



Figure 168.9 Compression Garments Length. (A) Knee-high. (B) Thigh-high. (C) Full-length.

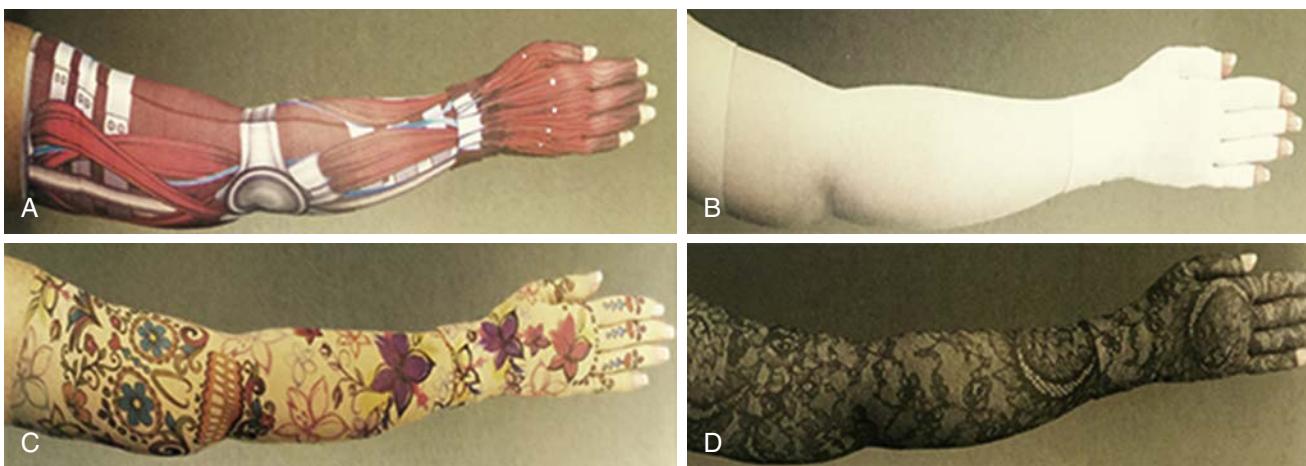


Figure 168.10 Compression Garments Materials. (A) Latex. (B) Cotton. (C) Spandex. (D) Nylon.

wide range of options is key to promoting acceptance and adherence. Good garment fit is critical. Garments should never be rolled at the top, creating the possibility of an obstructing tourniquet. Creases at the ankle or in the popliteal or cubital areas can create enough pressure to cause skin breakdown. Skin should be carefully inspected for chafing or irritation after any new garment is worn.

Nonelastic Compression

Commercial nonelastic support devices are well received by patients as an alternative to nighttime wrapping. The Circ Aid (Shaw Therapeutics, Rumson, NJ) uses Velcro fastenings to adjust a series of nonelastic support bands around the leg and ankle. Another form of nonelastic support, the Reid sleeve (Peninsula Medical Inc., Scott Valley, CA), is a tube of eggcrate foam, surrounded by canvas, with multiple wide Velcro bands to apply compression. Nonelastic compression options are most helpful for patients who are unable to manage a program of complex wrapping by themselves (Fig. 168.11). The efficacy of nonelastic devices has not been prospectively tested.

Sequential Pneumatic Compression

Sequential pneumatic compression (also called intermittent pneumatic compression [IPC]), is another method of

compression therapy.⁵⁴ Desai et al. reported 3-year outcomes of IPC in 232 extremities with secondary lymphedema. IPC resulted in a 28% decrease in absolute limb volume ($P < 0.001$), decrease in body mass index (BMI), improvement in SF-36 QOL ($P < 0.001$), and significant per capita direct cost savings with a subsequent decrease in hospitalization for lymphedema-associated complications of over \$3200 per patient per year.¹⁷

IPC is an ideal alternative to replace MLD for those patients who have difficulty performing the self-care MLD.^{66,67} With lymphedema there is no force available to mobilize, isolate, and propel stagnant fluid to the regions where lymphatics absorb and contract; this task needs to be replaced by external massage, of which the most effective seems to be the sequential IPC.⁶⁸ The intermittent nature of pulsatile external compression produces beneficial physiologic changes, which include hematologic, hemodynamic, and endothelial effects.⁶⁹ The device enhances lymph transport by generating intermittent inflation and deflation over the affected limb, which mimics the action of the muscle pump. There are two phases: (1) the preparation phase, where pressure is applied in a distal-to-proximal gradient; and (2) the drainage phase, where pressure is applied in the same manner.⁶⁶ IPC also reduces lymphedema by decreasing capillary filtration, and therefore decreasing lymph formation.⁷⁰ Also the pump will lead to evacuating the edematous



