the arterial cannula. Ultrasound sensors are attached to the arterial and venous cannulas, and 10 cc of isotonic saline is injected into the venous line, and the velocity of the blood dilution as it passes through the blood lines is measured by ultrasonography.

Any recirculation should be considered abnormal, but 10 % by the urea-based method and 5 % by the non-urea dilutional method should prompt further investigation into a cause for recirculation.

Management of Recirculation

Any recirculation should be considered abnormal, and a cause should be sought as it is most often a correctable cause – arterial or venous stenosis or misplacement of access needles. Therefore, routine measurement of recirculation in some centers can be used as a surveillance tool for problems with the fistula and an indicator of inadequate hemodialysis. However, in other centers where this is not routinely measured, other indicators may prompt measurement, such as inadequate reduction in potassium or BUN. If incorrect cannula placement is eliminated as a possible cause, ultrasound duplex followed by fistulogram should be performed to evaluate and treat any areas of stenosis [5].

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Dialysis Access-Related Steal Syndrome and Neuropathy

37

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Introduction

Management of hand ischemia or dialysis access-related steal syndrome following upper extremity dialysis access surgery remains a challenge. Although approximately 80 % of patients with arteriovenous (AV) accesses have evidence of physiologic steal phenomena in the form of retrograde arterial flow distal to the AV shunt or demonstrable reduction in perfusion distal perfusion pressures that is clinical silent, the development of symptomatic steal syndrome with hand ischemia as a complication of an AV access can be seen in up to 5 % of patients and can be a significant cause of patient morbidity. Presenting symptoms, which may include rest pain, ischemic neuropathy, tissue loss in the form of ulcer, and digital gangrene, may vary in degree.

Traditionally, arteriovenous fistula (AVF) ligation was the preferred method to address symptomatic upper extremity arterial steal syndrome associated with dialysis access; however, this required an additional operation to create new access and a period of time with an indwelling central catheter for dialysis. As a result, over the past three decades, a number of other techniques have been described to treat symptomatic steal syndrome while also preserving the access for dialysis. These include anastomotic banding, relocation of inflow both proximally and distally, and surgical bypass.

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Pathophysiology

All upper extremity AVFs shunt blood from the distal arm to a certain extent, and physiological reversal of flow distal to the AV anastomosis can occur in 70 % of radiocephalic fistulae and up to 94 % of fistulae based on brachial artery inflow [1, 2]. This physiologic steal phenomenon is due to the low vascular resistance in the area beyond the arteriovenous anastomosis, resulting in preferential retrograde blood flow in the artery at this level [3, 4]. Normally, there are compensatory mechanisms that maintain adequate distal perfusion including an increase in heart rate, cardiac output, and collateral arterial flow, as well as peripheral vasodilation. However, symptomatic steal may develop when these compensatory mechanisms fail to provide adequate distal perfusion and may be seen with diseased arteries whose ability to vasodilate is impaired. Hand ischemia that occurs during hemodialysis is likely a result of reduced perfusion pressures due to a decrease in venous return and subsequent cardiac output. Furthermore, symptomatic steal syndrome is more likely to occur in the setting of arterial occlusive disease, which can reduce arterial inflow and increase peripheral vascular resistance in the distal upper extremity causing symptoms even at rest [5]. The inability to consistently predict with certainty which patients will develop symptomatic steal syndrome despite preoperative, intraoperative, and postoperative diagnostic exams and risk factors underscores the complex nature of this complication following dialysis access construction.

Risk Factors

Symptomatic steal syndrome has been most frequently associated with AV accesses that are constructed with the brachial artery as inflow, and an incidence as high as 9 % may be seen for prosthetic arteriovenous grafts (AVGs) [6]. The incidence of hand ischemia is less with autogenous AVF based

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on the brachial artery and much less common for radiocephalic AVF (1–2 %) [3, 7, 8]. Although there is no definitive predictor as to which patients will develop clinically significant steal syndrome following AV access creation, several common risk factors have been described. Those at increased risk include patients who are >60 years of age, are female, have diabetes, have a history of previous ipsilateral access procedures, or have the presence of arterial occlusive disease. Gupta et al. identified additional risk factors among their large single-center experience of 114 patients with ischemic steal syndrome. Coronary artery disease, hypertension, and tobacco use were all found to be independent risk factors for ischemic steal syndrome [9]. The use of AVG based on brachial artery inflow may also predispose the occurrence of symptomatic steal syndrome [2, 4, 9–11].

Clinical Presentation

Since physiologic steal is a frequent occurrence following AV access creation, symptomatic steal syndrome is generally a clinical diagnosis. Patients typically report extreme rest pain and weakness of the hand. The clinical manifestation of steal syndrome presents along a spectrum ranging from transient coolness of the hand with mild paresthesias to frank digital gangrene with significant motor and sensory loss. Therefore, a grading system exists reflecting the degree of hand ischemia at presentation, which also correlates with management recommendations:

Grade 1 steal: includes coolness of the hand with numbness and paresthesias.
Grade 2 steal: is characterized by hand exercise intolerance or pain during hemodialysis.
Grade 3 steal: reflects severe arterial insufficiency of the hand and includes rest pain, motor weakness, digital ulceration, or gangrene.

Timing of Steal Syndrome Presentation

Although symptomatic steal syndrome can develop at any point following the access procedure, 50–66 % of patients who develop clinically significant steal syndrome will do so within 30 days of AV access creation [7, 12]. Those presenting with steal syndrome within the first 30 days of access creation typically experience intense hand pain. Steal syndrome that develops later generally presents with some degree of tissue loss.

Physical Exam Findings

Physical exam findings may show a pallorous hand that is tender to touch, diminished, or absent radial/ulnar artery pulse that becomes palpable or augments on Doppler with fistula compression, neurologic deficits including loss of motor function affecting the intrinsic muscles of the hand, as well as impaired wrist extension/flexion. It is important to note that an absent wrist pulse in isolation does not definitively rule in ischemic steal syndrome nor is an indication for intervention by itself. A report of 180 AV access procedures, where one-third of patients had no radial artery pulse, only 12 % developed symptomatic steal [13]. Patients with symptomatic steal also present with variable degrees of digital tissue loss in the form of ulceration to dry gangrene. Severe cases of ischemic steal syndrome may present with finger contracture and muscle atrophy of the hand muscles.

Diagnosis

Despite the multitude of diagnostic studies available, it is important to note that no study by itself is diagnostic for symptomatic steal syndrome but rather should be used to supplement the clinical findings predicated on patient complaints and physical examination.

Vascular Laboratory Evaluation

These include color duplex ultrasonography, digital photoplethysmography (PPG), pulse oximetry, digital blood pressure evaluation, and systolic pressure index evaluation. An arterial duplex should be performed with the access outflow compressed in order to assess the presence of more proximal inflow occlusive disease evaluated by arterial waveform analysis. Radial and ulnar artery waveform and velocities may also be evaluated with arterial duplex scanning using intermittent compression of the access outflow. In 1996 we described six patients with symptomatic steal who had augmentation in the radial and ulnar arteries on color duplex with fistula compression before surgery [14]. Similar augmentation phenomenon is observed with digital plethysmography upon access compression [7, 15]. In addition, digital pulse oximetry has been used to objectively support the diagnosis of clinically significant steal syndrome. Halevy demonstrated a rise in digital oxygen saturation to 90 % in five patients with symptomatic steal following compression of the access who had low pulse oximetry values at baseline [16]. An absolute digital systolic pressure of ≤50 mmHg has been used as a threshold to validate symptomatic

hypoperfusion of the hand in a number of reports [4, 17]. In addition to digital blood pressure evaluation, a systolic pressure index (ratio of the systolic forearm pressure of the symptomatic arm divided by the contralateral forearm pressure) of 0.5 or less has been used by some to characterize a critical threshold for hand ischemia following an access procedure [2, 8, 18]. Lazarides et al. observed both mild and moderate ischemic symptoms in 14 % of their access patients who had a systolic pressure index less than 0.4. In the same study, lower systolic pressure indices correlated with abnormal nerve conduction studies supporting an ischemic etiology for neuropathy [3].

Angiographic Evaluation

Hand ischemia due to proximal inflow occlusive disease if present should be corrected before any attempt at surgical revision of the access. Angiography of the entire arterial inflow from the aortic arch to the anastomosis and from the anastomosis to the hand should be performed.

Surgical Treatment Options and Outcomes

In the absence of inflow occlusive disease, a variety of techniques to address hand ischemia from steal syndrome have been described including fistula ligation, banding, proximalization of arterial inflow (PAI), revision using distal inflow (RUDI), and distal revascularization with interval ligation (DRIL).

Ligation

Surgical ligation of the AVF or AVG is the simplest and most effective way to address dialysis access-related hand ischemia. Ligation of the access brings arterial flow dynamics of the affected extremity back to native anatomic baseline, thereby maximizing perfusion to the hand. Though uncommon, patients who develop symptomatic steal syndrome following a radiocephalic fistula from inadequate retrograde flow through the palmar arch can be successfully treated with ligation of the radial artery distal to the arteriovenous anastomosis. Some have described coil embolization of the distal radial artery as a catheter-based alternative to ligation in this setting with reported clinical resolution of steal [19, 20]. Despite the reliability of fistula ligation for symptomatic steal syndrome, eliminating flow through the access conduit mandates the construction of a new access for dialysis, which can be potentially problematic in patients with limited access options. Therefore, ligation should be considered as a last-resort option or reserved for patients who develop ischemic monomelic neuropathy (IMN), which is discussed later.

Banding

Banding of the AVF or AVG aims to increase resistance through the access by mechanically restricting flow, thereby promoting antegrade perfusion to the distal upper extremity. Despite the minimally invasive nature of this technique and preservation of access for hemodialysis, successful banding has been inconsistent and remains a controversial method in the treatment of symptomatic steal syndrome. Although banding leads to increased perfusion of the hand, restricting the flow through the venous outflow puts the AV access at risk for thrombosis. Determining the optimal amount of flow restriction to allow improved distal tissue perfusion while maintaining long-term access patency has been a surgical challenge. Odland et al. reported their experience with banding in 16 patients using intraoperative digital plethysmography and digital brachial indices (DBI). Extent of banding was determined using digital pressures of at least 50 mmHg or DBI of greater than 0.6. All patients had relief of symptoms for steal; however, access patency was 63 % at 6 months and 38 % at 1 year [17]. Alternatively, Zanow et al. described using an intraoperative flow meter to measure the flow reduction of the venous outflow to gauge degree of banding. In their series of 78 patients with symptomatic steal syndrome and high flow accesses, banding was performed to restrict flow through the fistula to 400 ml/min for autogenous and 600 ml/min for prosthetic conduits. Eighty-six percent of patients had ischemic symptom improvement, and a 91 % 1-year patency for AVFs and 58 % 1-year patency for AVGs was achieved [21]. With a wide range of success and failures following banding, establishing objective criteria to determine the degree of banding has been a challenge. Although increasing the resistance through the fistula with banding has demonstrated improved perfusion to the distal extremity with symptom relief, wide adoption of this technique has been tempered by unacceptable rates of access thrombosis.

Proximalization of Arterial Inflow (PAI)

Since symptomatic steal syndrome is most commonly associated with dialysis accesses based on brachial artery inflow, novel techniques creating access using different sources of inflow such as the axillary artery in PAI or radial/ulnar artery in RUDI have been described. The PAI

technique involves ligation of the venous outflow at the anastomosis and construction of an interposition graft with a small-diameter prosthetic conduit using a more proximal source of inflow such as the distal axillary artery (Fig. 37.1) [22]. Theoretically, this configuration leads to a smaller pressure drop across the AV anastomosis promoting antegrade perfusion to the distal upper extremity while maintaining sufficient flow to the fistula for access. Moreover, the small-diameter prosthetic interposition graft may serve to restrict flow through the access, further increasing tissue perfusion of the hand. Zanow et al. reported their experience with PAI in 30 patients with dialysis access-related hand ischemia. They demonstrated a mean increase in DBI from 0.4 to 0.8 and complete resolution of ischemic symptoms in 87 % of patients and significant improvement in 16 %. Primary patency of the access was 87 % at 1 year and 67 % at 3 years [22]. In another series of 12 patients who underwent PAI for dialysis access-associated hand ischemia, all patients have preservation of their access; however, 22 % were more likely to require another procedure due to ongoing symptoms of steal [23]. Although the PAI technique addresses symptomatic steal syndrome and preserves access for hemodialysis, long-term patency of the fistula is compromised by converting an autogenous conduit to a prosthetic as well as the need for more procedures for continued symptoms of steal.

Revision Using Distal Inflow (RUDI)

Revascularization using distal inflow such as the radial or ulnar artery for dialysis access creation was first described by Minion et al. in 2005 [24]. This technique involves ligation of the access at the anastomosis and relocating the inflow to the proximal radial artery using an interposition vein graft or primary anastomosis with the existing matured vein if length permits (Fig. 37.2). This configuration allows for antegrade flow via the ulnar artery, thereby improving perfusion pressures in the hand. Minion et al. reported complete resolution of ischemic symptoms in all four patients treated with RUDI with functioning fistulae during a follow-up period ranging 4–14 months [24]. Leake and coworkers recently reported their 10-year surgical experience with steal. Among a total of 201 surgically treated patients, 21 underwent RUDI which resulted in preservation of access in 95 % of the cases and improvement in steal symptoms in 89 %; however, a 30-day complication rate of 37 % was observed [23]. Although limited

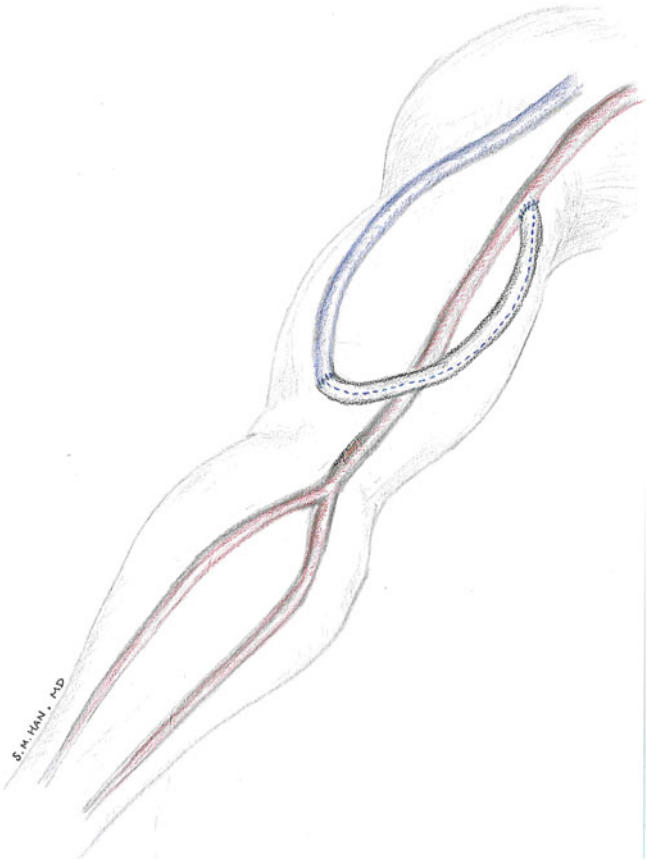

Fig. 37.1 Proximalization of arterial inflow (PAI)

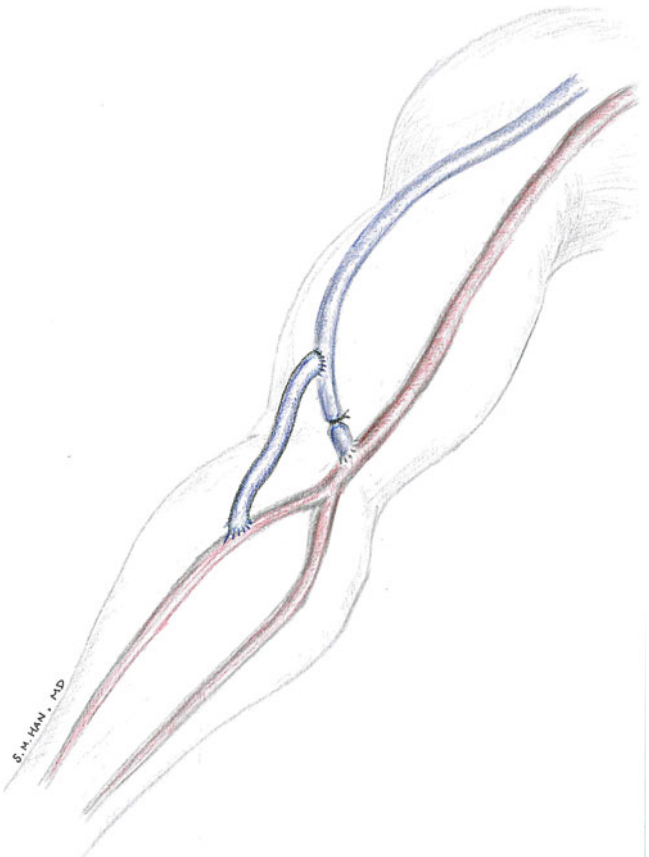

Fig. 37.2 Revascularization using distal inflow (RUDI)

experience with RUDI has shown clinical benefit for symptomatic steal syndrome, it has been suggested that this technique may compromise maturation and long-term access survival in women and patients with diabetes, the two groups most likely to develop steal syndrome [25, 26]. More experience with this technique may better characterize which patients will benefit most from RUDI over other similar alternatives to address symptomatic steal syndrome.

Distal Revascularization and Interval Ligation (DRIL)

In 1988, Schanzer and his colleagues developed a novel approach to the treatment of dialysis access-associated steal syndrome [5]. The technique involves ligation of the artery immediately distal to the anastomosis to eliminate retrograde flow from the hand and construction of a bypass using autogenous conduit distal to the flow interruption using a more proximal inflow source (Fig. 37.3). Over the following decade, this technique was increasingly used to manage dialysis-associated steal syndrome, and the acronym DRIL was later coined by Berman et al. in 1997 to describe critical features of this technique [7]. The bypass component effectively functions as a low-resistance collateral to the distal arm and restores the flow pattern to more physiologic conditions [4]. Illig et al. have quantified the hemodynamics of brachial artery-based AV accesses and demonstrated that a pressure sink that exists in the brachial artery proximal to the anastomosis is reversed with the DRIL procedure [4, 27]. Therefore, the antegrade bypass component in DRIL should originate as proximal as possible with a minimum of 10 cm proximal to the anastomosis to maximize arterial perfusion to the distal extremity and maintain adequate flow through the access.

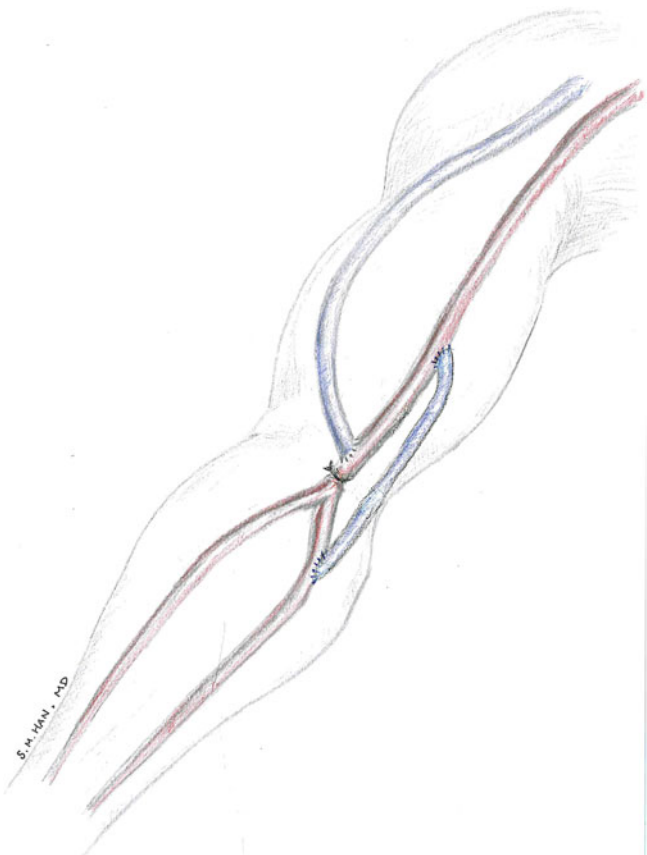

Fig. 37.3 Distal revascularization and interval ligation (DRIL)

Revascularization of the distal extremity coupled with interval ligation not only effectively addresses the ischemic component of steal but also preserves the existing access so that dialysis may continue immediately following DRIL. In 2004 Schanzer reported updated outcomes from his initial report using DRIL. Thirty-four of 42 patients had complete symptom resolution from steal with partial improvement in the remaining 8 patients, which was attributed to permanent neurologic deficits. Patency rates at 1 year were 96 % for bypass grafts, 100 % for AVFs, and 73 % for prosthetic accesses [28]. Knox and colleagues reported their experience with DRIL in 52 patients with hemodialysis access-induced ischemic steal syndrome in 2013. Substantial or complete relief of ischemic hand symptoms was achieved in 90 % of patients with an 80 % primary patency of bypass grafts at 4 years and 1-year AV access primary patency rate of 83 %. Fifteen of 20 patients with digital tissue loss had complete healing on follow-up [10]. A more recent experience by Scali et al. demonstrated symptom resolution in 82 % of patients and 85 % functional accesses following 132 DRIL procedures in 126 patients [29]. Several other single institutional case series with a moderately large number of patients have demonstrated the clinical effectiveness and durability of the DRIL procedure [7, 12, 23, 30, 31].

In 1994, we adopted the DRIL procedure as our preferred method for treating dialysis access-induced steal syndrome. Over an 18-year period, 81 DRIL procedures were performed on 77 patients for symptomatic steal syndrome associated with dialysis access. Complete symptom resolution was seen in 82 % for rest pain, 91 % for digital ulceration, 56 % for neurological deficits, and 83 % for digital gangrene. Fistula and bypass graft survival 5 years following DRIL was 56 % and 97 %, respectively. All patients not effectively treated by DRIL had resolution of ischemic-related complications following fistula ligation, local amputation, or repeat bypass.

Complications following DRIL are most commonly wound related involving the vein harvest site. A feared complication following the DRIL procedure is bypass graft thrombosis with subsequent acute limb ischemia. Although the effectiveness DRIL is predicated on interval ligation of the native artery distal to the AV anastomosis, bypass graft

thrombosis in this setting rarely leads to acute, irreversible ischemia. In our series, the overall complication rate following DRIL was 17 % with the majority being wound related. Among the 81 DRIL procedures performed, three bypass grafts occluded all within the first 4 months. The saphenous vein and prosthetic graft occlusions resulted in the development of ischemic rest pain, and in both cases, a repeat bypass with saphenous vein led to complete resolution of symptoms. The basilic vein bypass failure was discovered when a patient with digital gangrene was unable to heal from a local amputation. Fistula ligation resulted in prompt healing of the amputation site. Therefore, we believe the reticence in interval ligation of the axial artery in DRIL is not justified. Our experience has demonstrated excellent brachial bypass patency, especially when saphenous vein was used as conduit. In the rare instance of bypass graft occlusion, irreversible ischemia is unusual, and limb salvage can be achieved with a repeat bypass procedure or fistula ligation.

Ischemic Monomelic Neuropathy (IMN)

Ischemic monomelic neuropathy (IMN) is a rare but devastating complication following access creation that is distinguished by profound neurologic dysfunction in the distribution of the median, radial, and ulnar nerves in the absence of profound hand ischemia. The condition was first described by Bolton et al. in 1979 and later coined ischemic monomelic neuropathy in 1983 by Wilbourn and colleagues [32, 33]. Risk factors that have been consistently identified to be associated with those that develop IMN include older females with diabetes and accesses created using brachial artery as inflow. IMN is not observed with access creation based on radial or ulnar artery inflow. The pathogenesis of IMN is not entirely understood; however, some hypothesize that IMN is a result of transient ischemia exclusively to the nerve trunks due to flow diversion following access creation [34]. Some have demonstrated loss of flow through the vasa vasorum or an inherent watershed zone for the vasa nervosum in the antecubital fossa as possible mechanisms to explain IMN [34, 35]. It is generally believed that the threshold for ischemia is less for peripheral nerves than that of muscle, similar to the natural progression of symptoms seen in acute lower extremity ischemia with neurologic deficits precede soft tissue ischemic changes which may explain why some have describe IMN as steal syndrome isolated to nerves with preservation of the soft tissues of the distal upper extremity [33].

Patients who develop IMN do so within hours of access creation and present with acute hand pain; numbness in the distribution of the median, radial, and ulnar nerves in the distal upper extremity; and weakness or paralysis of the hand and forearm. The hand is typically warm with a palpable pulse often present without evidence of any skin or muscle ischemia. The diagnosis of IMN is often delayed, with the neurologic deficits usually being attributed to intraoperative positioning or from the effects of a regional nerve block. Any motor or sensory deficit recognized immediately following an access creation procedure should prompt an expeditious evaluation of the patient, and other potential causes to explain the deficits ruled out, including surgical nerve trauma or hematoma. Therefore, the use of regional blocks as an anesthetic for dialysis access procedures is controversial.

Treatment of IMN involves immediate action to improve arterial flow to the distal upper extremity by access ligation or revision such as DRIL, in order to expeditiously eliminate steal phenomena and maximize chances for neurologic recovery. Although access ligation achieves preoperative baseline arterial flow, neurologic recovery has been inconsistent with evidence of improvement in some and permanent loss in sensory-motor function of the affected limb in others. In our series, four of the seven patients with neurological deficits not responding to the DRIL procedure presented within 24 h of access creation with severe sensory and motor deficits out of proportion to the degree of ischemia observed. A number of these patients almost certainly had IMN, which might explain the inability of the DRIL procedure to improve their neurologic symptoms. The optimal management for IMN is still controversial since neurologic recovery has been inconsistent despite prompt recognition and immediate access ligation. We preferentially address IMN with DRIL so that the access is preserved for continued dialysis regardless of the degree of recovery.

Conclusion

In summary, hand ischemia from symptomatic steal syndrome is a well described but a relatively infrequent complication following dialysis access creation. Symptomatic steal syndrome is most frequently observed in older females with diabetes and occurs nearly exclusively with accesses created originating from the brachial artery. Fistula ligation is a very effective way to address steal syndrome but requires an additional procedure to create new access for dialysis and may also be a concern in patients with limited options for new access. Several other techniques to address the ischemic component of steal as well as preserve access for dialysis have been described including banding, proximalization of arterial inflow, and revision using distal inflow; however, we believe distal revascularization and interval ligation is the most reliable and durable approach in the management of symptomatic steal syndrome. Ischemic monomelic neuropathy is a rare but devastating complication following access creation in the upper extremity that can be treated with access ligation

or DRIL with varying degrees of success. As a result, the optimal approach to the treatment of IMN remains controversial.

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Cardiopulmonary Complications of Hemodialysis Access

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Mariel Rivero and Linda M. Harris

Introduction

Cardiovascular complications are the leading cause of morbidity and mortality in patients with end-stage renal disease (ESRD). The etiology and pathogenesis of the cardiovascular issues are multifactorial. Patients with chronic kidney disease (CKD) demonstrate altered pulmonary and cardiac status even prior to beginning hemodialysis, as compared to non-CKD patients. Factors, other than the typical comorbidities, have been implicated as playing a role in the higher than expected rate of cardiovascular complications in the CKD population, including volume overload, anemia, and uremia. Interestingly, arteriovenous (AV) access construction is also associated with an increased risk of cardiovascular death. Renal transplant has been shown to drastically improve the clinical picture, even if the access is not ligated.

Congestive Heart Failure

Patients with CKD have a higher prevalence of both atherosclerotic vascular disease and congestive heart failure (CHF) when compared to the general population [1, 2]. According to the most recent report of the US Renal Data System, 30.1 % of patients over 65 with CKD also have CHF vs. only 6.7 % of patients over 65 without CKD [3]. The majority of these patients have CHF associated with a low cardiac output. However, heart failure can also occur in the setting of high cardiac output states. These states include both physiological conditions (fever, pregnancy, etc.) and pathologic conditions [4]. The association between high-output CHF and hemodialysis access was first reported in the 1970s [5, 6]. The incidence remains poorly defined; however, it is presumed to be rare.

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Physiological Changes After Arteriovenous Access Creation

The relationship between arteriovenous fistulas (AVF) and increased cardiac output was first recognized during WWII era studies of traumatic AVF [7, 8]. In one of these studies, Epstein et al. placed PA catheters in seven young soldiers with traumatic AVF of the femoral and popliteal vessels and then examined the hemodynamic impact of AVF compression. At baseline these patients had elevated cardiac output ranging from 4.8 to 9.2 L/min. Compression of the AVF significantly decreased both the cardiac output and the heart rate [8].

Guyton and Sagawa sought to determine the mechanism by which an AVF causes an increase in cardiac output [9]. They directly evaluated the hemodynamic effects of creating large AVF in dogs that had been rendered areflex by spinal injections of anesthetic. They found that cardiac output increased by 75 % of the arteriovenous flow rate within the first 2–3 heartbeats following opening of an AVF. At the same time there was a significant decrease in peripheral vascular resistance (PVR) and an increase in venous return to the heart. By performing these studies in areflex dogs, they were able to demonstrate that the majority of these changes are due to mechanical compensation rather than a reflex response. The venous return and the cardiac output must be equal to maintain a functioning circulatory system. Creation of an AVF immediately decreases PVR which causes increased venous return to the heart. The stroke volume then increases in response to the increased venous filling as dictated by the Frank-Starling mechanism.

Emile Holman, a pioneer in the physiology of both congenital and acquired arteriovenous fistulas, understood an AVF as "a parasitic circuit engrafted upon the normal circulation and capable of producing serious deleterious effects" [10]. He described the AVF and the systemic circulation as two systems in parallel. The AVF is a short circuit with low pressure and low resistance, whereas the systemic circulation is characterized by high pressure and high resistance. As size of the connection between the two increases, there is

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increasing flow and sequestration of blood in the low resistance system, while the blood volume in the systemic circulation remains the same. The cardiac output increases in order to keep pace with the increased total blood volume and maintain adequate peripheral perfusion.

The same hemodynamic processes that underlie the physiology of traumatic arteriovenous fistulas have been demonstrated in the setting of vascular access fistulas. Ori et al. performed echocardiography on a series of patients immediately before placement of arteriovenous access and then repeated these studies an average of 12.9 days later. Stroke volume, ejection fraction, cardiac output, fractional shortening, and left ventricular end-diastolic diameter had all increased significantly, while systemic vascular resistance had decreased significantly [11]. In a similar study, Iwashima et al. evaluated a series of 20 CKD patients immediately before and then 3, 7, 10, and 14 days following creation of an arteriovenous fistula [12]. At each time point they obtained an echocardiographic study as well as measurements of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP). As in the study above, the cardiac output and left ventricle end-diastolic diameter increased significantly, with most of these changes occurring within the first week. Both ANP and BNP also increased significantly. Iwashima et al. postulated that the increase in ANP reflected an increase in blood volume, while the increase in BNP signified left ventricle pressure overload.

These hemodynamic changes are not innocuous. Over time they induce changes in both myocardial structure and oxygenation. Ori et al. followed a group of 12 CKD patients for the 3 months following creation of an AVF but prior to initiation of dialysis [13]. The patients were assessed by echocardiography prior to access placement and then again at 1 and 3 months. By 3 months there was a significant increase in left ventricular mass. Savage et al. followed nine CKD patients for the 6 months immediately following placement of a radiocephalic fistula [14]. The patients were assessed by pulse wave analysis prior to fistula placement and then every 6 weeks thereafter. The pulse wave analysis allowed calculation of the subendocardial viability ratio (SEVR) which is a marker of myocardial oxygen supply and demand that has been shown to correlate with the presence of myocardial ischemia. SEVR decreased immediately following surgery and remained below baseline in 8/9 patients at 6 months. Though both of these studies are small, they illustrate the significant functional impact of access placement on the heart.

Diagnosis of Hemodialysis-Related High-Output Heart Failure

The first requirement for diagnosing hemodialysis-related high-output heart failure is a high level of suspicion on the part of the clinician. Though the underlying physiology of high-output and low-output heart failure is different, both have a very similar presentation. Patients typically complain of dyspnea on exertion, orthopnea, fatigue, and edema. On exam both groups will often have inspiratory rales, jugular venous distention, peripheral edema, and tachycardia. However, one noteworthy difference between the two physiologic states is their effect on the pulse pressure; it is narrow in cases of low output and wide in cases of high output. Other findings that may arouse suspicion for high-output failure are the presence of peripheral vasodilatation, a hyperkinetic precordium, and a hypertrophic fistula [15, 16].

If heart failure is suspected, there are a number of investigations that can help to make the diagnosis and also to distinguish between low- and high-output states. A transthoracic echocardiogram will allow for assessment of left and right ventricular function. Patients with high-output heart failure typically develop compensatory LV dilatation and hypertrophy. However, they usually have a preserved ejection fraction as well. A venous blood gas with measurement of the mixed venous oxygen saturation (SvO_2) can also help to distinguish between high- and low-output failure. An $SvO_2 > 75\%$ suggests the presence of a high cardiac output state, while an $SvO_2 < 65\%$ suggests inadequate cardiac output [16]. However, the definitive diagnosis of high-output failure requires a right heart catheterization. The critical finding for diagnosis is a CO > 8 L/min or a cardiac index greater than 3.9 L/min/m^2 [17]. However, other typical findings include low systemic vascular resistance and pulmonary hypertension with a normal pulmonary vascular resistance [4, 15].

Once the diagnosis of high-output heart failure has been confirmed, the next step is to determine whether or not the AV access is making a substantial contribution to the cardiac output. Heart failure secondary to the presence of an AVF or AVG requires a high access flow rate (Q_a). At present neither the National Kidney Foundation (NKF) – Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines nor the literature contains a clear definition of a Q_a that is too high. Pandeya and Lindsay introduced the concept of the Q_a/CO ratio [18]. In their study on chronic hemodialysis patients, they found that the mean Q_a was 1.5 ± 0.6 L/min, while the mean Q_a/CO ratio was 22 ± 6%. MacRae et al. then evaluated numerous case reports of patients with high-output heart failure secondary to dialysis access and found that these patients consistently have Q_a/CO ratios greater than 30–35% [19]. Basile et al. examined the Q_a and CO in a series of 96 chronic hemodialysis patients, ten of which carried a diagnosis of high-output heart failure [20]. Through regression analysis they were able to show that a Q_a value > 2.0 L/min predicted high-output heart failure with a sensitivity of 89% and a specificity of 100%. The Q_a was more predictive than any of the Q_a/CO ratio tested. However, a Q_a/CO ≥ 20% had a sensitivity of 100% and a specificity of 74.7%. Nevertheless, the predictive values of Q_a and Q_a/CO have yet to be confirmed in prospective studies.

The studies described above will often be sufficient to make the diagnosis of high-output heart failure secondary to the presence of an arteriovenous access. However, the complexity of these patients, especially the presence of structural heart disease, can make it difficult to determine the relative contribution of the fistula itself. In these cases, manual compression of the fistula with simultaneous hemodynamic assessment is a useful adjunct. If there is high flow through the fistula, compression will cause a dramatic decrease in the heart rate, a finding known as the Nicoladoni-Branham sign. If there is also a significant decrease in cardiac output, the fistula is likely to be the cause of the failure, and these patients will benefit from either ligation or revision [21].

Treatment of Patients with High-Output Heart Failure Secondary to Dialysis Access

There are two goals to consider when treating patients with high-output heart failure secondary to dialysis access: (1) symptomatic relief and (2) preservation of the access. As discussed above, the increase in cardiac output is largely due to the high rate of flow in the fistula. Consequently, the primary treatment strategies involve flow reduction. As with the treatment of high-flow ischemic steal of the hand, the two primary techniques for flow reduction are banding and revision using distal inflow (RUDI).

The banding technique typically involves using a prosthetic cuff to create a surgical stenosis. However, it can be difficult to adequately reduce flow without causing thrombosis and loss of the access. The first report of using banding for the treatment of high-output cardiac failure was published by Ahearn et al. in 1972 [5]. Since that time there have been a number of small case reports, but each of them has had relatively limited information on both clinical outcomes and access patency [22–25]. Van Hoek et al. have published the largest series to date with nine heart failure patients [24]. AVF blood flow was monitored intraoperatively and used to guide the degree of banding. The procedure successfully decreased access flow from 3.2 L/min to 1.2 L/min. All fistulas remained open for at least 3 months postoperatively. They did not provide detailed information on clinical outcomes. However, they noted that two patients required repeat banding procedures for recurrent symptoms at 1 and 28 months postoperatively.

In RUDI, the arteriovenous fistula is ligated just beyond the anastomosis, and then inflow is reestablished using a smaller, more distal arterial inflow source. Parmar et al. described a case in which they used a segment of great saphenous vein to connect a brachiocephalic fistula to the ulnar artery [26]. They were able to reduce flow through the fistula from 10.4 L/min to 3.6 L/min. At 7 months the patient had both sustained improvement in his cardiac symptoms and a patent dialysis access. Chemla et al. reported a series in which they used RUDI to treat 17 patients with heart failure secondary to a high-flow upper arm arteriovenous fistula [27]. Unlike Parmar et al., they utilized a PTFE graft to connect the fistula to the radial artery. They were able to successfully reduce access flow from 3.1 L/min to 1 L/min and cardiac output from 8 L/min to 5.6 L/min. Over a median follow-up period of 16 months, access thrombosis occurred in five patients, and four patients required placement of a new access.

Although many groups have reported success with inflow reduction procedures, there is a subset of patients who ultimately require ligation of the fistula. Stern et al. reported on a patient who failed banding due to persistent shortness of breath and chest heaviness [15]. Her symptoms improved dramatically post-ligation, and at 6 months postoperatively, her ejection fraction had improved from 35 to 45–50 %. Multiple case reports have documented similar improvement in both symptoms and ejection fraction following AVF ligation [19, 23, 25].

As suggested by the case above, fistula ligation has been shown to cause not only symptomatic improvement but also reversal of cardiac remodeling. Using echocardiography Unger et al. prospectively studied the impact of AVF closure on a series of 17 renal transplant patients [28]. At 21 months postoperatively, the LV mass index (LVMI) had decreased significantly and the prevalence of LV hypertrophy had dropped from 65 to 18 % ($p = 0.008$). There were no changes in LVMI or LVH in a matched group of controls; therefore, the results cannot be attributed to the effects of renal transplantation. Similarly, van Duijnhoven et al. demonstrated a significant decrease in LVMI as early as 3–4 months following AVF ligation in transplant patients [29]. Movilli et al. studied the effects of AVF closure on dialysis-dependent patients that underwent conversion from an AVF to a tunneled dialysis catheter secondary to fistula failure [30]. Despite the fact that, by definition, all eligible patients had low flow in their AVF, closure was associated with a significant decrease in LV mass and an increase in LVEF. No significant changes were observed in a group of matched controls with well-functioning AVF.

None of the above studies on AVF closure included patients with high-flow fistulas. Therefore, the results are not strictly applicable to patients with access-related high-output heart failure. However, these results are the closest available proxy for the physiologic impact of AVF flow reduction in these patients.

Access Selection in Patients with Preexisting Heart Failure

The presence of an AVF has numerous effects on cardiac hemodynamics. Therefore, it is important to consider a patients' underlying cardiac function prior to selecting the type of dialysis access. However, there is very little data in the

literature to help providers identify patients at risk for high-output heart failure. What is clear is that high-output heart failure secondary to the presence of dialysis access is a relatively rare problem. While there are more than 400,000 patients on hemodialysis in the United States [3], most papers on dialysis-related high-output heart failure consist of isolated cases or series with less than ten patients. Furthermore, there is evidence that patients with symptomatic heart failure at baseline demonstrate a decrease in both LVMI and LVH following initiation of dialysis [31]. Overall, it appears that most patients with heart failure can tolerate the presence of an AVF.

The determination that a patient is at high risk for worsening heart failure with an AVF must be made on a case-by-case basis. However, as the hemodynamic impact of an arteriovenous fistula is largely dependent on access flow rates, there are multiple factors that can influence this risk. Several papers have shown that both Q_a and Q_a/CO are higher in patients with upper arm AVF when compared to patients with forearm AVF [20, 32, 33]. In addition, Begin et al. demonstrated that both male sex and the presence of a previous ipsilateral, more distal, AVF are associated with significantly higher access flow rates [33]. Therefore a patient's sex, access history, and available access sites all have a significant impact on the likelihood of developing high-output heart failure. When treating a patient with severe (NYHA class IV) heart failure with multiple risk factors for high access flow rates, it may be prudent to consider the use of either a tunneled catheter or peritoneal dialysis.