Figure 168.11 Nonelastic Compression.

fluid to the area with normal lymph flow through the squeezing effect of the pump.⁶⁷ However, the efficacy of IPC may depend on the clinical situation as well as on several variables associated with the devices.⁷¹ Bergan et al.⁷² randomized 35 patients with lymphedema to a 2-hour-long treatment session with one of three types of compression pumps: (1) a uni-compartmental pump using 50 mm Hg pressure; (2) a three-compartment pump with segmental pressures of 50 mm Hg in each cell; or (3) a multi-compartmental gradient pressure pump with 10 cells ranging in pressure from 80 mm Hg distally to 30 mm Hg proximally. The mean percentage volume change was +0.4% in the first group, +7.3% in the second, and -31.6% in the third. The authors concluded that multi-compartment sequential compression achieved the best reduction of limb volume after a single treatment for chronic lymphedema.

The IPC devices may be single or multiple chamber,⁷³ and some pumps permit adjustment of the amount of pressure in a particular chamber; however, for the management of patients with lymphedema, the ideal pressure for the pump is unknown. Some investigators have suggested that a pressure greater than 59 mm Hg may injure lymphatic vessels. The IPC treatment is usually applied daily or 5 times per week; the optimal duration of IPC is also unknown. Among various studies, sessions have varied in length (90 minutes to as long as 6 hours) and duration (2 days to 4 weeks).^{74–78}

After external compression therapy, a form-fitting, low-stretch elastic knit sleeve is usually applied to maintain edema reduction.⁵ Outcomes of using the pump have been studied, and it was concluded that the pressure generated from the pump at the limb lymphedema tissue will cause the formation of tissue channels that will work as pathways to help in clearing the accumulated fluid. The limb circumference is decreased or at least does not further increase, and the elasticity

of the target limb is increased and maintained. No local complications in limb texture were observed.⁵ The long-term, high-pressure IPC, long-inflation timed therapy can be safely recommended to patients with lower limb lymphedema.⁶⁷ Contraindications to the use of IPC include local or proximal malignancy, infection in the limb, deep vein thrombosis, and patients on anticoagulation medication.⁶⁶ Current trials have failed to show the effectiveness of the addition of an IPC to the routine management of breast cancer-related lymphedema.⁷⁹ It has been reported that IPC improved symptom relief, and reduced episodes of cellulitis and ulceration in lower-extremity lymphedema. It was well tolerated and should be recommended as supplemental to standard lymphedema therapy.⁸⁰

Pressure Level

Provided there is no underlying peripheral arterial disease, sustained pressure of 60 to 70 mm Hg has been suggested as a maximum upper limit to treat lymphedema. Therapeutic lower extremity elastic stockings designed for chronic venous insufficiency or lymphedema are available in a variety of lengths and compression strengths (20 to 30, 30 to 40, 40 to 50, and 50 to 60 mm Hg). Lower limbs with recalcitrant chronic lymphedema generally require 30 to 40 mm Hg of compression at the ankle; however, for patients with comorbidities (e.g., diabetes mellitus, arterial occlusive disease, arthritis, or other conditions that limit the use of high-compression garments), stocking pressures of 20 to 30 mm Hg or less may be more appropriate. Upper extremity garments are typically fitted with 20 to 30 mm Hg pressure; however, 15 to 20 or 30 to 40 mm Hg are available, but their use would depend on lymphedema stage and tissue turgor. Previous studies have shown that high-pressure (90 to 100 mm Hg) sequential external pneumatic compression (SEP) reduced both limb girth and volume in a lymphedematous extremity.⁸¹ Good evidence supporting the use of IPC for thrombosis prevention after surgery, in the treatment of post-thrombotic syndrome, and lymphedema, has been reported.⁸²

It also has been reported that IPC use with a pressure of 120 mm Hg inside the chambers effectively reduced a phlebo-lymphedema. Furthermore, it appeared that treatments with a pressure of 60 mm Hg were ineffective in lymphedema therapy, and perhaps are only useful in anti-edematous therapy.⁸³ Currently, the optimal frequency and duration of IPC therapy is unclear.⁷³ Little known adverse events have been reported using IPC. In one study, there were no significant adverse events reported; however, there were reports of discomfort in two patients with chronic venous edema treated with IPC at 60 mm Hg, but not at 40 or 50 mm Hg. Another patient reported skin irritation, while three reported discomfort at least once during therapy.⁸⁴ Current literature indicates that IPC devices have little detrimental effect on patient safety (Fig. 168.12).⁷³

After reviewing current literature regarding garment characteristics, the authors of this chapter recommend applying non-elastic graduated compression stocking with 60 to 70 mm Hg when appropriate in addition to CDT.