Pulmonary Hypertension

Pulmonary hypertension is a progressive, fatal disease, defined as a pulmonary artery pressure of greater than or equal to 25 mmHg as measured by right heart catheterization. Measurements are frequently estimated by Doppler echocardiography using the Bernoulli equation (PAP-4x (tricuspid systolic jet velocity)^2 + estimated right atrial pressure). Most studies use values of greater than 35 mmHg as a cutoff for pulmonary hypertension. Pulmonary hypertension is classified according to the World Health Organization Classification, most recently modified in 2008 (Table 38.1). CKD patients have components that fall into multiple categories. For example, class II includes heart failure, which is frequent in the CKD population, and class III includes sleep apnea and COPD, also not uncommon in CKD patients. Class IV includes thromboembolic issues, which may be seen with access thrombectomy, and is also more common in the CKD population than controls, and class V includes systemic diseases, including CKD with "unexplained pulmonary hypertension."

Survival of patients with pulmonary hypertension is markedly decreased, as compared to those patients without pulmonary hypertension 74 % vs. 94 % at 1 year, in a study by Ramasubbu [34]. Agarwal found pulmonary hypertension to be the strongest predictor of mortality in HD patients, with a HR of 2.17 by multivariate analysis [35]. Yigla also found pulmonary hypertension to be an independent risk factor for mortality in HD patients, similar to those with severe cardiac abnormalities [36]. In a recent study by Li, he found that pulmonary hypertension was an independent risk factor for both all-cause and cardiovascular mortality, with the incidence of cardiovascular events approximately doubled in pulmonary hypertension patients [37]. Mortality in PHT patients was 27.6 % vs. 14.4 % in those without pulmonary hypertension ($p = .008$). In another study by Yigla, pulmonary hypertension was associated with a significant decrease in survival (mortality 30.8 % versus 3.5 %) [38]. In this study, pulmonary hypertension was the strongest predictor of cardiovascular events, even more than existing CV disease, diabetes, hemoglobin levels, and malnutrition. This has led some to recommend evaluation of PAP, EF, and fistula flow 6 months after access creation [39].

Prevalence of Pulmonary Hypertension

The prevalence of pulmonary hypertension is difficult to estimate. The vast majority of the studies assessing prevalence exclude patients who fit the first four categories of the World Health Organization Classification system, leaving only those with "unexplained pulmonary hypertension," thereby underestimating the prevalence of PHT in the CKD V patient population. From a review of current series, the prevalence of unexplained pulmonary hypertension predialysis ranges from 0 to 39 %. For CKD V patients on HD, the

Table 38.1 World Health Organization classification of pulmonary hypertension

Group	Description	Causes/examples
1	PAH	Idiopathic, hereditary, drug/toxin induced, connective tissue, congenital heart, etc.
2	PH from left heart disease	Systolic or diastolic dysfunction, vale disease
3	PH from lung disease	COPD
4	Chronic thromboembolic disease	Multiple PE
5	Unclear/multifactorial	Myeloproliferative disorders, sarcoid metabolic, ESRD on dialysis

prevalence of pulmonary hypertension ranges from 14 to 86 %, with most studies finding rates of approximately 40 %, and 0–68.8 % on peritoneal dialysis. The difference in prevalence may or may not be related to dialysis methodology, as the two populations are not necessarily similar, with peritoneal dialysis patients often being healthier and frequently younger than those on HD.

Pulmonary hypertension has been shown to increase in prevalence after the creation of AV access and is noted to regress after temporary access closure [40]. There is conflicting data as to whether blood flow rate directly correlates with PAP levels, with the majority suggesting that a higher flow rate is associated with pulmonary hypertension. However, pulmonary hypertension has also been shown to decrease after renal transplantation, even with continued presence of a functioning AV access with PAP decreasing from a mean of 49.8–38.6 (0.028) [41].

Pathogenesis of Pulmonary Hypertension

The pathogenesis of pulmonary hypertension in the CKD population is not clearly understood but appears to be multifactorial in nature. Factors that have been implicated include cardiac dysfunction, volume overload, high cardiac output often associated with increased pulmonary vascular resistance due to hormonal and metabolic derangement, uremic toxins, inflammation, endothelial dysfunction, pulmonary vascular calcification, embolization microbubble from dialyzer or particulate from access with resultant chronic hypoxia, and sleep apnea. PHT also has been shown to be present in CKD patients prior to the onset of dialysis at a higher rate than the normal population. In a study by Yang and Bao, of patients with CKD 1–3, they found 28.9 % of patients had a PASP of ≥35 [42]. In this predialysis group, BNP, left atrial diameter and GFR were independent determinants of pulmonary artery systolic pressure.

Dialyzer membrane utilized may play a role in the incidence and extent of pulmonary hypertension. Walker first assessed this in an animal model in 1984 [43]. More recently, Kiykim compared biocompatible and bioincompatible membranes and found that pulmonary artery pressure significantly decreased after dialysis with the high-flux polysulfone membranes, but not with the cellulose acetate membranes [44]. Patients with ESRD have acquired endothelial cell dysfunction, which reduces their ability to tolerate the elevated cardiac output associated with AV access creation. Havlucu and associates evaluated AVF flow by Doppler sonography and found a positive correlation with systolic pulmonary artery pressure and AV access flow rates [45]. Further, AVF compression decreased systolic pulmonary artery pressure from 36.8/10.7 to 32.8/10.5 mmHg. Hemodialysis and dry-weight reduction also decrease systolic pulmonary artery pressure. Nakhoul and coworkers studied the role of endothelin-1 and nitric oxide in the development of pulmonary hypertension after surgical access creation [41]. They found elevated endothelin levels in all dialysis patients, with 48 % of them having pulmonary hypertension. Those with pulmonary hypertension had a greater cardiac output than those without pulmonary hypertension. Hemodialysis increased nitric oxide metabolites in patients without pulmonary hypertension more than in those with PHT. Temporary closure of the access resulted in a transient decrease in cardiac output and systolic pulmonary artery pressure, suggesting that part of the mechanism of pulmonary hypertension may be related to the increased flow secondary to AV access. Harp and coworkers evaluated the relationship of access thrombectomy and pulmonary hypertension and found pulmonary hypertension in 52 % of all dialysis patients after at least one thrombectomy, versus 26 % in patients without thrombectomy [46]. Twenty-six percent of dialysis patients had either moderate or severe pulmonary hypertension, whereas in controls, the incidence of moderate to severe pulmonary hypertension was only 12 %. In patients with ESRD without thrombectomy, the prevalence of pulmonary hypertension was 42 %, with 14 % having moderate to severe hypertension. They concluded that thrombectomy was not a significant factor in pulmonary hypertension; however, the presence of ESRD was associated with a 2.7-fold increased risk of pulmonary hypertension. A study by Yigla and associates compared patients with long-term AV access, peritoneal dialysis patients, and those with chronic renal insufficiency [38]. Pulmonary hypertension was found in 37 % of AV access patients, in no peritoneal dialysis patients, and in one patient with renal insufficiency. Cardiac output was also found to be significantly higher—6.9 L/min versus 5.5 L/min—in patients on hemodialysis. Further, they found that pulmonary artery pressure increased in 66 % of patients after beginning hemodialysis. They concluded that both long-term hemodialysis and AV access creation appear to be associated with a high incidence of pulmonary hypertension by affecting pulmonary vascular resistance and cardiac output. Many authors have found a higher prevalence of pulmonary hypertension in patients with HD as compared to patients with peritoneal dialysis.

Treatment for pulmonary hypertension in ESRD patients

Treatment for pulmonary hypertension in ESRD patients requires accurate diagnosis of the etiology, as different causes require different therapies. The majority of this evaluation is not the purview of the vascular surgeon. Treatment includes right heart catheterization with vasoreactivity testing to determine etiology and permit focused therapy. Targeted therapy is indicated for those in Category I, while those in Category III require treatment of the underlying cause, i.e., COPD. Diuresis may be appropriate for Category II patients with CHF and may be appropriate in most CKD patients with ESRD. Treatment may include optimization of volume status and avoidance of peripheral vasodilators. Pharmacologic management,

Table 38.2 Pulmonary hypertension prevalence in patients with chronic kidney disease

Author/year	Country	Definition of PHT (mmHg)	No. of patients/ controls	ESRD patient PHT prevalence		
				Pre	PD	HD
Amin/2003 [47]	Egypt	35	51			29.4 %
Yigla/2003 [38]	Israel	35	58			39.7 %
Yigla/2004 [48]	Israel	35	49			57 %
Nakhoul/2005 [41]	Israel	35	42/20			48 %
Tarrass/2006 [49]	Morocco	35	86			26.74 %
Havlucu/2007 [45]	Turkey	35	25 HD; 23 Pre	39 %		56 %
Kumbar/2007 [50]	USA	35	36		42 %	
Yigla/2008 [51]	Israel	35	12	0		
Adelwhab/2008 [52]	Egypt	35	45/31	32.3 %		44.4 %
Mousavi/2008 [53]	Iran	35	62			49.3 %
Mahdavi-Mazdeh/2008 [54]	Iran	35	62			52 %
Acarturk/2008 [55]	Turkey	>25	32			43.7 %
Issa/2008 [56]	USA	35	215	25 %		58 %
Bozbas/2009 [57]	Turkey	30	500			17 %
Unal/2009 [58]	Turkey	35	135		12.5 %	
Yigla/2009 [36]	Israel	35	127	13.4 %		29 %
Dagli/2009 [59]	Turkey	30	116			21.6 %
Beigi/2009 [39]	Iran	30	50			14 %
Yu/2009 [60]	Taiwan	35	39			61.53 %
Unal 2010 [61]	Turkey	35	20			30 %
Ramasubbu/2010 [34]	USA	35	90			47 %
Kiykim/2010 [44]	Turkey	30	74		68.8 %	
Zlotnick/2010 [62]	USA	35	55	14 %	0	86 %
Etemadi/2011 [63]	Iran	35	34 HD; 32 PD		18.7 %	41.1 %
Fabbian/2011 [64]	Italy	35	29 HD; 27 PD		18.5 %	58.6 %
Agarwal/2012 [35]	USA	35	288			38 %
Pabst/2012 [65]	Germany	25	62	71 % symptomatic		65 % symptomatic
Ogyar/2012 [66]	Cyprus	35	77 HD; 28 PD		35.7 %	33.8 %
Unal 2013 [67]	Turkey	35	50 HD; 20 PD	0	10 %	34 %
Fadaii/2013 [68]	Iran	35	102			66 %
Abedini/2013 [69]	Iran	25	90 HD; 73 PD; 83 txp	5 %	8.3 %	31.6 %
Li/2014 [37]	China	35	278			35.3 %
Yang/2014 [42]	China	35	101	28.91 %		
Harp [46]	USA	35	82/100/117 CKD			52 % thrombectomy, 42 % thrombectomy

PHT pulmonary hypertension, *HD* hemodialysis, *PD* peritoneal dialysis, *ESRD* end-stage renal disease

including anticoagulants, diuretics, digoxin, and oxygen, as well as calcium antagonists, is appropriate for many patients, as is exercise training therapy. Treatment of pulmonary hypertension associated with AV access can also include ligation of the access, distalization of the access to reduce flow, alternative modes of dialysis (e.g., peritoneal), or renal transplantation (Table 38.2).

Conclusions

While care of the CKD patient by vascular surgeons is typically limited to access creation and maintenance, it is important for the surgeon to be aware of factors that may impact life expectancy and quality of life for these patients. Patients with underlying congestive heart failure should be carefully assessed prior to access creation, to prevent exacerbation of their underlying condition. Patients who develop signs and symptoms of CHF after access creation should undergo full evaluation, including an assessment of the contribution of the access to the cardiac issues, to determine whether intervention on the access may be warranted. Patients with underlying pulmonary issues, or other factors that may place them at higher risk for pulmonary hypertension, need further consideration prior to creation of an AV

access, as peritoneal dialysis or transplant may be better options. Flow rates in fistulas should also be considered in patients at high risk, and these patients may warrant closer monitoring, and possibly intervention, if symptoms develop or pulmonary hypertension becomes worse or consideration of catheter-based AV access for those with underlying pulmonary hypertension, with more limited life expectancy, or who are not candidates for transplant. While cardiopulmonary issues are not the primary purview of the vascular surgeon, it is critical that we be aware of these issues in the creation and maintenance of the dialysis access.

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Part VII

Hemodialysis Alternatives

Renal Transplant Referral and Criteria

39

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Introduction

Kidney transplantation is considered the ideal form of renal replacement therapy for people with advanced chronic kidney disease (CKD) and end-stage renal disease (ESRD). Multiple studies have demonstrated that a successful kidney transplant leads to improved quality of life and longevity when compared to remaining on dialysis [1–3]. In addition, kidney transplantation is cost-effective [4].

In the United States the number of patients on dialysis is on the rise due to the increasing growth of the aging population with a high rate of comorbid conditions such as obesity, hypertension, heart disease, and diabetes [5]. The number of patients waiting on the transplant list has progressively increased, while the organ donation rate is static, widening the gap between the people waiting on the transplant list and the number of organs available every year (Fig. 39.1). As of 2012, 114,813 people were waiting on the transplant list with only 16,487 undergoing transplant [5].

The important first step to a successful kidney transplant is a timely referral for transplant evaluation. It requires collaboration and effective communication between the primary nephrologist, dialysis unit, and the multidisciplinary transplant team, which includes transplant nephrologists, transplant surgeons, nurse coordinators, pharmacists, dieticians, social workers, and financial counselors. There are a number of barriers to early referral for kidney transplant evaluation. These include a lack of complete understanding of the process and the advantages and disadvantages of kidney transplantation as a therapy for CKD and ESRD by both patients and physicians [6, 7].

Late referrals can lead to missed opportunities for preemptive transplantation [8]. Kidney transplantation performed prior to initiation of dialysis is associated with better outcomes of graft and patient survival [9]. Other advantages are the avoidance of morbidity associated with dialysis and dialysis access procedures. A large portion of preemptive transplants are performed using living donor kidneys. Recipients of preemptive kidney transplants tend to be white and of higher socioeconomic status. Late referrals are known to occur with ethnic minorities, patients with lower socioeconomic status, and geographically disadvantaged patients with limited access to specialized care [10].

Kidney Donors

Kidney transplantation can be from either deceased or living donors. Living kidney transplantation could be from related or unrelated living donors. Living donors constitute a very significant source of the best quality organs. Living kidney transplants have a better graft survival, despite poor HLA matching when compared to well-matched deceased donor kidneys [11, 12].

In the United States, most *kidney transplants* come from deceased kidney donors (Fig. 39.2). The average waiting time for a kidney is at least 3–7 years depending on blood type and the region of residence [5]. Deceased donors could be either brain-dead donors or donors after circulatory death (DCD). Kidney transplantation from DCD donors have similar allograft and patient survival compared with kidney from donation after brain death; however, DCD transplantation has higher incidence of the delayed graft function (need for at least one dialysis treatment during the first week after transplantation) when compared to the brain-dead donor kidneys [13].

There exists variability in the quality of deceased donor kidneys that are used for transplantation. The use of kidneys

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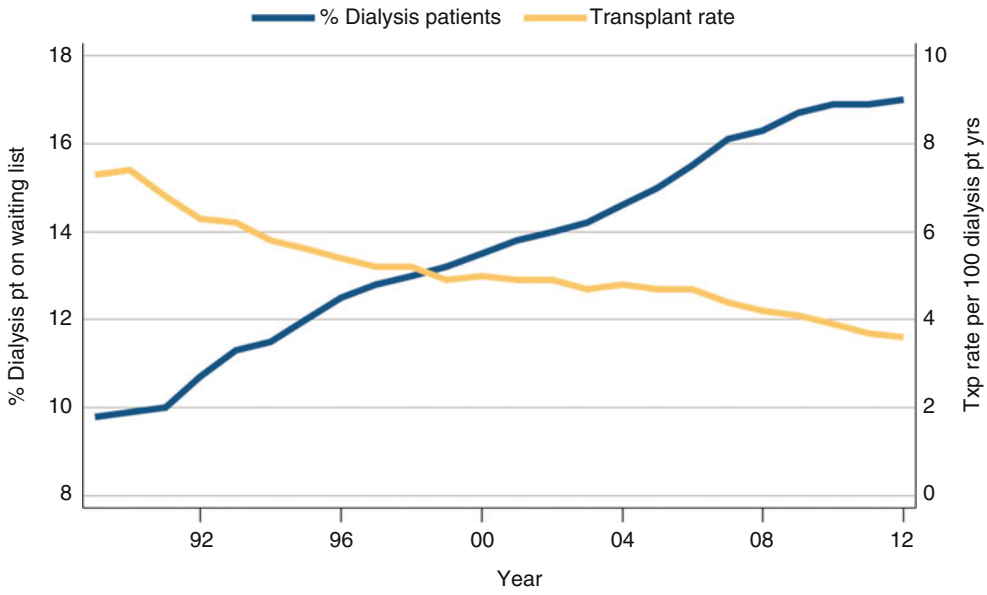

Fig. 39.1 Trends in transplantation: unadjusted rates, waiting list counts, waiting time, counts of transplants per year, and total functioning transplants. Percent of dialysis patients wait-listed and unadjusted and transplant rates (vol 2 Fig. 6.1)

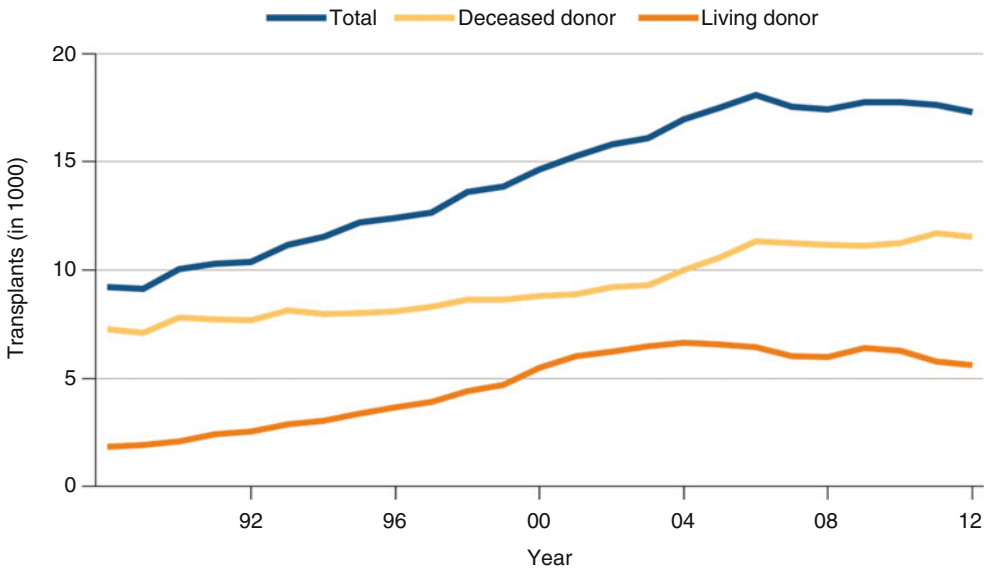

Fig. 39.2 Trends in transplantation (vol 2 Fig. 6.1), Counts of Transplants

from older donors with multiple comorbidities previously known as expanded criteria donors (ECDs) is a way to address the shortage of organs. Although organs from such donors produce suboptimal results compared with standard donors, these results are still better than remaining on dialysis [14]. At the present time, the quality of the donor kidneys is defined by the kidney donor profile index (KDPI). KDPI combines ten donor factors – age, height, weight, ethnicity, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C virus (HCV) status, and donation after circulatory death (DCD) status – into a single number and summarizes the risk of graft failure after a kidney transplant. Lower KDPIs are associated with better donor quality when compared to higher KDPI kidneys [15].

The Process of Transplant Referral

The referral to a transplant center is done by the treating primary nephrologist. Most centers require a substantial level of involvement by the patient who will demonstrate good understanding of the transplant process, understand the importance of effective communication, and have good social support. The decision to be considered for transplantation is based on the complete evaluation by the transplant team. Patients with ESRD tend to have significant comorbid conditions. With advances in transplantation, some of these candidates can be considered for transplantation after careful evaluation. This is more likely with living donor transplantation as it allows for optimization of the recipient while

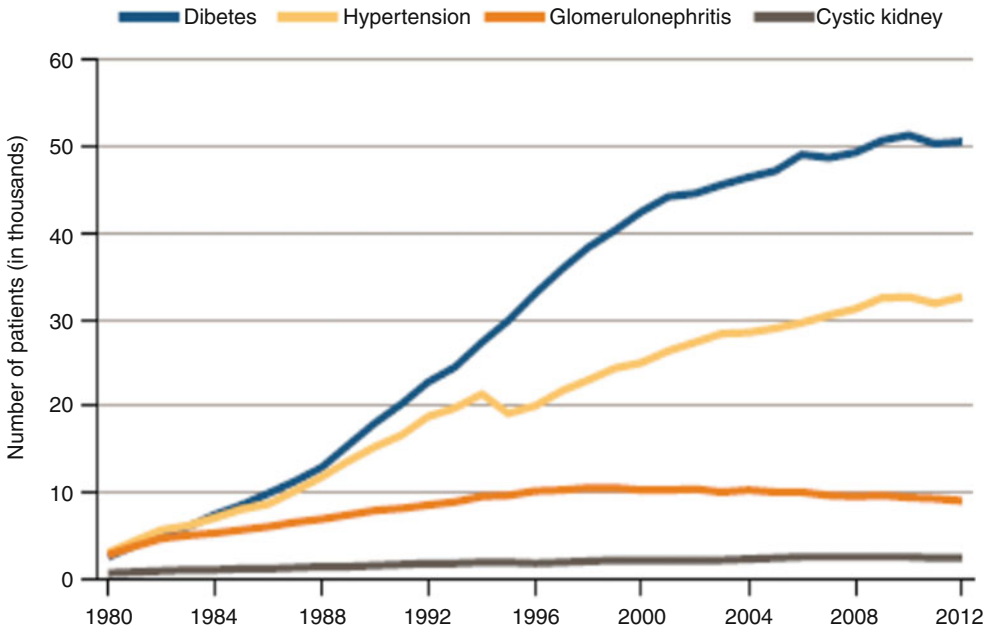

Fig. 39.3 Trends in ESRD incident cases, in thousands by primary cause of ESRD, in the US population, 1980–2012 (vol 2 Fig. 1.7)

planning for the procedure. The following are some of the guidelines and evaluation criteria:

1. *Renal function*: Patients with advanced chronic kidney disease (CKD stages 4–5, eGFR < 29 ml/min/1.73 m^2) are appropriate for referral for consideration for kidney transplantation. Studies have demonstrated that progressively worsening CKD increases mortality with time [16]. Single center studies have shown that longer waiting times on dialysis have a negative impact on posttransplant graft and patient survival [17]. Consequently, it is ideal for a patient to be transplanted preemptively or within a short time after initiating dialysis in order to achieve better outcomes.
2. *Age*: In the past older age was considered a contraindication for transplant, however, now increasing numbers of older patients are being transplanted. Studies have shown that kidney transplantation can improve the longevity of patients over the age of 60 when compared to remaining on dialysis [18]. It has also been shown that it is safe to transplant older individuals with acceptable comorbidities. Using donor kidneys with higher KDPI score (previously known as ECD) has been shown to be beneficial in this age group as it may potentially reduce the time on the wait list [19].
3. *Comorbidities*: Patients with ESRD tend to have multiple comorbidities related and unrelated to their kidney disease. In the United States, diabetes mellitus is a number one cause of kidney disease (Fig. 39.3) [20]. Cardiovascular disease is present in 63 % of patients with advanced CKD, compared with 5.8 % of adults without CKD [21]. Significant peripheral vascular disease is a relative contraindication for transplantation. Anemia is very prevalent in patients with kidney disease, and its prevalence increases with worsening kidney function. Patients with anemia before a kidney transplant are known to have more hematologic and cardiovascular complications [22]. During the evaluation of the patient, all comorbidities are carefully considered prior to patient's approval for transplantation.
4. *Active chronic infection*: There is a risk of reactivation of chronic infection in recipients of kidney transplant, and thus thorough screening and testing of the recipient is important. It is also important to recognize and treat infections that can be exacerbated or reactivated after immunosuppression; examples of these are tuberculosis, coccidioidomycosis and histoplasmosis, or strongyloidiasis [23].

HIV-positive individuals now have a longer survival due to highly effective antiretroviral therapy. HIV infection and the antiviral medications increase the risk of developing chronic kidney disease [24, 25]. While in the past HIV infection used to be viewed as a contraindication to transplantation, now kidney transplantations in patients infected with HIV have resulted in good outcomes. The legalization of the use of the organs from HIV infected donors in November 2013 by the *HOPE Act* will increase the number of organs available for transplantation [26, 27].

While there is no consensus on how hepatitis B and C infections affect graft and patient survival, many studies seem to suggest that the graft survival is lower in patients

with these infections. To understand the effects of newer anti-hepatitis C, treatments on kidney graft survival will require time [28].

5. *Alcohol and substance abuse*: Both are known to cause and progressively worsen renal disease [29]. A strong personal history of ongoing substance abuse can be a harbinger of medication noncompliance, causing an increased risk of early graft failure [30]. Ascertaining this history during the initial evaluation is very important. If identified, these patients must be directed toward rehabilitation. Patients have to demonstrate adequate recovery and sobriety, stable social support, and adequate coping skills in order to proceed with the transplant process.
6. *Psychological factors*: Transplantation is a very involved process, and it can be very emotionally and psychologically demanding. There are studies that show that kidney transplant is better than dialysis for patients with anxiety and depression, but there are also studies that show the process of transplantation to be stressful and anxiety provoking. It is vital to screen patients who are being evaluated for transplant for preexisting mental health issues to ensure adequate and continued support [31]. Immunosuppressive therapy can further worsen psychological symptoms. It is also important to assess for drug interactions with the psychiatric medications and immunosuppressants.
7. *Obesity*: A high BMI is considered an exclusion criterion in the majority of transplant centers. Although the exact cutoff may vary from center to center, people with BMIs over 35 are generally cautiously approached. Many studies have shown an increase in posttransplant complications in obese patients compared to nonobese patients. These include wound complications such as wound infections, dehiscence, and hematomas as well as urologic complications such as urine leaks and strictures [32, 33]. Patients with high BMI have increased incidence of delayed graft function and a higher mortality rate [34, 35].
8. *Malignancy*: Patients with active malignancies are strictly not considered for transplantation due to the concerns of progression of the existing malignancy with immunosuppression. The patients are required to be disease-free prior to transplantation for various periods of waiting time after definitive therapy. The waiting time depends on the type of cancer, stage of the disease, and curative nature of treatment received. It is for the same reason that patients are required to have completed age-appropriate cancer screening. The identification of previous malignancy is important in deciding the choice of immunosuppressant as mTOR inhibitors which have been shown to be beneficial in certain types of cancers [36].
9. *Previous transplant*: While patients with a previous failed transplant could be complex, retransplants are routinely done after careful consideration of the risk of recurrence of the primary disease, reason for graft failure, and long-term risks of immunosuppressive therapy [37].

Transplant Evaluation

The candidates referred for kidney transplantation undergo a comprehensive evaluation by the transplant nephrologists, transplant surgeons, nurse coordinators, pharmacists, nutritionist, social workers, and financial coordinators. The process includes patient education, medical evaluation, surgical evaluation, and social evaluation.

The medical and surgical risks and benefits of renal transplantation, the potential adverse effects of immunosuppression, and the importance of compliance with immunosuppressive therapy are discussed with the potential candidates. The advantages and disadvantages of deceased versus living donor renal transplantation are discussed in detail.

The transplant nurse coordinator provides education regarding the transplant evaluation process, listing for transplant, the waiting time, and patient responsibilities before and after transplant and serves as a primary link between the patient and the rest of the transplant team.

Medical evaluation is done by the transplant nephrologists, who perform a thorough review of the history, physical examination, review of medications, and tests. It is important to identify the etiology of the kidney disease as it can predict the outcome and the risk for disease recurrence. A number of laboratory tests and imaging studies are performed to help in the process of assessing the candidacy. The patients are also evaluated by the transplant surgeons who review the history and perform the physical examination while focusing on recognizing any potential surgical issues. History of peripheral vascular disease and bladder dysfunction should be elicited.

Pharmacists focus on reviewing the patients' current medication list and look for possible interactions with immunosuppressants, anticoagulants that may pose a bleeding risk during or after the surgery, medication allergies and possible clues to medication nonadherence, and prescription narcotic overuse.

Transplant psychiatrists and psychologists look for major exclusion criteria like active substance abuse, serious debilitating ongoing psychiatric disease, and cognitive impairment with lack of support.

Social workers have various responsibilities including helping to identify the transplant patient's caretaker after the surgery. Financial coordinators ensure that finances or insurance status do not pose restrictions to the quality of health care delivery.

Investigations

1. *Laboratory Testing*: Comprehensive metabolic panel; HLA typing and immunologic studies; viral serologies for cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella-zoster virus (VZV), and hepatitis B and C and HIV; rapid plasma reagin (RPR); purified protein derivative (PPD) testing for latent tuberculosis; strongyloides and coccidioides serologies for recipients from endemic areas; urinalysis; and vaccination profile are performed [23].
2. *Cardiac Evaluation*: Noninvasive cardiac testing includes EKG, echocardiogram, and stress test [38]. Based on the results of these tests, a cardiac catheterization may be required to evaluate the coronary vessels. Therapeutic interventions are performed as required prior to transplantation. Severe cardiac disease may preclude transplantation.
3. *Pulmonary Evaluation*: Smoking cessation is required [39]. Chest X-ray and pulmonary function tests are done if there is a history of a known chronic lung disease that may cause complications during anesthesia [40].
4. *Screening for Peripheral Vascular Disease*: Vascular Doppler studies and other imaging modalities, including CT scan, are performed to rule out poor circulation to the lower extremities and to assess suitability of blood vessels for transplantation [41].
5. *Urologic Testing*: Patients who have bladder dysfunction and history of multiple urinary tract infections are referred for urologic evaluation (urodynamic studies, cystoscopy) [42].
6. *Cancer Screening*: Comprehensive cancer screening, including colonoscopy, Pap smear, mammogram, and PSA, is done based on the candidate's age and family history. Abdominal imaging including US and CAT scan is performed to rule out renal cell carcinoma which is more prevalent in dialysis patients than in the general population [43].
7. *Dental Workup*: An updated dental examination and treatment of abnormalities and infections if found are performed. In the posttransplant period, occult infections can flare, and healing will not be as effective after a procedure in the immunosuppressive state [44].

Multidisciplinary Meeting

Once all the tests and evaluations are completed, the patient's candidacy is discussed by the committee. In most transplant centers, a multidisciplinary meeting is held once a week where all the providers involved in the initial evaluation process are present and each patient is discussed individually. The meeting encompasses an active discussion about the pros and cons of listing a person, and then the decision is communicated to the patient. Patient selection for kidney transplantation is a complex process. The goal is to choose a candidate who can safely tolerate the surgical procedure, perioperative state, and immunosuppressive therapy and who will obtain maximum benefit from this transplantation. There is continued surveillance of these patients while they are awaiting transplant. This requires effective communication between the patient and their primary care providers, including nephrologists and the transplant team.

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Peritoneal Dialysis

40

Jared Kray and W. Kirt Nichols

Introduction

Interest in using the peritoneal membrane as a method for eliminating waste from the body began after it was recognized as a semipermeable membrane by Wegner in 1877. Since that time, many have made contributions to the concept of using the peritoneum to filter accumulated wastes. Today, peritoneal dialysis has evolved into its current state as a viable alternative to hemodialysis for patients with end-stage renal disease.

This chapter will discuss the surgically relevant aspects of peritoneal dialysis with a focus on current state of peritoneal dialysis, basic pathophysiology of peritoneal filtration, access options, and complications inherent to using this method for dialysis.

History of Peritoneal Dialysis

The peritoneum was first described by Wegner as a semipermeable membrane capable of transporting solutes in 1877 [1]. However, it was not until 1923 that Putnam [2] described the peritoneum as a dialyzing membrane in his animal studies, and reports were made by Georg Ganter regarding his attempts in treating a uremic patient using peritoneal dialysis. Progress, however, seemed to halt until 1945 when a group at Beth Israel in Boston began to revisit the subject at the direction of President Franklin D. Roosevelt.

The initial clinical system used by doctors Frank, Seligman, and Fine at Beth Israel utilized a closed system of continuous inflow and outflow through temporary placed peritoneal catheters. However, this system required constant bedside attendance of a nurse to refill, sterilize, and reconnect tubing (effectively opening the previously closed system) and had a high complication rate from peritonitis. This system continued to be refined initially with changes to the catheters from end-hole rubber catheters which were prone to omental occlusion as well as significant inflammatory reaction, to harder nylon designs with small distal perforations.

Modern peritoneal dialysis technique is largely attributed to the changes made by Morton Maxwell. He sought to simplify and make the system more universally available and made a number of changes to the previous system. First, he introduced the previously described multiple side-hole catheter to improve performance as well as changed the catheter to a semirigid nylon design to prevent kinking. He then began to use the "paired bottle" technique in which instillation was performed with gravity – the tubing was clamped, still primed near completion of instillation, at which point the solution would be allowed to dwell. These same bottles would then be lowered to the floor, unclamped, and allowed to drain. He also replaced the previous sodium bicarbonate solution with lactate. This change allowed lactate to be added to the solution without the need to sterilize bicarbonate separately to prevent the precipitation that would occur and permitted the ability to produce a commercially available solution.

Up to this point, peritoneal dialysis was only being used as an acute method for treating renal failure. In the early 1960s, Boen and Merrill et al. began using peritoneal dialysis to treat patients with chronic renal failure. Boen developed a Silastic button that had Teflon disks that were inserted with one in the peritoneal cavity and the other in the abdominal musculature. This tubing allowed capping and repeated access to the peritoneal cavity. This, however, was not particularly successful and was largely abandoned for repeated puncture techniques.

It was not until the mid-1960s when Dr. Henry Tenckhoff recognized the need for a better designed

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indwelling catheter if home dialysis was to become an option. He worked with Dr. Wayne Quinton (who was successfully using hemodialysis at the time) to develop a silicon rubber tubing which could be implanted for repeated usage. This initially was a single-cuffed, straight tube design that underwent multiple revisions until the final design became a silicone rubber tube with a coiled intraperitoneal portion and two Dacron cuffs, one at the fascia/peritoneal level and the other at the subcutaneous level, to promote tissue ingrowth. This catheter remains the most common in use still today.

Throughout the 1970s, 1980s, and 1990s, refinements and improvements continued to be developed. These principally involved the switching from bottles to plastic bags, using different tubing sets for delivery of the dialysate, and improved "connectology." Automated peritoneal dialysis was introduced and the management of the exit site and the understanding of microbiology improved. Most of these changes improved outcomes but did not change the basic placement of the catheter.

Other than the continued issue with the development of peritonitis, surgically implanted catheters have been plagued by problems with leakage around the exit site. Additional catheter changes have been made, including the addition of the Dacron cuffs and Silastic beads at the posterior fascia/peritoneal level to help eliminate this problem. Another procedural change to help combat this problem was the creation of a long tunnel to prevent or minimize exit site leakage and pericatheter migration of bacteria.

Current State of Peritoneal Dialysis

Overall, peritoneal dialysis (PD) has been a relatively consistent entity accounting for around 11 % of patients receiving dialysis of some type. This encompasses nearly 197,000 patients worldwide. According to a recent global study, developing countries are adopting this technique at a higher rate than more industrialized countries. In fact, data from 1997 to 2008 suggests that the rate of end-stage renal disease patients undergoing PD has had a 2.5-fold increase. In the United States, there are greater than 26,500 patients receiving PD as their main source of renal replacement therapy [3].

Physiology of Peritoneal Dialysis

The peritoneal structure contains a circulatory system – referred to as the microcirculation – composed of thin walled capillaries as well as postcapillary venules that allow solute and fluid exchange. The peritoneum allows blood flow of 50–100 ml per minute. Peritoneal clearance is not blood flow limited and is also responsive to vasoactive substances in peritoneal dialysis fluid.

Mechanisms of solute transport in peritoneal dialysis are through convection, diffusion, and absorption. These models have all been studied extensively, and their discussion is beyond the scope of this chapter. A clinical prediction model, the Peritoneal Equilibration Test, developed by Twardowski et al. is clinically relevant in describing transport rates. This is clinically relevant in that it allows identification of patients who are "high transporters" or "low transporters." Those who have faster transportation of solutes across the peritoneal membrane do better with shorter dwell times and possibly with automated peritoneal dialysis. Patients who transport slowly and require longer dwell times are better served with continuous ambulatory peritoneal dialysis.

Patient Selection

Successful adoption and maintenance of PD as the modality of choice does depend on patient selection. There are very few absolute contraindications to peritoneal dialysis which include active peritoneal infection such as severe inflammatory bowel disease, diverticulitis, etc., or an uncorrectable pleuroperitoneal connection. The majority of contraindications are relative and depend largely upon institutional and physician comfort with the modality. Studies have shown that the majority of patients presenting for initial evaluation for dialysis access are candidates for PD ranging from 75 to 83% [4–6].

As peritoneal dialysis accounts for only 11 % of all active dialysis, there are clearly other intangible issues that account for the fact that although a majority of patients with end-stage renal disease are candidates for PD, only a small fraction end up on PD. We attribute this mostly to a combination of patient factors as well as the comfort level of the nephrologist. For the purposes of this chapter, we will discuss the patient factors.

Peritoneal dialysis patients need to be adequately educated on the technique and lifestyle associated with performing their own dialysis and, as such, must have help at home in order to be successful. This requires that the surgeon/nephrologist team is able to accurately assess the patient and family's medical literacy and home social structure.

Once the patient has been determined to have the functional capability of performing his or her own dialysis, the relative surgical contraindications must be taken into consideration. Traditionally, obesity has been listed as a relative contraindication. In the current era of increasing obesity, we have found that obese patients are able to have adequate peritoneal dialysis using standard methods; however, the

presternal tunneling method has allowed easier access and care of the catheter and tubing.

Preoperative Evaluation

The preoperative evaluation of a patient desiring PD should, of course, include a thorough surgical history and physical exam with attention paid to previous surgical history and inspection for surgical scars. Previous open abdominal surgery is not a contraindication to PD catheter placement, but surgical history and previous incision location may have bearing on operative planning. Adhesions formed to the anterior abdominal wall increase the risk of catheter placement and subsequent function. In addition, those with significant pelvic surgical history may have adhesions, making placement of the catheter in the pelvis difficult. In the present era, both of the previously described instances should prompt consideration for laparoscopic inspection at time of operation (Fig. 40.1).

Once the patient has been determined to be a good candidate for peritoneal dialysis through the evaluation of their ability to perform PD and deemed an acceptable surgical risk, there are a number of surgical techniques that can be considered to provide long-term access to the peritoneum. First, however, a choice of catheter must be made.

Implantable Catheters

Although there are currently a variety of catheters on the market today for use, there are two main designs, each with multiple variations, which encompass the vast majority of catheters used for access. The Tenckhoff catheter was developed in mid-1960 and remains the most widely used catheter on the market. The Tenckhoff design has silicone rubber tubing with (usually) two polyester (Dacron) cuffs. It is made with both straight and coiled intraperitoneal portions.

The first variation in catheter design worth discussing is in the number of cuffs on the catheter itself. Prior to cuff introduction, persistent leakage around the catheter tubing was a significant concern. The introduction of cuffs has since been shown to have a twofold advantage. The first polyester cuff placed at the peritoneal junction helps to allow tissue ingrowth to seal the catheter tract. The addition of a second cuff helps to decrease leakage through tissue ingrowth but has also decreased peritonitis rates by inhibiting of bacterial translocation down the tubing in the subcutaneous tunnel.

The second major catheter design difference was the introduction of the "swan-neck" design. This manufacturing change introduced a permanent bend to the catheter tubing. The impetus for this design change was from a retrospective review of Tenckhoff catheters which showed that the lowest complication rates occurred when both of the cuffs on the Tenckhoff catheter were directed downward [7]. It was noted, however, that the downward direction of both cuffs on the Tenckhoff catheter led to, by placing the straight catheter in an arcuate shape, an increased rate of cuff extrusion. Introduction of a permanent bend to the catheter tubing eliminated the "shape memory" forces which caused extrusion. The "swan-neck" catheter design is the second most commonly used today.