Figure 168.12 Sequential Pneumatic Compression. (A) Basic pump. (B) Entré system with up to 18 inflatable chambers. (C) flexitouch system with up to 32 inflatable chambers.

Exercise

Exercise may be beneficial to individuals with lymphedema.⁸⁵ It provides an improved life quality⁸⁶ and a therapeutic intervention instead of worsening the lymphedema symptoms⁸⁷ by enhancing protein resorption⁸⁸ and maintaining lymphatic flow.^{87,89,90} During the inspiration phase of the exercise, there is a decrease in the intrathoracic pressure, which leads to an improvement of infra-diaphragmatic lymph flow.⁹¹ It can be concluded that with more exercise there is more pulmonary work, which enhances lymph flow and decreases the lymphedema.⁶³ Exercise will help weight reduction, which, in turn, will augment the clearance of lymph and decrease the swelling.⁶³ It is worth mentioning that patients with lymphedema associated with breast cancer may benefit from resistance exercise, and it is safe when it is done under the supervision of an experienced trainer to decrease symptoms exacerbation.^{92,93}

Skin Care and Nail Care

Skin and nail hygiene is recommended to decrease the amount of cutaneous fungal and bacterial on the skin. Low pH moisturizers should be applied to keep skin from drying and cracking.⁹⁴ Cracks and dry areas of the skin are entry points for bacterial and fungal infections.^{95,96} Regular use of a moisturizer can help to avoid skin cracking. For arm lymphedema, good hand hygiene and softening the cuticles with proper cuticle moisturizer are recommended.⁹⁷

Therapeutic Approach Based on Clinical Stages

Multimodal therapy consists of general measures of self-care applicable for all stages of lymphedema. Treatment should be

based on the stage of the disease. The intensity of compression and physiotherapy will also vary by stage. There are two general phases of therapy. The goal of phase I (intensive phase) is to mobilize accumulated protein-rich fluid and initiate the reduction of fibrosclerotic tissue (if present), while the goal of phase II is to reserve and improve the success achieved during phase I (Table 168.3).

Level of Evidence

CDT, including all the components, is recommended for practice.^{98–105} Based on recent research, each component of CDT has different expected outcomes (Table 168.4).

SURGICAL TREATMENT

Physiological Intervention

Two modalities of physiological treatment are surgical options for patients with lymphedema. Lymph node transplantation involves donor node implantation into the lymphedematous limb and the attachment of the arterial and venous system.¹⁸ Lymphovenous bypass is a second physiological surgical intervention option. Lymphovenous bypass involves draining lymph into the venous circulation or the lymphatic system proximal to the area of obstruction.¹⁹

Excisional Procedures

The goal of excisional treatment of lymphedema is to remove the deposited fibrofatty tissue by the use of either liposuction

TABLE 168.3

Therapeutic Approach Based on Clinical Stages

Stages	Duration	Phase I (Decongestion)	Phase II (Maintenance)
Stage I	2–3 weeks	<ul style="list-style-type: none"> • MLD 1–2× per day • Short-stretch bandages • Skin care • Remedial exercises 	<ul style="list-style-type: none"> • MLD • Compression garments • Skin care • Remedial exercises
Stage II	3–4 weeks	<ul style="list-style-type: none"> • MLD twice a day • Short-stretch bandages • Skin care • Remedial exercises 	<ul style="list-style-type: none"> • MLD as needed 1–2× per week • Compression garments • Skin care • Remedial exercises • Repeating phase I (1–2×)
Stage III	4–6 weeks	<ul style="list-style-type: none"> • MLD 2–3× day • Short-stretch bandages • Skin care • Remedial exercises 	<ul style="list-style-type: none"> • MLD as needed 1–2× per week • Compression garments with bandages • Bandages at night • Skin care • Remedial exercises • Repeating phase I (3–4×) • Plastic surgery may be indicated

MLD, manual lymphatic drainage.