Another design difference worth addressing is the selection of coiled versus a straight intraperitoneal segment of tubing. During fills, there has been a phenomenon described as "jet effect" which has been associated with discomfort on filling. A coiled intraperitoneal segment catheter design has

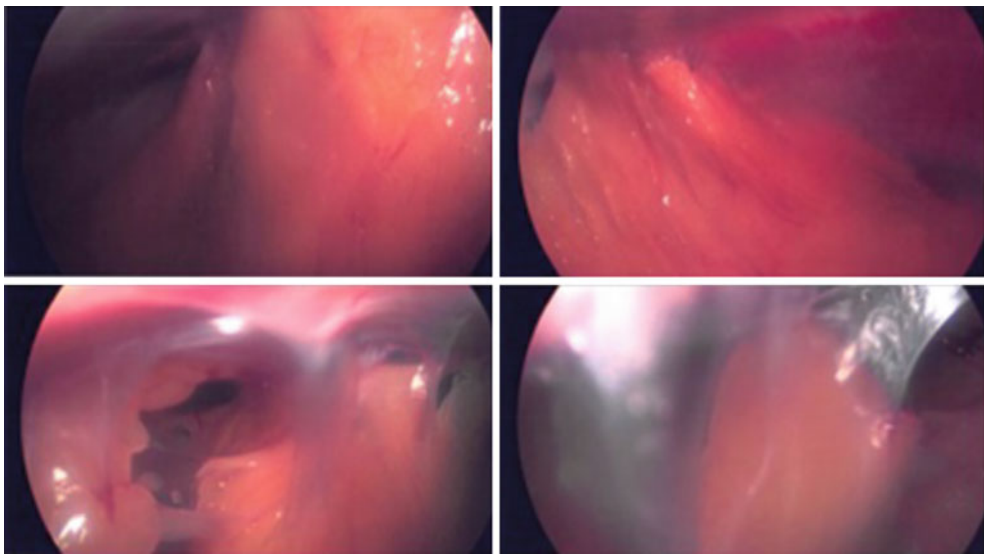

Fig. 40.1 Laparoscopic revision of a "trapped" catheter

been associated with a decreased rate of reported discomfort during filling and is our preference.

Surgical Technique

There remain three major techniques for establishing permanent access to the peritoneum for dialysis, and they include traditional open surgical placement, laparoscopic insertion, and peritoneoscopic techniques. In this section we will discuss the technique as well significant merits associated with each of these insertion methods.

Open Technique

Open surgical placement of peritoneal dialysis catheters should begin with standing evaluation of the patient noting the belt line as well as marking with indelible ink identification of this landmark, which is not obvious when the patient is supine on the operating room table. We also advocate supine examination with the patient lifting his or her head off the table. This maneuver, much like in preoperative marking for ostomy sites, allows easier identification of the rectus musculature. Proper identification of the rectus ensures that the incision will allow transrectus placement of the catheter. This has been shown to decrease not only pericatheter site leakage, but also catheter tract infections which can predispose toward peritonitis by allowing better tissue ingrowth into the cuffs [7].

The patient is positioned supine. Arm positioning is surgeon dependent, however, we find it easier to perform the presternal tunneling and chest incision with the patient's arms tucked into the side and padded. After induction of appropriate anesthesia, a 3–5 cm incision is marked, usually lateral to the approximate location of inferior epigastric vessels, and the incision made. Electrocautery is used to deepen the incision and self-retaining retractors (such as a Weitlaner retractor) are used to facilitate exposure. Care should be taken to have meticulous hemostasis, as postoperative hematoma can be a source of catheter infection. The incision is deepened to the anterior rectus sheath, which is opened transversely.

Once encountered, rectus fibers are separated with a muscle-sparing technique by spreading a hemostat in a cephalad-caudad direction. This exposure is maintained by a self-retaining retractor. Once the posterior sheath is encountered, a small incision is then made through the posterior sheath/peritoneum and a purse-string suture of approximately 1.5 cm diameter is placed. Elevation of this incision with forceps grasping the edges allows air to enter the abdomen creating pneumoperitoneum and separates the viscera from the anterior abdominal wall.

The catheter of choice is then prepared on the back table by soaking the Dacron cuffs in saline and then flushing the catheter. At this point, a stiffening stylet is placed into the catheter. This provides extra support in a straight catheter to facilitate positioning and straightens the coiled catheter so that it may be placed in the pelvis more easily. Care should be taken in both the straight and coiled catheter to leave approximately 1 cm of soft catheter beyond the stylet to make the placement more atraumatic to the viscera during placement.

The catheter with a stiffening stylet is then guided carefully, by feel, into the pelvis. This is accomplished by elevation of the posterior sheath/peritoneum and by directing the stylet anteriorly and caudally until the area of the pubis is reached and then allowing it to fall posteriorly into the pelvis. If any resistance is felt, the catheter should be pulled back and redirected. Once placed, the catheter is held in place and the stylet removed. Each catheter variation is then placed to its appropriate level (e.g., Missouri catheter placed so that the purse string can be tied above the bead, or Lifecath disk folded and placed with disks beneath the peritoneum and one on the anterior sheath) (Fig. 40.2). Once the defect is closed in the posterior sheath, a short (approximately 1.5 cm) tunnel is created in the cephalad direction through the anterior sheath and the catheter pulled through the sheath into the subcutaneous space. At this point, a tunneling trocar can be used to facilitate externalization of the tubing. One liter of saline is then allowed to infuse via gravity, and bag is then placed on the floor to allow drainage. Once good flow is confirmed, the anterior rectus is closed as well as subcutaneous tissue and skin with absorbable sutures in multiple layers.

If one desires to place a Missouri Swan-Neck Presternal Peritoneal Dialysis Catheter (Fig. 40.3), the steps of placement are unchanged until after the small tunnel through the anterior rectus is created. At this point, creation of a small pocket on the chest wall is accomplished using a vertical incision to the left of the sternum/manubrium. This pocket needs to be wide enough to allow the preformed curve to again lay flat on the chest wall. At this point, the presternal catheter containing two further Dacron cuffs is tunneled subcutaneously down to the previous incision. These catheters are then connected using a supplied titanium connector (Fig. 40.4). At this point, a 0 Ethibond suture is hand-tied around the connector on each end and then tied together. This creates a reinforced connection that is sturdy enough so that we have never seen separation of the catheters in the tract. Once satisfied with the catheter length and flow, the chest wall catheter should be externalized approximately 3 cm below the superficial cuff using a sharp trocar attached to the PD tubing. At this point, we recommend closing all incisions with absorbable suture in multiple layers.

Placement can also occur in a "blind" fashion using either a Tenckhoff trocar or percutaneous technique. Each method

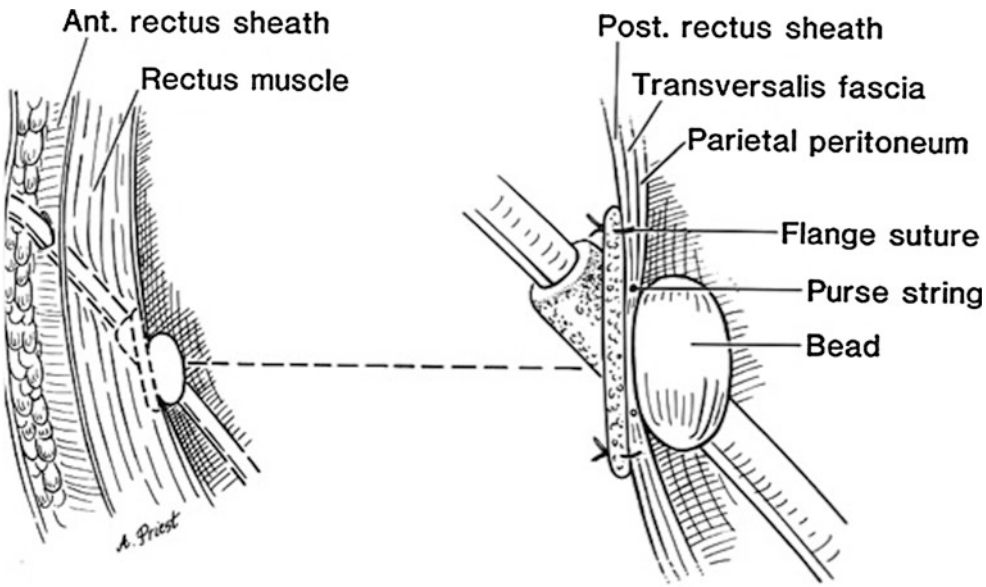

Fig. 40.2 Missouri Swan-Neck placement

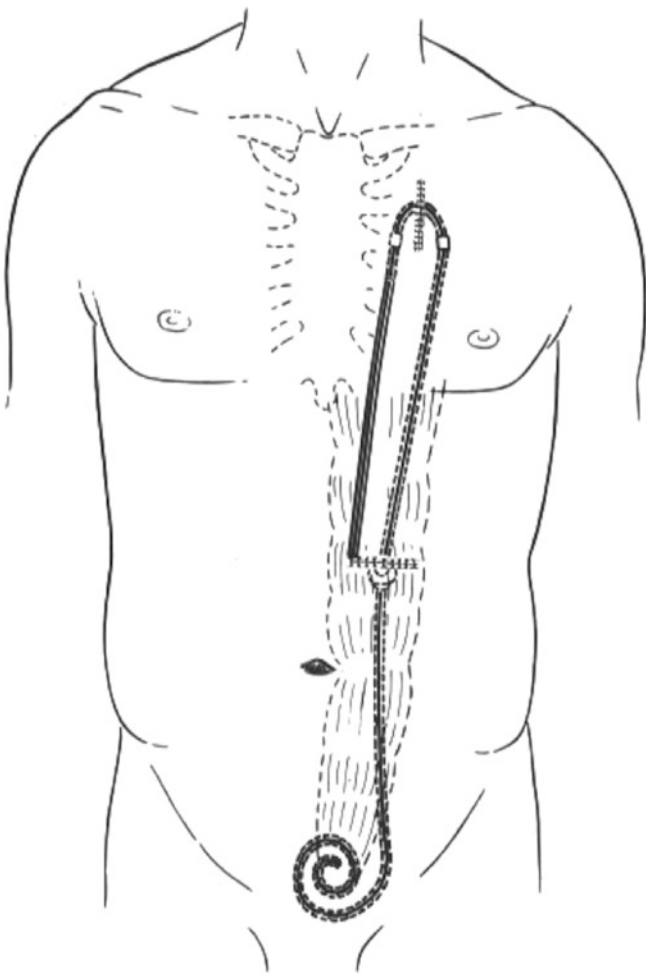

Fig. 40.3 Insertion of Missouri Swan-Neck catheter

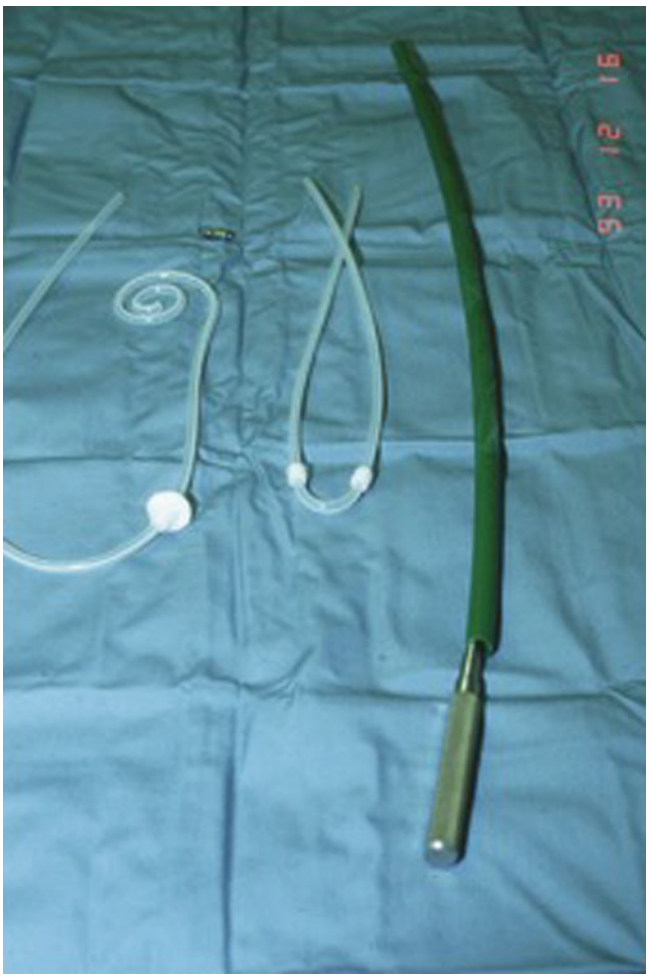

Fig. 40.4 Contents of Missouri swan kit + Scanlan tunneling device

requires a 2–3 cm skin incision that allows introduction of a trocar or large bore needle. Once access to the abdomen is confirmed, dialysate or saline is allowed to infuse in the abdomen and the tract dilated until it will accept the Tenckhoff style of catheter. This catheter is then advanced through the sheath until the first cuff can be placed at the level of the abdominal musculature. A tunneling trocar is then used to place the second cuff approximately 2 cm from the decided exit site.

Laparoscopic Technique

The advent and growth of laparoscopic surgery has also become of use to dialysis access surgeons. The ability to obtain minimally invasive access has had an increasing role in both the initial placement of peritoneal dialysis catheters as well as in revisions. The discussion of optimal method of abdominal entry technique is beyond the scope of this chapter; however, we suggest each surgeon use the technique he or she is most comfortable using. Advances with the laparoscopic approach now allow patients who may have previously been turned down as PD candidates the ability to dialyze at home.

Generally, for laparoscopic placement, a double-cuff coiled Tenckhoff catheter is chosen. The patient is positioned supine and is used after a probable catheter site is marked preoperatively on the abdomen. Arms can be positioned either extended or to the sides. Generally, a supraumbilical 5 millimeter (mm) incision is made and blunt dissection carried down to the level of the anterior sheath. A Veress needle is then introduced into the abdomen and insufflation of CO2 is begun after confirmation of intra-abdominal placement. Once the abdomen is insufflated a pressure to 15 mmHg, a 5 mm trocar is introduced through this tract and camera placed. Visual inspection of the abdomen is then carried out. Upon determination that access to the pelvis is possible, placement of two additional 5 mm trocars under direct visualization into the right lower quadrant and the left lower quadrant (avoiding inferior epigastric vessels) is performed. A blunt grasper is then placed through the site of eventual catheter placement and brought through the opposite trocar. The portion of the catheter to be externalized is then given to the grasper, which is now through and through, and withdrawn carefully until the coiled portion of the catheter is in the abdominal cavity, and the catheter exits the trocar on the opposite side from where it was introduced. At this point, another blunt grasper can be introduced through the free trocar to facilitate placement in the true pelvis.

Once the coiled catheter is satisfactorily positioned in the pelvis, the trocar with the external catheter is withdrawn until the deep cuff proximal to the coil is just above the level of the peritoneal opening. The trocar is completely withdrawn and the incision widened. A tunneling trocar is attached to the end of the catheter now protruding from the wound and used to tunnel the catheter to the previously marked external site for the peritoneal dialysis catheter being careful to not kink or twist the tubing during tunneling. Once this is done, the abdomen can be decompressed and saline instilled into the abdomen and then subsequently be allowed to drain. After a functioning catheter is confirmed, heparin lock is placed into the tubing and all incisions are closed in layers. Sterile dressings are applied to each site as well as to the PD catheter site. One should avoid placement of sutures at the exit site for the catheter due to potential compromise of the tube lumen, direct catheter damage, or promotion of exit site infection (i.e., stitch abscess).

Other Techniques

Peritoneoscopic placement of peritoneal dialysis catheters is preferred by some nephrologists, interventional radiologists, or access surgeons. The basic technique usually involves a Y-tec® peritoneoscope as well as a Quill® type dilator sheath. Much like the blind technique, a 2–3 cm incision is created and then the trocar is advanced until the surgeon feels entrance into the abdominal cavity is likely. The peritoneoscope is then advanced, and visual confirmation of successful access into the abdomen is confirmed. Gas (most often CO2) or fluid is infused into the abdomen to create space for the placement of the PD catheter. The Quill® sheath is placed and then dilated to 6 mm for acceptance of the Tenckhoff catheter. The catheter is placed to the level of the abdominal musculature and held in place, and the sheath is split without withdrawing the catheter. The catheter is then connected to a tunneling trocar and placed so that the superficial cuff is approximately 2 cm from the exit site.

Complications Associated with Peritoneal Dialysis Catheter Placement

Immediate Complications

Surgical complications associated with peritoneal dialysis catheter placement are infrequent but not negligible and should be discussed with the patient preoperatively. The most frequent immediate complication associated with PD catheter placement is minor bleeding. This usually occurs due to inadequate surgical hemostasis at the time of implantation. The risk for minor bleeding complications is somewhat higher when placing a presternal catheter due to the need for a long subcutaneous tunnel that must be created, as well as the abundant vasculature of the anterior chest wall.

The risk of intra-abdominal injury is also pertinent. The risk is highest in patients with previous abdominal surgery. However, injury can occur during either initial entry into the abdomen or during the placement of catheter in the pelvis with the positioning stylet during a traditional open surgical placement. In patients with a history of previous abdominal surgery, we suggest consideration be given to the use of initial laparoscopy to evaluate the feasibility of access into the pelvis for placement of the catheter. Through the use of alternative points of entry in those with previous abdominal surgery (e.g., Palmer's point), one can inspect for adhesions that could present difficulty with either entry into the abdomen or proper catheter positioning.

Pericatheter leaks are also considered an early complication. To avoid this, we recommend early implantation of PD catheters prior to the anticipated need for renal replacement therapy. A minimum of 2–4 weeks will allow time for ingrowth into the Dacron cuffs which will decrease the likelihood of developing leaks. During this period, low-volume flushes can and should be performed weekly to ensure catheter function and also to help prevent omental blockage of the side-hole perforations. As described in the preceding section, the tunneling of the catheter is also important to eliminate a simple route for leakage.

The other major immediate complication worth discussing is that of immediate catheter dysfunction. This is seen usually as a failure to drain the majority of fluid instilled into the abdomen during the time of placement. If failure to drain occurs, the catheter should be inspected for any evidence of kinking or malpositioning. If no obvious technical problem is found with the catheter, and the position is confirmed to be in the pelvis with intraoperative radiograph or fluoroscopy, one can proceed and finish the case. The catheter can then be monitored for function during the subsequent 2–4 weeks when the patient should be having weekly fills and drains at their dialysis center. Often, the catheter will improve its function during this time period and become a viable route for dialysis.

Delayed Complications

The major reason for cessation of peritoneal dialysis is the development of catheter-related infection. As previously mentioned, success of long-term maintenance of PD does require a significant amount of education and adherence to sterile technique on the part of the patient and their caregivers. Infectious complications can range from minor exit site infections to florid peritonitis.

Minor exit site infections are not infrequent among those who use PD as their primary means of renal replacement therapy. Exit site infections can usually be treated with topical antibiotics. We have found that, especially given the increasing size of the patient population, the presternal catheter offers a significant benefit in this area. By moving the exit site higher, we feel, self-care of the catheter becomes easier. Patients are often able to perform their own cleaning of the site using a mirror while still having the ability to use both hands. Inspection and care of exit sites on the increasingly protuberant abdomen may prove too difficult for many patients to adequately perform.

If repeated exit site infections are seen (Fig. 40.5), one should inspect the catheter carefully to ensure that there is no extrusion of the external catheter cuff and no occult involvement of the superficial cuff (Fig. 40.6) which can predispose to repeated infection. Cuff extrusion (Fig. 40.7) is particularly common when attempts were made to place the exit site of a straight catheter in a caudad direction. Placing catheter cuffs aimed caudally actually does seem to decrease the chances of recurrent catheter or exit site infection. A solution to this problem, for those who believe that the caudad vector of the exit site is associated with fewer progressive infections, has been the development of the swan-neck catheter. By having a permanently bent section of tubing, this catheter eliminated the forces that would be placed on a traditional catheter during tunneling downward.

Should one encounter a cuff extrusion, the catheter may still be salvaged. A simple BIC-type razor, fine iris scissors, or 10 blade can be used to carefully remove the Dacron from the cuff, which can be very irritating to the skin, after sterilizing with 70% alcohol. Using a careful technique, you should drag the razor across the Dacron and slowly rotate the catheter after each swipe until the tubing is free from Dacron. The operator should use extreme care to avoid injury to the catheter itself.