or resection. **Liposuction** is particularly effective in the upper extremity, and it has few side effects. Lymphedema patients treated with liposuction have substantial long-term decrease in limb volume and improved quality of life when used alongside compression garments.²⁰ Radical resection is a treatment option used only after failure of other treatments, and is much more likely to result in substantial morbidity due to the increased level of invasiveness.²¹

OTHER TREATMENT

Besides the established therapies mentioned in Table 168.4, the benefits and effectiveness of several other therapies have been investigated. **Pharmacotherapy** has not shown to be beneficial; neither diuretics nor coumarin alleviate lymphedema. **Low-level laser therapy, hyperbaric oxygen, and intermittent negative pressure** have limited data to support effectiveness (Fig. 168.13). For example, the results from one low-level laser therapy study indicated edema reduction after treatment, which

TABLE 168.4

Level of Evidence for Lymphedema Current Treatments

Therapy	Outcome	Evidence
Manual lymph drainage	Effectiveness not established	(112), (113), (114), (115)
Compression bandaging/compression garments	Recommended for practice	(61), (116), (117), (118)
Pneumatic compression	Effectiveness not established	(106), (119), (120)
Exercise	Likely to be effective	(121), (122), (123)
Skin care	Expert opinion	None

was sustained for several months.¹⁰⁶ Also, hyperbaric oxygen therapy studies for breast cancer-related lymphedema has had mixed results (see Fig. 168.13 for summary).^{107,108}

As mentioned below, additional treatments have been investigated. It is likely, in the future, that gene therapy will be used to develop new lymphangioles in the affected limbs, which could be a potential clinical remedy. The potential efficacy of this approach was illustrated in a mouse model with lymphedema acquired by inactivating VEGFR-3 mutation, similar to that in congenital hereditary lymphedema (Milroy disease). Virus-mediated therapy with the gene for VEGF-C, which activates VEGFR-3, led to the generation of functional lymphatic vessels.¹⁰⁹

Intralymphatic steroid injections also have been used in an attempt to decrease fibrotic occlusion in lymph nodes and to improve lymphatic transport. In a pilot study of 20 patients with primary lymphedema, 8 showed improvement for as long as 9 months after treatment.¹¹⁰ Yet, to date, the effectiveness of steroid treatment has not been established; however, investigators in Japan attempted to treat secondary lymphedema by injecting autologous lymphocytes into the main artery of the affected limb. Five of the seven patients showed a short-term improvement.¹¹¹ Also, the results of a larger series, which used a combined approach of lymphocyte injection and compression therapy, reported that 34 of 46 patients experienced edema reduction.¹¹² However, these studies have not been replicated.

Researchers found a significant decrease in the thickness of lymphedematous ears in a rabbit animal model following **extracorporeal shock wave therapy**. The results indicated that there was a significant increase in the density of lymphatic vessels. The authors suggested that extracorporeal shock wave therapy may be a novel, feasible, effective, and noninvasive treatment for lymphedema.²

SUPPORTING EVIDENCE

Besides the standard lymphedema management and treatment techniques, there is limited information on the efficacy of other non-traditional therapies (see Fig. 168.13). For example, there is no evidence that diuretics are effective. Some reports are supporting the use of coumarin^{113,114} and laser therapy.^{6,106,115–119}