Malpositioning of the catheter also occurs on occasion. A change in the function of a previously working catheter is generally the first sign of a malpositioned catheter. Patients may also report sensory changes during fills or having difficulty draining fluid. The diagnosis can be made using a flat

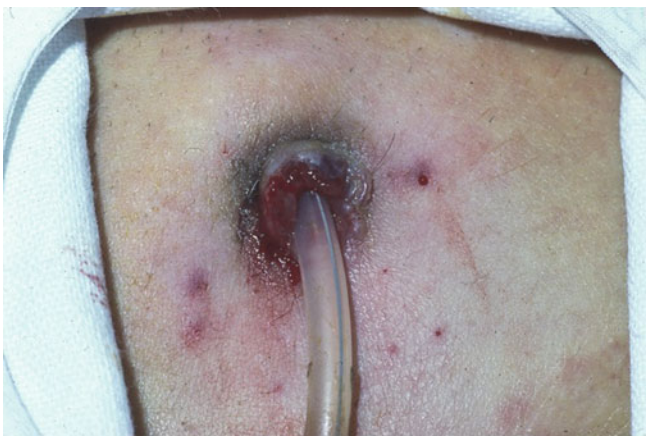

Fig. 40.5 Exit site infection

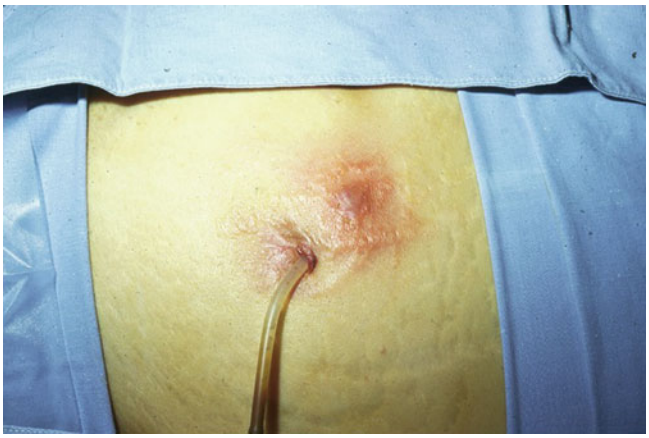

Fig. 40.6 Superficial cuff infection

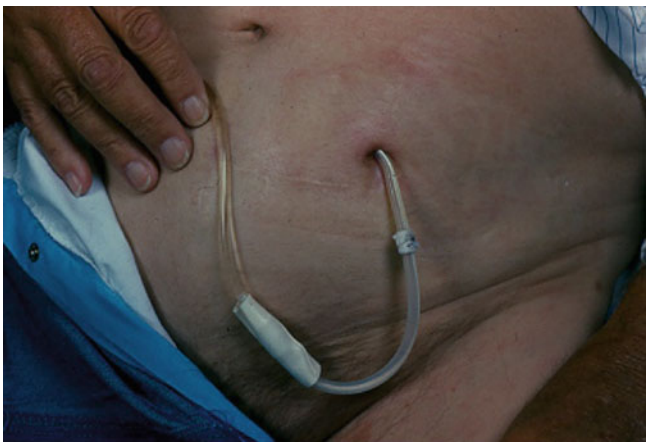

Fig. 40.7 Cuff extrusion

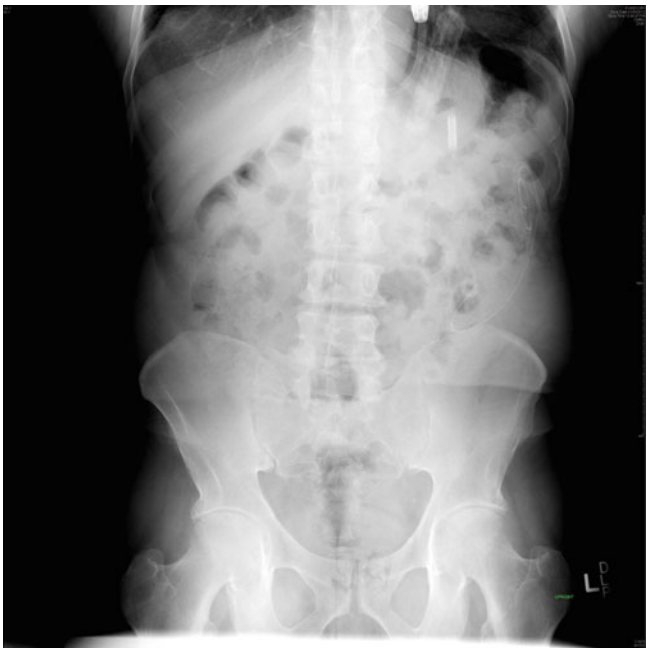

Fig. 40.8 Malposition. Catheter in RUQ

plate abdomen x-ray or kidney-ureter-bladder (KUB) film (Fig. 40.8). Occasionally a contrast catheterogram can aid the diagnosis of a malplaced catheter. If catheter tubing is noted to be out of the pelvis, consideration should be given to surgical revision using laparoscopy.

In today's era, laparoscopy is of significant benefit in the revision of malpositioned catheters (Fig. 40.8). During revisional surgery, we prefer to use the implanted catheter as a route of insufflation by hooking the insufflation tubing to the PD catheter (either prepped into or out of the field depending upon its location) for instillation of CO_2. Once a pneumoperitoneum has been accomplished, a direct visual entry technique can be used and the abdomen inspected. Omental creeping and "wrapping" around a proximal portion of the catheter is the usual culprit for malpositioning, and once released, the coil is usually repositioned in the pelvis (Fig. 40.9). If an abundance of omentum is present in the abdomen, an omentopexy can be performed. Alternatively, one can choose a position along the anterior abdominal wall to "pexy" the catheter anteriorly to avoid further malpositioning. A Carter-Thomason® or Endo Close™-type suture passer can be used to pass a 0 or 2-0 permanent suture which can be loosely tied to keep the proximal portion of the catheter near the abdominal wall until it enters the pelvis.

Peritonitis and associated peritoneal dialysis catheter infection is the truly feared late complication that results in up to 12–25 % of PD patients changing over to hemodialysis within the first year [8]. Peritonitis in PD patients is a source of significant mortality with reports of overall mortality greater than 15 %. Diagnosis of PD catheter-associated peritonitis can be confirmed with peritoneal fluid aspiration sent for Gram stain and cultures. In the setting of bacterial peritonitis, intraperitoneal administration of appropriate antibiotics through the dialysis catheter is recommended and surgical removal of the catheter may often be unnecessary in this setting.

Fungal peritonitis is, however, a much more difficult problem affecting PD patients. Mortality rates of ~25 % are reported with confirmed cases. Once catheter infection with fungal organisms is confirmed, the catheter should be removed in its entirety. *Candida* species are most common and usually present after treatment with antibiotics, and not uncommonly after treatment for bacterial peritonitis. Intraperitoneal treatment for fungal organisms presents a problem as amphotericin B causes chemical peritonitis and subsequent pain. Intravenous administration of amphotericin as well as other antifungals generally results in poor peritoneal availability due to adhesion formation.

An episode of peritonitis frequently results in at least a temporary change of dialysis modalities. After

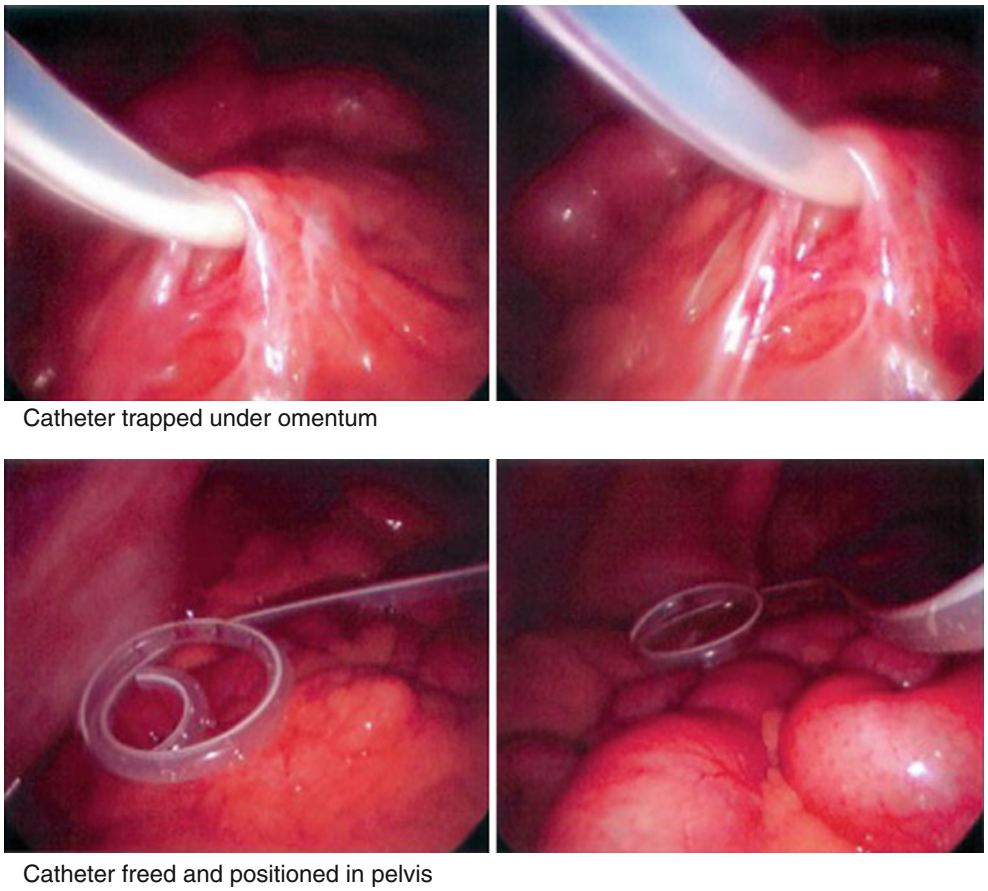

Fig. 40.9 Laparoscopic revision of malpositioned catheter

resolution of infectious peritonitis, patients may have a subsequent attempt at peritoneal dialysis via a new secondary catheter. We suggest a minimum of 6–8 weeks after resolution of clinical peritonitis prior to attempting replacement of a PD catheter. Laparoscopy should be considered to evaluate for any adhesions which may have formed which might prevent placement of catheter into the true pelvis.

Peritoneal Dialysis Catheter Removal

Peritoneal dialysis catheter removal is an infrequent procedure. It is typically done for one of three indications: (1) catheter not needed after kidney transplant, (2) for patients with recurrent peritonitis, and (3) patients changing from peritoneal dialysis to hemodialysis, usually for a reason of non-malfunction.

The design of a chronic peritoneal dialysis catheter should ensure excellent tissue ingrowth into the cuffs to fix the catheter in place and prevent leakage. This very design characteristic means that the catheter needs to be removed operatively and not at the bedside.

A general anesthetic is required. The patient's abdomen and chest are prepped and draped in a typical fashion.

In the case of an abdominal catheter the old abdominal incision is reopened and the catheter is identified by palpation. The sheath around the catheter is opened and the dissection is carried to the level of the cuffs. The cuffs are freed up with a combination of electrocautery and sharp dissection. Once the cuffs and/or flange are freed up, the purse-string suture at the peritoneal level is divided and the catheter pulled from the abdomen. The small defect into the peritoneal cavity is closed usually with a single suture 2-0 Prolene. Any additional cuffs in the subcutaneous tissue are likewise freed up using electrocautery. The catheter is divided in the subcutaneous space and the external portion of the catheter is pulled free. Any fascia defects are closed with nonabsorbable suture, and the subcutaneous tissue and skin are closed with monofilament absorbable suture. A gauze wick is inserted in the exit site to act as a drain for a few days.

If the patient has a presternal catheter, the removal of the abdominal portion is done exactly the same as above. The presternal portion of the catheter is ligated and divided through the abdominal incision, and the

abdominal portion is removed. The presternal incision is reopened and the catheter identified by palpation. The sheath surrounding the catheter is opened and both subcutaneous cuffs are freed up with electrocautery. The distal ligated portion of the catheter is pulled up into the wound, and the catheter is divided just beyond the superficial cuff just beneath the exit site. The upper portion of the catheter is submitted as a specimen. The wound is closed in a normal fashion using 3-0 monofilament sutures in the subcutaneous tissue and a 4-0 monofilament subcuticular suture. A piece of gauze is tucked in to the exit site to act as a wick drain.

Outcomes

Several studies have evaluated the overall clinical outcomes of patients with end-stage renal disease. When evaluating the mortality rate, it is important to keep in mind that the life expectancy of those with end-stage renal disease is only roughly 20–25 % less than the general population. Despite improvements in dialysis over the years, only 54 % of HD patients and 65 % of PD patients are alive at 3 years after ESRD onset. In studies comparing trends in dialysis patients, however, there are a number of interesting observations that have been made.

It should first be noted that overall mortality related to end-stage renal disease is significant. Many studies have been done to try to understand the reasons including those related to the modality of dialysis chosen. One fairly consistent trend that is elicited from the dialysis population data is that PD offers an early survival advantage over HD. Peritoneal dialysis patients are routinely seen to have significantly lower mortality rates in the first 2 years with dialysis-dependent end-stage renal disease [9, 10]. The reasons for this are not entirely clear; however, this effect is consistently noted. We also consistently see that patients who are transferred from PD to HD suffer an increased mortality risk in the first 6 months after the changeover. This is likely due to the generally poorer health of those who suffer a peritoneal dialysis catheter complication necessitating at least temporary transfer to hemodialysis. After the initial survival advantage, rates equalize, and by 5 years there appears to be a slight, but not statistically significant, increase in survival for HD patients [11].

Patient preference related to dialysis modality remains important. One of the risk factors consistently associated with increased mortality is lower overall health-related quality of life [12]. This has also been a factor in multiple studies comparing peritoneal to hemodialysis. The results of these studies have not been consistent. A recent meta-analysis was completed to help solidify the conclusions of previous studies; no statistically significant difference in health-related quality of life was found among the data confirming better quality of life using one modality of dialysis over the other [13].

Summary

Peritoneal dialysis offers an excellent alternative method for renal replacement therapy for a wide range of patients. The importance of patient selection cannot be understated. Patients must have an adequate understanding of the lifestyle they are choosing, since the patient or their care givers are the ones directly responsible for taking care of their access. Failure to properly care for the site, as well as the catheter, can result in loss of access due to infectious complications.

Surgical placement of peritoneal dialysis catheters encompasses a range of techniques which the individual surgeon can tailor to his or her own practice. However, patient criteria should also be evaluated as patients will have better ability to care for their access when placed in an easily visible location, and this can help to prevent late infectious complications. Our preference for more than 20 years has been the Missouri Swan-Neck Presternal Peritoneal Dialysis Catheter placed with a minimally invasive open technique.

Regional practice patterns will continue to play a role in the prevalence of peritoneal dialysis as an alternative method of renal replacement therapy. As the vast majority of end-stage renal disease patients are determined by nephrology referral patterns, any access surgeon performing PD catheterization procedures should make attempts to educate local nephrologists that PD access can be used for appropriate candidates. Although no study consistently confirms an improvement in health-related quality of life, there are many patients with end-stage renal disease that find the ability to perform their own renal replacement therapy to be liberating.

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Home Hemodialysis

41

Brent W. Miller

Introduction

Although its use has diminished in the United States and currently stands at about 2%, hemodialysis performed in the patient's home has been a safe and effective form of dialysis therapy for over 40 years and was a predominant form of dialysis therapy in the 1960s and 1970s [1]. With the advent of newer technology and the increasing cost structure of center-based hemodialysis therapy, home hemodialysis is likely to become more prevalent. Thus, the physician managing vascular access will need to be cognizant of the specifics of hemodialysis at home. This chapter will focus on the differences between center-based dialysis and home hemodialysis and discuss self-cannulation principles and ergonomics, changes in dialysis frequency and length, and clinical monitoring of the access from a remote location.

History

Hemodialysis has been performed successfully in patients' homes for over 50 years. In fact, prior to the development of large-scale outpatient hemodialysis facilities, home hemodialysis was a major form of delivery of the therapy. When legislation granted coverage for hemodialysis to most citizens regardless of age in the 1970s, there was a rapid expansion of outpatient hemodialysis and a movement away from home hemodialysis [2].

With the introduction of new technology and easier to use dialysis machines, home hemodialysis has increased in popularity slightly over the last decade. The suggestion of improved outcomes with longer dialysis sessions and/or more frequent hemodialysis, which can be practically accomplished at home, has also renewed interest in home hemodialysis (Table 41.1).

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Technical Concerns

Machine

The choice of a machine is important not only for the patient but also for the home dialysis program. Machines will differ in their cost, maintenance, physical footprint, portability within and outside the home, plumbing and electrical requirements, training time, setup and breakdown time, and water and dialysate preparation. While it is feasible and sometimes helpful to use multiple hemodialysis machines within a home program, this will introduce more required training, knowledge, and experience of the entire staff. Almost any dialysis machine can and has been utilized in the patient's home.

Several dialysis machines have been studied for safety and efficacy in the home and approved for home use by the US Food and Drug Administration [3, 4]. The *NxStage System One* utilizes a cartridge-based extracorporeal circuit and dialysate of up to 60 L with lactate as a buffer. Its maximum dialysate flow is 300 ml/min. The *Fresenius 2008 K@home* is based on a traditional hemodialysis machine requiring water treatment similar to traditional hemodialysis and bicarbonate as a buffer. Four other hemodialysis machines designed specifically for home hemodialysis are under development: the *Tablo hemodialysis machine* from Outset Medical with an integrated patient interface and production of dialysate from tap water; the *PAK hemodialysis system* from Fresenius Medical, a sorbent-based hemodialysis system; the *Vivia hemodialysis machine* from Baxter which reuses the dialysis membrane and bloodlines; and the *SC+ hemodialysis machine* from Quanta Fluid Solutions which also uses a cartridge-based setup.

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Table 41.1 Common types of home hemodialysis

Type	Blood flow (ml/min)	Dialysate flow (ml/min)	Ultrafiltration rate (ml/kg/h)	Frequency per week
Staff assisted	350–500	500–800	10–15	3
Traditional	350–500	500–800	10–15	3–4
Short daily	350–500	100–350	5–10	4–6
Nocturnal	200–300	100–300	1–3	3–6

Water

Successful dialysis starts with the production of water free from microbiological and chemical contaminants that can harm the patient [5]. The Centers for Medicare and Medicaid Services (CMS) has applied water quality and testing standards developed by the Association for the Advancement of Medical Instrumentation (AAMI) since 1987. These standards are updated approximately every 5 years [6]. While water production in the outpatient unit is similar in each unit, each patient's home installation will be unique. In the home environment, the water system will be unique in every installation while adhering to the same AAMI standards.

While the cost of providing water and dialysate in the outpatient unit is usually less than 2 % of the overall cost of the treatment, it is a major cost in home hemodialysis and also may entail cost to the patient for additional electricity, water usage, sewer drainage, and plumbing.

Dialysate

Dialysate can be provided in a patient's home in a number of methods: bagged dialysate delivered to the patient's home similar to peritoneal dialysis, dialysate prepared in the patient's home prior to dialysis, or in-line dialysate from an appropriate water source mixed at the machine. Cost, convenience, storage, installation, and maintenance all factor in the type of dialysate to utilize.

Bagged dialysate similar to peritoneal dialysis has the advantage of providing a sterile, ultrapure dialysate to the patient. However, limitations accompany this advantage. Practical considerations of delivery, storage, cost, and logistics generally limit this method to approximately 30 l of dialysate yielding a single-pool urea Kt/V ($spKt/V_{urea}$) of approximately 0.7 in the typical 80 kg adult, whereas most current guidelines for thrice weekly hemodialysis recommend a $spKt/V_{urea}$ of approximately 1.2. Thus, in the absence of significant residual renal function, hemodialysis will need to be performed more than three times per week. Second, lactate is typically the base in bagged dialysate fluid for stability, compatibility with calcium, and microbiological concerns. Lactate showed improvement in tolerability over acetate as a hemodialysis buffer before the widespread introduction of bicarbonate-based buffer [7]. Yet, in hemodialysis with a lactate buffer, serum lactate levels will be increased slightly during the treatment, and patients with significant liver dysfunction, higher volumes of dialysate, and/or poorly controlled diabetes may not tolerate lactate.

Attempting to replicate dialysate production similar to the outpatient unit or the acute care setting in the hospital also has limitations. Typically either a reverse osmosis (RO) machine or a deionized (DI) water system must be installed in the patient's home. A disadvantage of the RO system is another machine to install, maintain, and monitor. The DI system usually requires an outside vendor to change the tanks and regenerate the beads in addition to plumbing installation delivering the water to the machine in the home.

Several systems that produce water and dialysate in novel methods in the home are being developed. These include the use of sorbent, distillation, and miniaturization of the dialysate production.

Management of the Vascular Access

For the home hemodialysis patient, several additional aspects of vascular access management need consideration: patient training, technique, ergonomics, safety, remote management of potential infection, and clinical monitoring of the vascular access outside of the dialysis clinic. All types of vascular access utilized in center-based dialysis have been successfully utilized in patients at home. The type of access should not be a deterrent to a patient dialyzing at home.

Rarely is fear of cannulation an insurmountable obstacle to home hemodialysis training. Currently, approximately half of home hemodialysis patients cannulate themselves and half have caregivers performing cannulation. Since all dialysis patients may be taught self-care in any aspect of their therapy, it is often helpful to begin cannulation training in the outpatient dialysis center before starting home hemodialysis training (unless the patient is new to hemodialysis).

For the patient with the arteriovenous fistula (AVF), either the rotating site ("rope-ladder") or single-site ("buttonhole") method of cannulation can be chosen. Although many practitioners believe the self-cannulator has less discomfort and easier needle insertion, this has not been adequately studied, and the infectious risk appears higher as currently practiced with buttonhole cannulation [8–10].

The sites of cannulation should be chosen with careful collaboration between the training nurse and the patient. The patient should give significant input to the ergonomics of cannulation and decannulation, while the nurse should choose the safest sites. For example, the nonmedical person choosing a site to insert a needle may inappropriately see the top of an aneurysmal dilatation as the easiest site to be successful. Removal of the needle also demands careful attention especially for the self-cannulator. The synchrony of safe needle removal, placement in an appropriate waste container, pressure, and hemostasis is often more technically difficult than needle insertion. Another ergonomic factor for the self-cannulator at home is the insertion and subsequent removal of both arterial and venous needles in a proximal or upward direction in both AVF and AVG.

Similar to peritoneal dialysis, aseptic technique cannot be emphasized, monitored, and retrained enough. Aseptic technique is often a foreign concept to the new home hemodialysis patient.

Unlike peritoneal dialysis, the signs and symptoms of an access infection in a home hemodialysis patient can be subtle. The threshold for a clinical evaluation, potential blood cultures, and possible preemptive antibiotics should be low. How and where to perform these should be determined prior to the end of patient training for each patient so no delay will occur when a potential problem develops. With a documented access infection, the patient's aseptic technique should be reviewed, observed, and adjusted as needed. Similarly, the home hemodialysis program should monitor their rate of bloodstream infections carefully.

Changes in the vascular access should be noted for possible intervention. An unexplained decline in urea kinetics would be one measure. Reports from patients of changes in blood flow, increased venous pressure during dialysis, or a change in bleeding after pulling needles may indicate a problem with the access. One of the advantages of home dialysis is that a full exam of the access can occur monthly by the physician without needles in place and a complete range of motion of the limb. Assessing the appearance, thrill, bruit, augmentation, temperature, and location of the cannulation sites is easy to do in the home patient during a clinic visit by both the nurse and physician.

Safety Considerations

Home hemodialysis as currently practiced has an excellent safety record [11]. In one review of two home hemodialysis programs, only seven serious events were noted over 500 patient-years, and most of those events were operator errors that could be prevented by a combination of technology and education. However, several specific topics merit discussion.

Hypotension

Some have estimated that intradialytic hypotension, defined as the need to stop ultrafiltration and administer saline intravenously, occurs in up to 20 % of conventional hemodialysis treatments. Hypotension in the home environment poses a clear safety risk and must be minimized. The most common cause of intradialytic hypotension in the home environment is incorrect calculation or entry of the ultrafiltration volume. Some of the strategies to reduce hypotension in the outpatient center also are available in the home such as limiting the ultrafiltration rate to ≤ 10 ml/kg/h, decreasing the dialysate temperature, and avoiding antihypertensive medications prior to the dialysis treatment.

Bleeding

Miscannulation of AVF or AVG should be reported promptly to the home dialysis nurse to determine the cause such as incorrect location, angle, depth, or advancement of the needle. Infiltration of blood into a misplaced venous needle can cause significant blood loss and pain and impair the future function of the access. Venous dislodgement of a needle with the arterial needle still in place with the blood pump engaged can lead to life-threatening blood loss quickly, particularly if the patient is performing a nocturnal hemodialysis treatment while sleeping. Fortunately, this is a rare event but moisture detectors placed near the venous needle can help prevent this from occurring.

Outpatient Follow-Up

One of the most surprising aspects of home hemodialysis is the effort the provider must provide after successful training. Most nephrologists perform a face-to-face encounter monthly with their home hemodialysis patients, usually in conjunction with a multidisciplinary team of nurses, social workers, and dieticians.

Since the use of the vascular access occurs outside the purview of the dialysis team, managing the vascular access can be challenging. However, since the patient is not undergoing dialysis at the time of the evaluation, a comprehensive exam of the access can be performed in addition to a monthly review of other parameters of the access which are:

- Cannulation sites
- Change in appearance of access
- Difficulty with cannulation
- Increased time to hemostasis
- Change in the thrill of the access

- Assessment of the venous outflow with elevation of the arm
- Venous pressure in access at initial blood flow
- Venous pressure in access at final blood flow
- Unexplained change in urea kinetics
- Unexplained elevation in plasma potassium

The outpatient clinic visit often works best if a multidisciplinary approach including the dialysis nurse, dialysis social worker, and renal dietician is utilized. Treatment logs for the month are reviewed for problems. Most patients draw their monthly blood work themselves and bring it to the center for analysis. Full medical waste containers can be exchanged for empty containers. While many supplies may be delivered to the patients' homes, it is often more cost-effective to have the patient pick up smaller supplies such as needles, gauze pads, syringes, etc., at this visit.

As with all forms of dialysis, problems will occur that require medical attention. A clear communication strategy should be in place for the patient. Technical problems with the machine should be routed to either the biomedical technician of the dialysis center or the technical support staff of the dialysis machine manufacturer. Medical problems should be routed to the home dialysis nurse or nephrologist on call. Many home dialysis programs will post this contact information physically on the dialysis machine for patient ease.

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Portable and Wearable Dialysis Devices for the Treatment of Patients with End-Stage Renal Disease

42

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Introduction

The outcomes of patients with end-stage renal disease requiring chronic renal replacement therapy remain dismal with respect to quality of life, morbidity, and mortality. Current dialysis systems are limited considering that their efficacy is approximately 10 % of a normal human kidney. Blood is filtered by the native kidneys for 168 h a week. In comparison, filtering the blood only for 12 h per week, the typical dialysis schedule, with inefficient current systems, is insufficient. Closely simulating the filtration of the kidney by increasing dialysis time has been shown to improve outcomes in patients. The potential advantages of continuous dialysis are numerous including improved volume control due to improved sodium retention, along with improvement of hyperphosphatemia, appetite and nutrition, hypertension, hyperkalemia, anemia, acidosis, and serum albumin level. Indeed, studies have shown that shifting patients from the typical three sessions of dialysis per week to daily dialysis leads to significant improvement in the quality of life (i.e., less dietary and fluid restrictions) and overall cardiovascular outcomes. Continuous dialysis leads to significant reductions in medication requirement, hospital admissions, and overall reduction in morbidity and mortality.

There is a growing need for a practical "around the clock" solution that significantly increases time on dialysis while increasing efficiency and reducing overall cost (which is compounded by the need for dedicated manpower and facilities). The next leap forward in renal replacement therapy, short of a kidney transplant, would be to provide a dialysis system which offers continuous treatment, is wearable and truly portable, and allows patients the freedom to resume their daily activities. There is currently no device available on the market that meets these criteria, but there are several in various stages of development. This chapter discusses the current advancements in portable and wearable dialysis technologies.

Wearable Peritoneal Dialysis Devices

Currently available continuous ambulatory peritoneal dialysis could be argued to have achieved the goal of liberalizing the patient to some extent; however, no more than 10 % of patients requiring renal replacement use this modality. Despite advancements in catheter technology, peritonitis remains the most common problem encountered by peritoneal dialysis. Long-term, hypertonic glucose exchanges risk the development of life-threatening peritoneal sclerosis and infective peritonitis. A wearable peritoneal dialysis system that allows fewer connections and disconnections could potentially reduce the risk of peritonitis (Fig. 42.1). Patients currently perform three to four exchanges per day with continuous ambulatory peritoneal dialysis or connect themselves to an automated overnight cycler, both of which require a static electrical supply and fresh dialysate. Portable and wearable peritoneal dialysis devices must address two issues: the ability to operate using compact battery-powered pumps and overcome the need for fresh dialysate [1, 2, 3]. To achieve freedom from daytime exchanges or overnight machines, several attempts have been made to develop a sorbent-based system to regenerate spent dialysate. This could

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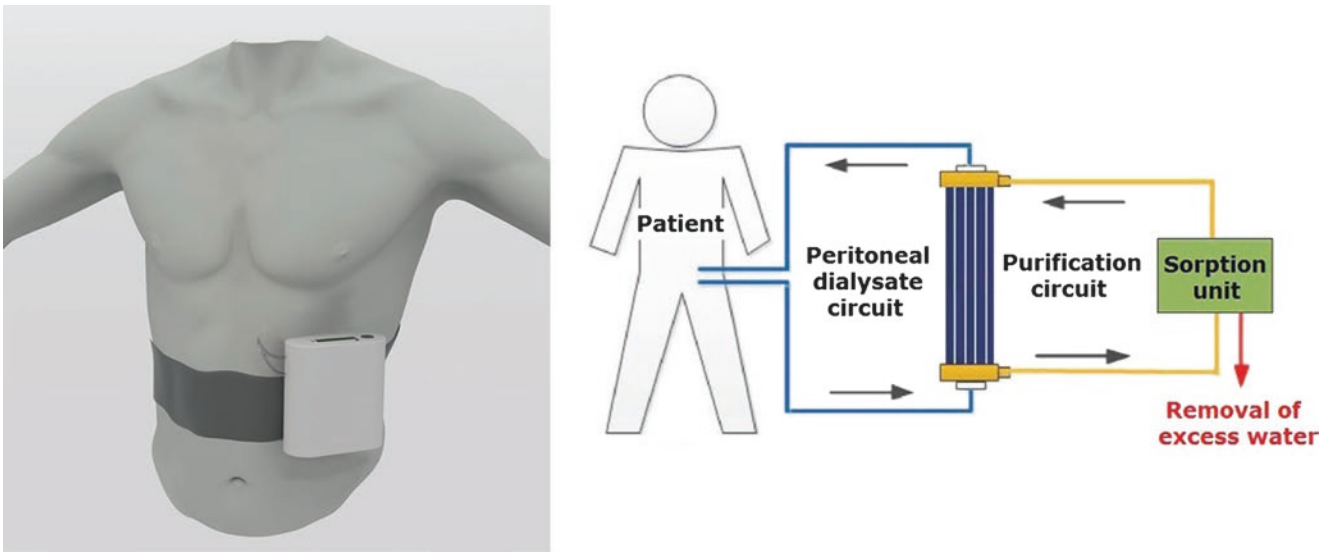

Fig. 42.1 Conceptualized wearable peritoneal dialysis system

be performed by two separate peritoneal dialysis catheters or a single coaxial design with a battery-operated pump designed to pump the dialysate into and out of the peritoneal cavity, with an additional pump to regulate ultrafiltration.

Vincenza Wearable Artificial Kidney

The developers of the Vincenza wearable artificial kidney (ViWAK) conceived a wearable system consisting of a double-lumen peritoneal catheter with a miniature rotary pump [4]. The system would employ a circuit for dialysate regeneration using parallel waterproof cartridges containing a mixture of activated carbon and polystyrene resins, a filter for deaeration and a dialysate inflow line. The device is controlled remotely by a handheld computer. ViWAK is designed to weigh approximately 2 kg and a standard glucose-based dialysate would be used. The dialysate is allowed to dwell for 2 h and then recycled through the double-lumen peritoneal dialysis catheter allowing continuous flow peritoneal dialysis powered by a lightweight battery-powered pump. After an initial 2 h period, peritoneal dialysate is then continuously recycled by the passage of spent dialysate through a series of sorbents. Sorbents have difficulty clearing urea and most sorbent designs have incorporated urease to clear urea to ammonium and carbon dioxide. Consequently, the dialysate effluent would be pumped first through degassing chamber before returning to the patient. In the evening the patient would drain out the dialysate and instill a fresh bag of 7.5 % icodextrin to aid solute clearance and volume control. The device provides good creatinine and β2-microglobulin clearance of 12–14 l/day. ViWAK would require the patient to perform two standard peritoneal dialysis exchanges per day.

Potential limitations of ViWAK revolve around the stability of dialysate composition as it is recycled. Spent peritoneal dialysate effluent contains proteins in low concentration, including fibrin, but with reuse cumulative protein buildup in the circuit would occur. Additional filters would be required to prevent protein coating of the sorbents, which degrades their efficiency. With these obstacles added to the costs of replacing the sorbents each day, the ViWAK has not progressed from the bench to clinical trials.

The Automated Wearable Artificial Kidney

The automated wearable artificial kidney (AWAK) is another wearable peritoneal dialysis device with technology focused on dialysate fluid regeneration. AWAK uses a standard single-lumen peritoneal dialysis catheter and unlike the ViWAK is a discontinuous flow system of peritoneal dialysate [2]. The primary difference between current peritoneal dialysis and AWAK is that patients do not have to reestablish the dialysate regularly as it is continuously regenerated. There are two modules, one designed to be changed on a

daily basis and the other to be changed monthly. The outflow circuit with spent dialysate in the AWAK pumps the effluent through fibrin filters to produce a protein-free ultrafiltrate. The ultrafiltrate is then passed through sorbents containing urease and then through a degassing chamber before being retained in a storage chamber. The refreshed dialysate is then pumped back into the patient.

Sorbent capacity is a key factor in designing a wearable and portable peritoneal dialysis system. Smaller sorbent quantities will mean earlier saturation and sorbent exhaustion leading to increased frequency of sorbent exchanges. Additional sorbent will reduce the frequency of sorbent exchanges at the cost of adding weight to the system. The AWAK design has two proposed versions, one weighing around 1 kg and the other 3 kg determined by the size of the sorbent cartridges. Replacing sorbent cartridges currently requires the patient to drain out peritoneal dialysate and then re-instill fresh dialysate. Therefore, it is imperative that sorbents have the capacity for at least 24 h to prevent the patient having to perform additional peritoneal dialysis exchanges. Clinical trials aimed at testing sorbent capacity for the AWAK are expected in 2015.

Given that it is based on peritoneal dialysis therapy, the AWAK shows the same limitations as the ViWAK with regard to dialysate stability and the use of glucose-based exchange solutes.

Wearable Hemodialysis Devices

Early developers of a wearable hemodialysis system were confronted with technical challenges including vascular access, circuit anticoagulation, device size, and mechanical reliability. Some conceived devices used an arterial blood supply, and those that worked with venous flow required a fail-safe pump and a continuous electrical power source. Ideally, the device must be able to deliver proposed creatinine clearance targets of 30 ml/min and an ultrafiltration target of 30 ml/min. Importantly, connecting to the patient's circulation requires additional safety features to prevent air emboli and blood loss and a mechanism to halt the ultrafiltration pump if such events should occur. Hence, pumping systems are the most critical components of the entire device. Advancements in nanotechnology have led to miniaturization of pump mechanisms and circuits that led to the current devices being developed and on clinical trial.

The Wearable Artificial Kidney (WAK)

The wearable artificial kidney (WAK) is a hemodialysis device developed by Gura and colleagues at the University of Washington in Seattle and was recently granted an Expedited Access Pathway status by the US Food and Drug Administration after a successful performance in its first US clinical trial, at the University of Washington Medical Center in Seattle (Fig. 42.2) [5]. The device employs a double-lumen catheter and a shuttle pump. The standard hemodialysis machine pumps blood into the dialyzer at a relatively constant pressure and is based on delivering a highly efficient but short-duration treatment. For lower efficiency systems as in wearable devices, this could result in an unwanted protein deposition on the dialyzer membrane over time that degrades dialysis efficiency. The WAK system uses a shuttle pump to generate pulsatile flow across the dialyzer membrane to reduce protein deposition. The device draws blood from a double-lumen catheter which is anticoagulated with heparin from a reservoir using a micro-pump. The blood is then circulated through the blood channel of the WAK shuttle pump and into the dialyzer. A low-sodium sterile dialysate is pumped through the dialyzer and then through a series of sorbents containing urease to remove urea and zirconium-containing sorbents to remove ammonium and hydrogen ions. The blood then returns to the venous side of the double-lumen catheter. As with the AWAK, carbon dioxide microbubbles develop within the extracorporeal circuit. Conventional hemodialysis circuit has an arterial expansion chamber and a venous bubble chamber; the WAK has no such chambers; thus, parts of the plastic tubing in the circuit have been designed using gas-permeable plastics. The current prototype of the WAK is constructed in a belt format and weighs approximately 5 kg. WAK is probably the most studied and closest to commercial release; however, there are other devices in the pipeline being developed for wearable hemodialysis (Fig. 42.3).

The main problem of a wearable hemodialysis device is that there is a risk of clotting in the extracorporeal circuit, which did occur with the WAK in some patients. It is important to design the blood circuit in the system to prevent turbulence and stagnation. Access catheter design and placement also have to be regarded in reducing the risk of clotting in the extracorporeal circuit. The risks of long-term anticoagulation also have to be considered. There are downsides to prolonged anticoagulation with

Fig. 42.2 (**a**) Belt-based wearable hemodialysis unit, the wearable artificial kidney (WAK) (Courtesy of Stephen Brashear for UW Medicine). (**b**) Chuck Lee was the first US patient to don the wearable artificial kidney in a clinical trial of the device, at UW Medical Center standing in contrast to two less-portable dialysis options (Courtesy of Sandy Lee for UW Medicine)

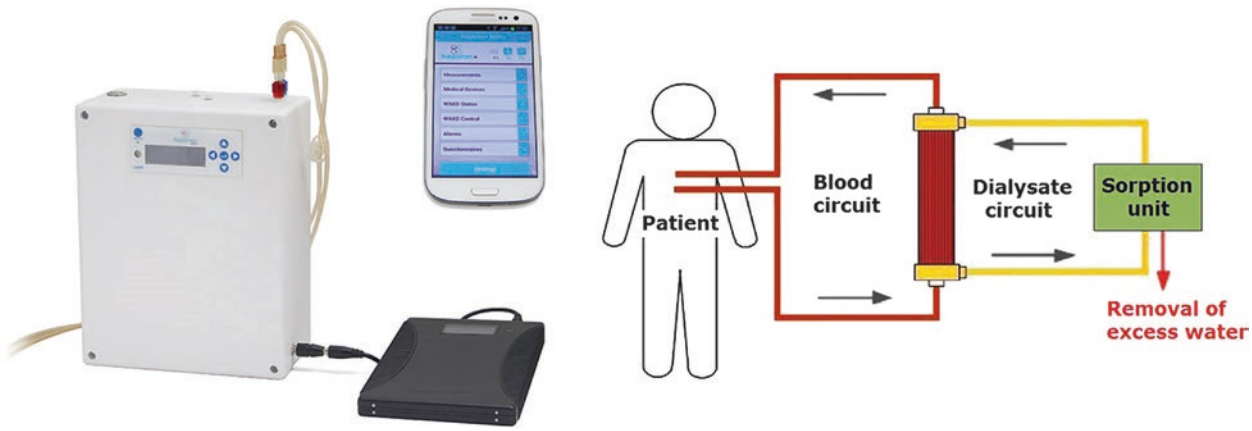

Fig. 42.3 Portable hemodialysis unit concept from NANODIALYSIS (Netherlands)

heparin, including osteoporosis. The use of oral anticoagulation in the setting of extracorporeal circuits has to be studied. Consequently, future designs of wearable hemodialysis devices will require alternative anticoagulant strategies.