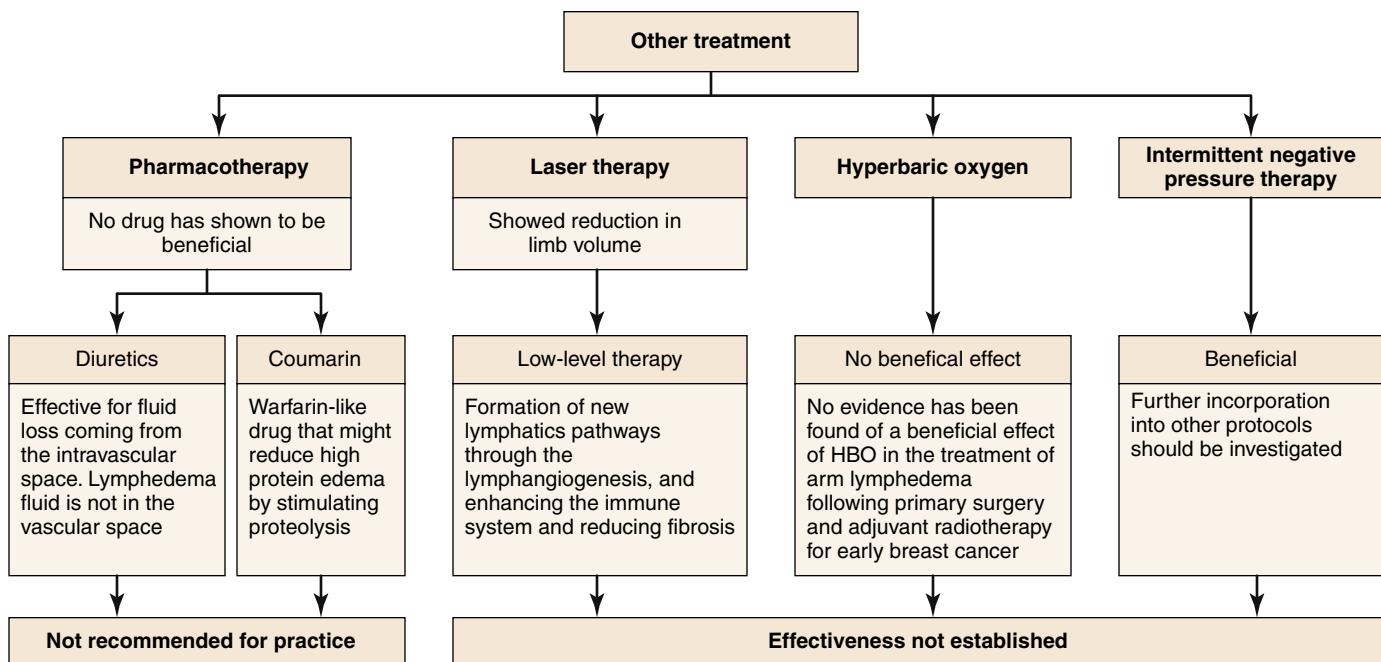


Figure 168.13 Other Treatment Algorithm.

On the other hand, published reports have failed to show any benefit for the use of hyperbaric oxygen^{120,121} or intermittent negative pressure therapy.¹²²

COMPLICATIONS

Skin Infections

Skin infection itself is both a triggering factor for lymphedema, and a consequence of untreated lymphedema. Lymphedema is a protein-rich fluid, which is also an excellent medium for bacterial and fungal growth that may contribute to an increased risk of infection. Lymphedematous tissue serves as an entry site for bacteria and developing erysipelas,¹²³ recurrent infections, and lymphangitis.^{94,123–126} Approximately 20% to 30% of lymphedema patients develop lymphangitis, erysipelas,⁹⁵ and cellulitis, especially those patients undergoing lymph node dissection.^{55,127} Early recognition and treatment of skin infections are essential to prevent progression of lymphedema.

Malignancy

A rare, secondary, malignant tumor, called "lymphangiosarcoma," can be the result of chronic lymphedema of any origin and be associated with its development.¹²⁸ It is usually seen in patients with massive and protracted edema,¹²⁹ and has been classically described as occurring in the post-mastectomy patient (Stewart-Treves syndrome),^{130–132} or with primary lymphedema and chronic filarial lymphedema.^{133–135} The tumor originates in vascular endothelial cells of the affected arm with lymphedema, not the lymphatic vessels.¹³¹ It may initially appear as blue-red or purple skin lesions with a macular or papular shape. Multiple lesions are common and subcutaneous

nodules may appear. Such skin lesions should be carefully evaluated in patients with chronic lymphedema.

Late-onset malignancies are a potentially devastating, but rare, complication of long-standing lymphedema. In most cases, they develop in no more than 1% of patients with lymphedema. The most common malignancies are angiosarcomas¹³⁶ and lymphangiosarcomas,¹³⁷ which are thought to represent the neoplastic transformation of blood vessels and lymphatics, respectively.

Histologically and clinically, it is difficult to distinguish these two sarcomas from each other. The occurrence of angiosarcoma (or lymphangiosarcoma) in the setting of lymphedema is commonly called Stewart-Treves syndrome.¹³⁶ Sarcomas can develop in patients with long-standing lymphedema of any cause: primary lymphedema or lymphedema secondary to filariasis,¹³⁵ hysterectomy,¹³⁸ trauma,¹³⁹ or mastectomy.¹³⁹ Other malignancies, including Hodgkin and non-Hodgkin lymphoma,¹⁴⁰ Kaposi sarcoma,¹⁴¹ squamous cell carcinoma,^{142,143} and malignant melanoma,¹⁴⁴ have been associated with chronic lymphedema, but a causal link has not been established.

Psychological Impairment

Chronic lymphedema continues to be an incurable and disabling condition.¹⁴⁵ The intensity of symptoms may differ from one patient to another; however, overall, most patients will have psychological impairment¹⁴⁶ and/or decreased quality of life, including social, functional, and emotional components.^{147,148} Psychological and functional impairments associated with lymphedema are significant.²⁷ The psychological impact of long-term disfigurement, especially in adolescents, needs to be considered. The disturbance of body image is the underlying cause for younger women to have psychological distress, and often for older women to have depression.¹⁴⁹ Kim

et al. found that lymphedema secondary to pelvic lymph node dissection among gynecologic cancer survivors decreased their quality of life due to the related symptoms and financial difficulty.¹⁵⁰ Winch et al. found the potential to accentuate sexual issues caused by lymphedema secondary to breast cancer, and women were reluctant to discuss these issues with anyone other than their partner.¹⁵¹ Park et al.²⁷ found that 12% of patients reported that they were limited to jobs working at a desk or that allowed frequent sitting. Effective management of lymphedema may improve patient quality of life and reduce interference in daily activity.¹⁵²

INSURANCE ROLE

From our local lymphedema clinic, it was reported that most insurance coverage plans cover CDT, but managed healthcare systems often limit the number of visits or units (e.g., 15-minute increments of care). In some cases, more visits may be requested with the submission of documentation. Typically, successful CDT treatment requires five visits/week for the first 2 weeks and then three visits/week for an additional 2 weeks. Hopefully, following CDT treatment, the size and volume of interstitial fluid has reduced to the point where a good assessment can be made. After this, compression garments can be fitted and patients are provided with instruction for donning, along with self-care instructions, and home protocols are provided to achieve the best compliance and long-lasting results. As there is no cure for lymphedema, in most cases there are few problems with coverage based on severity, as lymphedema is always progressive, if not appropriately managed. Unmanaged lymphedema places patients at great risk of infections.⁹⁴ However, it has also been reported that some third-party payers have suggested that edema is a cosmetic problem; consequently, they deny reimbursement for both treatment and garments. Such policies or beliefs often require repeated communications between payers and physicians to gain approval for treatment.¹⁵³ As part of a reconsideration of coverage policy, the Centers for Medicare and Medicaid Services requested a systematic review of the evidence on the use of pneumatic compression devices in the home environment for the treatment of chronic venous insufficiency (CVI) and venous ulcers.¹⁵⁴ "The Lymphedema Treatment Act is a federal Bill that aims to improve insurance coverage for the medically necessary, doctor-prescribed compression supplies, which are the cornerstone of lymphedema treatment."¹⁵⁵

Although the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database exists and reports claims of lymphedema in patients >65 years old,²² Medicare does not yet cover compression garments, while the lymphedema population is the one that could benefit the most. There is a rather lengthy application and a corresponding \$25 fee paid by the patient. If approved, then they are eligible for one set of garments and may apply again each year. However, the time and effort are well rewarded as thigh- and knee-high garments per leg are approximately \$480 and \$280 (USD, 2016), respectively.

In one study, researchers found an association between significant reductions in episodes of cellulitis and outpatient care and costs following the use of advanced pneumatic compression devices in patients with both cancer-related and non-cancer-related lymphedema. Since the publication of this study in the *Journal of the American Medical Association (JAMA)*,¹⁵⁶ healthcare payers have been more willing to reimburse for such treatments. Hopefully, these results will encourage healthcare providers to purchase comparable equipment, such as the Flexitouch System by Tactile Medical, because trial and treatment adjunct is very expensive.

IDEAL OUTPATIENT LYMPHEDEMA CLINIC

First and foremost, assessments, consultations, and treatment for lymphedema should take a multidisciplinary and team approach. The multidisciplinary team could include – but would not be limited to – specialists in nursing, podiatry, dermatology, plastics, oncology, physiotherapy, vascular, and psychology. The clinic should be a participating member of the National Lymphedema Network (NLN) because it is a good resource for healthcare professionals as well as patients. The Marilyn Westbrook Garment Fund is administered by NLN and provides garments to member patients who are in financial need and are treated by NLN-affiliated therapists. The lymphedema clinic should have a minimum of three certified lymphedema therapists who are certified by the Lymphedema Association of North America (LANA). Preferably there should be two physical therapists: one occupational and one physical, and at least one therapist experienced and certified in wound care. There should be a certified fitter for custom garments available at least 1 day a week. Also, the clinic should have a working relationship with garment and supply vendors who provide dependable and timely service.