Conclusions

For many patients needing renal replacement, dialysis is the focal point around which their life revolves. The associated time required to travel to a facility, the dietary and fluid restrictions, and the complex medication requirements result in significant burdens on the patient as well as on society overall. As such, the development of wearable and portable dialysis devices has been a "quest for the grail" in end-stage renal disease since the inception of renal replacement therapy. Although there are still substantial technical challenges with regard to safety, operation, and effectiveness, advances in nanotechnology are making it possible for the development of a number of wearable and portable devices based on peritoneal dialysis and hemodialysis.

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The Outpatient Dialysis Access Center

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Deepak Nair

Introduction

An outpatient dialysis access center (DAC) is a facility specializing in radiographic imaging and interventional procedures required for the care of vascular access in patients with end-stage renal disease (ESRD). Surgical and angiographic procedures continue to shift to the outpatient arena. There is a steady increase in the number of office-based angiographic centers that perform hemodialysis access procedures. These are owned and operated by cardiologists, nephrologists, radiologists, surgeons, as well as dialysis companies and other private entities. There is a decrease in hospitalization rates for vascular access-related management problems as procedures shift from the inpatient to the outpatient setting. This has paralleled the growth of DACs (though this does not necessarily signify causation). These centers alleviate the strains hemodialysis access maintenance puts on healthcare delivery. Access-related problems, often thrombosis or prolonged bleeding, are not considered emergent and are relegated to the add-on schedule at the end of the day in interventional radiology suites and operating rooms. This is due to these facilities operating at or near capacity with scheduled and emergent cases. Sometimes access procedures are delayed for more than 24–48 h. This invariably results in missed dialysis treatments and increased catheter usage to allow for urgent dialysis. An inability to promptly address access-related issues can often lead to hospital admission and inpatient dialysis treatments.

The outpatient DAC consolidates dispersed vascular access care among multiple hospitals and multiple interventionists to one location and one group of dedicated individuals. The triage of a dialysis access problem is simplified by providing a single source to rapidly evaluate and treat most issues. Patients come to the DAC from several points in the healthcare system. This allows for improved communication with the providers who referred them, better documentation, less scheduling delays, more consistent techniques, and better outcomes. The outpatient DACs' efficient integration of care decreases access-related hospitalization and missed outpatient dialysis treatments likely due to the Hawthorne effect (i.e., improvements are attributable to greater scrutiny). Greater focus and attention is given to the global concept of vascular access in such centers. Patients are thus sent less often to hospital emergency rooms and seldom hospitalized for access-related issues. When well coordinated, there are less missed dialysis visits and better care of the ESRD patient.

All varieties of clinical practice have successfully demonstrated integration of a DAC into their business model. DACs are most commonly seen in private practice, most likely due to an inherently increased entrepreneurial milieu. However, office-based angiographic suites are now part and parcel of academic and hospital-based practices. Employed physicians enjoy the improved efficiencies (i.e., faster turnover in between cases) and revenues generated for themselves and their departments, just as much as private practitioners. If a provider is paid on a relative value unit (RVU) scale, it is important to factor in the technical fees generated by the work done in the center when calculating the RVU.

Procedures Performed at Outpatient DACs

DACs perform many similar access-related procedures but vary in other interventions they offer. Dialysis access-related angiograms, angioplasties, and stents are offered by nearly all outpatient centers. Most also provide placement of (tunneled and non-tunneled) catheters and percutaneous access thrombectomies ("declots"). Angioplasty of more central veins (the subclavian, innominate, and iliac veins) can be performed but may be more suitable for an in-hospital setting in case of uncontrollable hemorrhage. Interventions on the

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vena cava should be done only in symptomatic individuals with the utmost care and preparation due to the potential for significant morbidity and mortality. These should be done in the hospital with surgical backup available. Thrombolysis procedures of access grafts are done in select outpatient centers due to the increased risk of bleeding with thrombolytic agents. Centers may offer this if they have full anesthesiology support and are close to inpatient care. Many DACs also offer peripheral arterial and venous interventions to dialysis and non-dialysis access patients. This is often based on the providers who staff the centers (i.e., cardiologists, interventional radiologists, and vascular surgeons will often offer more non-access-related services at these centers than interventional nephrologists) and the sophistication of the equipment (basic low-powered c-arms are adequate for dialysis procedures but not suited to more advanced arterial or venous endovascular interventions).

Safety in Outpatient DACs

Dialysis access interventions are widely performed in outpatient DACs and may be considered relatively simple when compared to other peripheral vascular interventions. Interventional procedures on dialysis access, however, are not without their share of risk. The patients are often more frail than patients with only peripheral arterial disease. The variability in the quality and timing of dialysis treatments these patients receive also means that they may not be physiologically optimized when seen in the DAC for their procedure. The relative risk of cardiopulmonary arrest and medical emergencies during access interventions performed in a hospital setting was 5.5 in a study at the University of Pennsylvania [1]. Beathard et al. [2] reported an overall complication rate of 3.54 % on 14,067 dialysis access interventions performed at 11 freestanding outpatient interventional facilities in different regions of the United States. Most adverse events occurred in fistula and graft declotting procedures, just as they did in the inpatient setting [1, 3]. No cardiopulmonary arrests or deaths were described in the outpatient study. A more recent experience reported 20 cardiopulmonary resuscitations (0.032 %) and 96 medical emergencies (0.155 %) among 62,089 hemodialysis access procedures performed in nonhospital settings [4]. Thrombectomy procedures had 6.4 times the rate of cardiopulmonary arrests and 4.3 times the rate of medical emergencies compared to fistulagram or angioplasty procedures [4]. Dialysis patients who have not had their regularly scheduled treatments are more prone to mortality [5]. Thus, thrombectomy patients and those who have had a long interval since their last dialysis treatment need to be more carefully assessed and managed during their interventions. These patients in particular may be better suited in an inpatient setting since they will likely have more physiologic derangements (fluid overload, electrolyte abnormalities, uremia) than those with functioning but failing accesses or those who had a more recent dialysis treatment.

Quality and Outcomes in an Outpatient Dialysis Center

Quality and outcomes in an outpatient DAC have been shown to surpass both the inpatient and outpatient hospital settings. Patients treated in outpatient DACs experienced lower payments per member per month for access-related care, lower mortality rates, lower rates of hospitalization, and lower rates of infection [6]. Patients who were treated in a freestanding office-based center lived longer and cost the healthcare system less. Certainly, this may be related to sicker, more technically complex patients being treated in an inpatient setting. Nevertheless, the decreased resource utilization and better outcomes in treating dialysis vascular access in the outpatient setting [7–10] have been reported by interventional radiologists, nephrologists, and vascular surgeons. A reduction in access thrombectomies by intervening on failing access earlier has allowed for improved care of the patient. The result is also a 20–50 % decrease in global costs compared to similar care provided in the hospital [7].

Patients are generally more satisfied with their care in the outpatient DAC. Compared with the national benchmark of 54 %, 77 % of patients having their procedures performed in the outpatient setting had an overall visit satisfaction of excellent or very good. In addition, 76 % of the 79 % of patients who had similar procedures in a hospital reported greater satisfaction in the outpatient facility [11].

Getting Started

There are many things to consider when getting involved with an outpatient DAC. The initial challenge is whether there is enough patient volume to justify building a DAC. The viability of the center depends on an initial pro forma that is financially viable. The start-up year should be, at least, revenue neutral. This involves a retrospective evaluation of cases performed in the past 1–2 years and accurately predicting how many of them could have been done in the future office-based center. A referral base of at least 600 dialysis patients, with at least four patient visits a day, is a conservative estimate for initial financial sustainability. Viability may be difficult to achieve if there are not enough patients referred to the center. To address the challenges of an inadequate referral base of dialysis access patients, many centers are expanding their service lines and offering other procedures

(i.e., peripheral arterial and venous interventions, pain management, etc.). This allows for increased utilization of the physical infrastructure and human resources.

State laws and respective Department of Health regulations must be strictly adhered to. Unlike ambulatory surgery centers, prior approval is not often required due to the fact that the DAC is an extension of an established office practice. Procedures performed here are considered billable as "in-office" procedures. Nevertheless, legal counsel should be sought to clarify any relevant *Safe Harbor Statute* or *Certificate of Need* issues. If sedation is to be used, state law and policy must be followed. There are strict guidelines that vary from state to state regarding certification of radiology suites and the ability to administer conscious sedation. A review of the federal *Stark Statutes* is important, especially if partnering with other physicians or nonphysician entities.

Another consideration is deciding between involvement in a stand-alone center or a partnered center. A stand-alone DAC will require a greater amount of oversight from the provider operating it. The reward for doing this is greater independence in decision-making and, potentially, more financial profit. A partnered center can be created with the help of established companies known for managing outpatient angiographic suites (American Access Care, National Vascular Centers, RMS Lifeline, Vascular Access Centers, etc.). The advantage of partnering with such corporations is that they will assist with much of the legal, accounting, and human resource issues. The price to involve them is a share of the profits and, often, a share of the DAC. Another option is to obtain funding from outside the medical arena. Collaboration with other medical specialties or nonmedical investors allows for more control but less financial outlay, especially if not encumbered by day-to-day management concerns. Accurately forecasting the costs of the space, capital equipment, supplies, and labor will allow for a realistic pro forma. Cooperation and approval by others in the practice are vital to the success of the endeavor. This is an effort that should bring individuals together, not break them apart. The right strategy is dependent on the needs, wants, and personalities of the people creating the outpatient center.

Physical Space Needs for a DAC

There needs to be enough room in the center to be comfortable, safe, and functional. 2000–3000 square feet will be needed if operating one procedure room in the facility. A room lined with lead for radiation protection will house the angiographic suite. Some fixed fluoroscopic units (Fig. 43.1) will require higher ceilings (at least 9 feet) and more floor support (often as reinforced concrete under the machine and bed). Newer models, with their lower profiles and less weight, have allowed for easier setup and less ceiling height and floor support requirements. Portable units (Figs. 43.2 and 43.3) have the lowest profile and price, but at a compromise of imaging quality and field of view. As technology improves, the quality of portable imaging is rapidly approaching that of the fixed units. An appropriately sized waiting room, preoperative and recovery area (Fig. 43.4), supply room, decontamination room, and administrative office are all other minimum considerations that one will need to include when deciding how much space is required.

Fig. 43.1 Fixed ceiling mounted Philips system with table and setup to perform a fistulagram. Radiation protection is provided via transparent shield in front of image intensifier and via lead shielding underneath floating bed. Ultrasound is placed next to the arm to facilitate evaluation and access

Management of the center needs a dedicated team. Though it is an extension of your office, the DAC needs its own group of dedicated individuals including management personnel and a physician champion. Support staff should include registered nurses, medical and surgical assistants, and sometimes a radiologic technologist (depending on state laws). They should all have Basic Life Saving (BLS) certification; the nurses and physicians should be Advanced Cardiac Life Support (ACLS) certified. The initial team hired for the center should all have experience in the pre-procedure and post-procedural management of the patient

Fig. 43.2 Portable fluoroscopy unit with vascular package made by Ziehm Imaging

Fig. 43.3 The portable unit is in a 14 foot by 11 foot space

Fig. 43.4 Recovery room has four beds and ample space for transit

with femoral arterial punctures. Dialysis unit technicians and nurses who have extensive experience in cannulating patients may be an option if the center limits itself to dialysis access interventions.

Patient Selection

Patient selection must be conservative. There are no intensive care units, operating rooms, ventilators, blood banks, nor thoracotomy trays in an outpatient DAC. Hemodialysis patients are inherently at increased risk of cardiovascular morbidity and mortality [12]. It is important to be keenly aware of their history and physical condition prior to a procedure. Their volume status, coagulation profile, and respiratory state are essential factors to consider before the ambulatory procedure. Abnormalities in these specific systems portend an increased risk for complications. In addition to competency at BLS and ACLS, establishment and practice of protocols to deal with allergic reactions (many times radiologic contrast induced) should be instituted.

Contraindications for performing an access procedure in the outpatient center should include airborne disease, contact isolation for infection, ventilator dependence, severe anxiety, poor pain tolerance, documented severe dye allergy, heparin

allergy (including heparin-induced thrombocytopenia), and morbid obesity (i.e., most manufacturers do not recommend moving the table top on anyone over 300–350 lbs.). Most importantly, there should be access to and a relationship with a nearby hospital to accept patients with complications or cardiovascular instability.

Airway assessments must be carefully made. Rapid access to equipment required to manage a respiratory crisis is necessary. This is important even if the patient is receiving no sedation but only local anesthesia, as recumbent positioning and anxiety can result in a change in the respiratory state of fragile patients. Moderate sedation must be cautiously managed. Employing an anesthesiologist or contracting with one is the safest course of action when performing procedures in the outpatient angiographic suite. This allows for the best clinical expertise in airway management and sedation to be available if anything untoward happens.

Radiation Safety

Radiation safety is paramount in an outpatient angiographic suite. A radiation safety officer is often hired as an independent contractor. Education for all staff regarding radiation safety policies and procedures is part of all state regulatory agency requirements. Radiation exposure must be minimized to staff, physicians, and patients. A policy for measuring the dose all individuals receive, including patients, should be in place. The delivered dose of radiation should be recorded and followed. Fluoroscopy time can be used as a surrogate of exposure. Lead aprons and other radiation protective devices and garments should be checked periodically for defects.

Imaging Needs

Multiple imaging modalities within an outpatient DAC may allow for optimization of dialysis access care [13]. Duplex ultrasound (DUS) allows for rapid noninvasive assessment of the dialysis access and can determine whether or not an intervention is required. Vein mapping prior to access placement can also be offered as a service. Many surgeons now request vessel mapping prior to dialysis access surgery. Preoperative vessel mapping has improved the placement and success of dialysis access creation [14]. This mapping is done in the DAC, but access creation is, currently, still required to be performed in an in-hospital setting for reimbursement from payers. Ultrasound can also be used to gain access to vasculature that is not readily palpable. This can improve the safety, success, and speed of peripheral vascular intervention performed in the outpatient center. Computed tomographic angiography (CTA) can complement ultrasound imaging by assessing structures not readily seen on sonography (i.e., central venous system). Magnetic resonance angiography (MRA) without contrast may also be an option as software and technology improves. Since CTA and MRA require an expensive capital purchase or lease arrangement, realistic forecasting and financial planning should be done prior to commitment to these technologies. In stark contrast, duplex ultrasound machines are less expensive and have more applicability to dialysis access patients.

Patient Transportation Issues

Lack of access to care due to transportation difficulties, hours of operation, and health insurance continue to be obstacles for most outpatient facilities. Transportation to obtain medical care is a problem for some hemodialysis patients. Employing a social worker or coordinating with social workers in the dialysis units can help to solve many transport issues. Municipalities often have dedicated programs to help those who need to travel for medical care. The challenge is often in navigating the bureaucratic system. Contracting with a taxi service may be an option for ambulatory patients. Medical transport services are options especially for poorly mobile patients. The ideal DAC would have hours that mimic that of the referring hemodialysis center. This often means keeping the doors open on weekends and late afternoons. Many times this is not practical as there are cost and quality of life constraints for staff and providers. Outpatient DACs that have robust patient populations can, and do, offer flexible hours and more comprehensive availability. Some have relationships with local emergency departments and handle access emergencies, thereby avoiding hospital admissions for these patients. Emergent procedures comprise 20 % of the workload in a DAC. Kian and colleagues demonstrated that 61 % of patients referred emergently had successful dialysis within 24 h (90 % had successful dialysis within 48 h) [8]. Lack of access due to poor or no insurance coverage has been the hardest obstacle to overcome for nearly all outpatient DACs.

Accreditation, Outcomes Reporting, and Quality Initiatives

Accreditation, outcomes reporting, and quality initiatives are necessary for the future success of office-based procedures. Currently many different organizations accredit outpatient angiographic facilities – i.e., Accreditation Association for Ambulatory Health Care (AAAHC), Joint Commission on Accreditation of Health Care Organizations (JCAHO), etc. Though accreditation is not required, nor currently linked to reimbursement, it is highly recommended. It currently fills the vacuum that exists for setting standards for these facilities. Surrogates for quality are actively being sought in the delivery of healthcare, and accreditation will likely be a

Table 43.1 Common procedures performed in the outpatient dialysis access center

CPT code	CPT description	In-hospital payment	Outpatient DAC payment	Work RVU	Total RVU
36140	Introduction of needle; extremity artery	$107	$445	2.01	3.00
36147	Introduction of needle and/or catheter, arteriovenous shunt created for dialysis (graft/fistula); initial access with complete radiological evaluation of dialysis access, including fluoroscopy, image documentation, and report (includes access of shunt, injection[s] of contrast, and all necessary imaging from the arterial anastomosis and adjacent artery through the entire venous outflow, including the inferior or superior vena cava)	$195	$850	3.72	5.44
36148	Introduction of needle and/or catheter, arteriovenous shunt created for dialysis (graft/fistula); additional access for therapeutic intervention (list separately in addition to code for primary procedure)	$51	$266	1.00	1.44
36160	Introduction of needle or intracatheter, aortic, translumbar	$129	$504	2.52	3.62
36200	Introduction of catheter, aorta	$161	$636	3.02	4.50
36870	Thrombectomy, percutaneous, arteriovenous fistula, autogenous or non-autogenous graft (includes mechanical thrombus extraction and intra-graft thrombolysis)	$314	$1865	5.02	8.77
35476	Transluminal balloon angioplasty, percutaneous; venous	$283	$1452	5.10	7.91
75978	Transluminal balloon angioplasty, percutaneous; venous	$26	$138	0.54	3.85
37238	Transcatheter placement of an intravascular stent(s), open or percutaneous, including radiological supervision and interpretation and including angioplasty within the same vessel, when performed; initial vein	$334	$4184	6.29	9.35
37239	Percutaneous, including radiological supervision and interpretation and including angioplasty within the same vessel, when performed; each additional vein (list separately in addition to code for primary procedure)	$158	$2065	2.97	4.43

strong candidate. Outcomes reporting is robust in the inpatient setting, but it is very inconsistent in the outpatient arena. This is currently the Achilles heel of the outpatient DAC. By prospectively showing the quality and efficacy of the work done in the DAC, paradigms will shift. Quality initiatives relating to hemodialysis vascular access exist in the fields of nephrology, interventional radiology, and vascular surgery. Reporting through the DAC rather than disparately through multiple society registries will allow more comprehensive reporting and real-world analysis.

Reimbursement

Bundled payment structures and reduced reimbursements are the economic realities in the outpatient DAC. This requires efficient use of human and material resources. These are skill sets that most physicians do not enter practice with. Many do not develop it even after years of clinical practice, because it is seldom asked of them. In the outpatient setting, operational management determines the financial viability of the center. Knowledge of the most recent *Current Procedural Terminology* (CPT) codes relevant to the outpatient setting is important in assessing the procedures that will result in profit for the facility. Common procedures along and respective reimbursements in the hospital setting compared to the outpatient DAC, along with work RVUs and total (taking into account the outpatient facility fee) RVUs [15] are listed in Table 43.1. Since payments are often bundled, the facility is at risk of financial loss if the procedures end up costing more than what they are reimbursed. It is often not easy to predict the outcome of a particular procedure. Extra time and materials may be required to get a satisfactory result (i.e., use of extra wires, catheters, balloons, stents, etc.). If the majority of cases are cost-effectively performed with excellent results, the facility, patient, and payer will all benefit.

Conclusions

Healthcare is moving to an increasingly more cost-effective and collaborative model. The outpatient DAC is in line with this philosophy as it avoids the cumbersome and hard to navigate hospital system and replaces it with a more patient-centered facility. The result is a facility where there is more time dedicated to the care and service of the patient. Since patients come to the outpatient DAC from several points in the healthcare system, the DAC provides an ideal location to offer coordinated, comprehensive access care. Costs to the system are fixed, and the financial risk of the care delivered is taken on by the provider. Costs are not compromised at the expense of safety or quality. Improved efficiency and better outcomes have been demonstrated in treating both elective and emergent

dialysis access issues in the outpatient setting. These centers can obviate the need for the hospitalization of many access-related issues. Appropriate patient selection and monitoring combined with procedural planning and vigilant care allow for the safe and successful performance of interventions. Accreditation and quality initiatives will need to be developed and promoted for future success and validation of the DAC.

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