The necessary supplies for providing CDT should be maintained on-site. Also, under-stockinets of various sizes, compression foam of varied density, and short-stretch bandages in various sizes should be kept in stock. For example, one leg could require three boxes of foam, two 8-cm short-stretch, and four 10-cm short-stretch bandages. The clinic should work with patients to remove any financial barriers that may restrict treatment. It is beneficial for patients to receive arm and leg kits before starting therapy; starter kits can be expensive especially if treatment is necessary for both legs and arms. Also, two sets are needed, one to wash and one to wear. Finally, the treatment room must have a sink, no carpeting, and be large enough to accommodate large patients. The treatment table needs to be safe for supporting up to 600 pounds and can be elevated.

HELPFUL RESOURCES

See Table 168.5 for Sources and websites.

TABLE 168.5 Helpful Resources

Source	URL
Alberta Lymphedema Association	http://www.albertalymphedema.com/
British Lymphology Society	http://www.lymphoedema.org/
International Society of Lymphology (ISL)	https://isl.arizona.edu/
Lymph Notes	http://www.lymphnotes.com/
Lymphatic Education & Research Network	http://lymphaticnetwork.org/
Lymphedema in the News	http://paper.li/bluebonnetfield/1313342568
Lymphedema People	http://www.lymphedemapeople.com/
Lymphedema Treatment Act	http://lymphedematreatmentact.org/
Lymphedema Diary	https://lymphedemadiary.com/
National Association for Rare Disorders	http://rarediseases.org/
National Lymphedema Network Support Community (Inspire)	http://www.inspire.com/groups/national-lymphedema-network/
Ready-Made vs. Custom Sleeve	https://www.lymphedivas.com/sites/default/files/readymadevscustom.pdf
Prognostic and Therapeutic Uncertainty in Lymphedema	https://www.lymphedivas.com/sites/default/files/PrognosticUncertainty.pdf
What You Didn't Know About Compression Garments	https://www.lymphedivas.com/sites/default/files/WhatWeDontKnow.pdf
Exercise for Lymphedema	https://www.lymphedivas.com/sites/default/files/ExerciseforLymphedema.pdf
Lymphedema Risk During Air Travel	https://www.lymphedivas.com/sites/default/files/LymphedemaAirTravel.pdf
Modern Day Compression Garments	https://www.lymphedivas.com/sites/default/files/ModernDayCompressionGarments.pdf

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A complete reference list can be found online at www.expertconsult.com

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Lymphedema: Surgical Treatment

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INTRODUCTION

The lymphatic system is the least understood part of the vascular system. Lymphatic malformations such as chylous disorders, cystic hygromas, and lymphocysts are rare; acquired disorders such as lymphoceles and chylous effusions are also uncommon. However, local interruption and obstruction of the lymphatic vessels occur frequently from either congenital or acquired

causes (see Ch. 167, Lymphedema: Evaluation and Decision Making). In developed countries, most acquired lymphatic obstructions are iatrogenic, caused by medical procedures. In developing countries, the most frequent cause of lymphatic obstruction resulting in chronic lymphedema is filariasis.

The development of lymphedema can be described as an imbalance between the lymphatic load (the amount of lymph that has to be cleared from a body part within a given time)

and the lymphatic transport capacity (the amount of lymph that can be transported out of a body part within a given time), which is dependent on the number and function of lymphatic vessels and nodes (see Ch. 10, Lymphatic Pathophysiology).¹ Reduced lymphatic flow due to obstruction leads to secondary tissue changes, a process that is not yet fully understood. Lymphatic outflow disorders are manifested mainly with advanced secondary changes and chronic lymphedema, a condition that can be difficult to treat unless the underlying problem of reduced lymphatic outflow is resolved. Historically, secondary tissue changes leading to excess fibrous and adipose tissue were treated solely by excisional procedures, without correcting the underlying cause. However, modern surgical concepts have been developed to attempt to correct the underlying pathophysiologic mechanism to the extent possible.

Because conservative therapy consisting of limb elevation, compression garments, complex decongestive therapy, and compression pump therapy should be the first step (see Ch. 168, Lymphedema: Nonoperative Treatment), the question arises whether and at what time surgery is indicated. If the only purpose of surgery is resection, it is wise to reserve it as a last option. If, however, surgical reconstruction is possible, this procedure should be considered and offered to the patient early in the course of lymphedema.

HISTORICAL PERSPECTIVE

Excisional Operations

Surgical Excision

The most radical excisional approach is the classic operation first described by Charles in 1912.² It involves complete and circumferential resection of the skin, subcutaneous tissue, and deep fascia, followed by split-skin grafting. However, this procedure is associated with significant complications, and follow-up studies revealed hyperkeratosis, papillomatosis, and ulcerations in the grafted areas.^{3,4} Modifications of this technique, using the resected skin for grafting and performing the surgery in two stages,⁵⁻¹¹ reduced the surgical trauma and the rate of complications.

Liposuction

A less invasive way to reduce the amount of subcutaneous tissue is liposuction. It was first described by Illouz as a method for treating lymphedema.¹² More recently, Brorson and Svensson demonstrated lasting volume reduction if elastic compression garments are worn after the surgical procedure; this can result in an extremity that is even slimmer than the healthy limb.¹³

Functional Procedures (physiologic +)

Early Techniques

The first attempts to divert lymph from the subcutaneous to the muscular compartment through partial or complete resection of the fascia were described by Lanz and Kondoleon.¹⁴⁻¹⁶ Redirection of lymph from the superficial to the deep compartment is also a component of the Thompson method. Thompson resected the fascia along with parts of the subcutaneous tissue, created a flap in two stages, and de-epithelialized the

rim of the flap to allow the outflow of lymph. Subsequently, he buried the flap near the deep vessels to facilitate the creation of spontaneous lymphatic anastomoses.¹⁷⁻²⁴

The use of veins for the reconstruction of an interrupted lymphatic system was investigated by Holle and Mandl experimentally and performed in two patients clinically.^{25,26} Campisi and colleagues reported on a larger series using this technique.²⁷

Modern Techniques

Currently, the most common way to drain lymph from edematous tissue is the construction of connections between the lymphatic (Fig. 169.1) and venous systems in the periphery. The first reports on lymphonodular and lymphovenous anastomoses were provided by Laine and Howard,²⁸ Nielubowicz and Olszewski,²⁹ Rivero and coworkers,³⁰ and Allen and Taylor.³¹ Degni designed a special needle to facilitate the insertion of lymphatic vessels into veins.^{32,33} Further improvements were described by O'Brien and colleagues using microsurgical techniques.^{34,35} In some patients, excisional methods were combined with lymphovenous shunting. A large cohort of patients successfully treated with microsurgical lymphovenous anastomosis was reported by Campisi and associates.³⁶

However, experimental studies revealed problems with thrombotic occlusion at the site of anastomosis, with a patency of 20% after 5 months of follow-up.³⁷⁻³⁹ Specific preparations that ensured an undisturbed connection to the venous valve led to an improved patency rate of 44% after 6 months.^{40,41} Gloviczki and colleagues reported on results of experimental microsurgical end-to-end anastomoses between normal femoral lymph vessels and a tributary of the femoral vein in dogs and noted a 50% patency rate up to 8 months after the operation.⁴²

Direct reconstruction of the lymphatic system became a possibility only after the development of microsurgery. Before that time, it was commonly thought to be impossible to anastomose lymphatic vessels because of their extremely small diameters. Hence, Danese approximated lymphatic vessels as close to each other as possible and waited for spontaneous regeneration. He was able to demonstrate transport of contrast medium (through the lymphatics) with this technique.⁴³ In a patient with lymphedema of the arm, he mobilized two lymphatic channels proximally and distally, approximated them in the axilla, and achieved a reduction in edema.⁴⁴ Subsequent approaches included interpositioning veins between lymphatic vessels,²⁵⁻²⁷ implanting microsurgical lymph node grafts,^{45,46} and implanting free flaps with lymphatic vessels.^{47,48}

The question of optimal reconstruction material has been the subject of two experimental studies. In a series of 14 rats, 100% of the autologous lymphatic grafts were patent (observations made between days 7 and 119 postoperatively), whereas allogeneic lymphatic grafts were patent only until day 21 after transplantation. When lymphatics were replaced by small veins ($n = 10$), a patency of 70% was observed. Expanded polytetrafluoroethylene implants ($n = 10$) used as lymphovascular conduits were already thrombosed by day 7.⁴⁹ In a comparison of lymphatic and venous interpositional autografts in 71 dogs, all 26 lymphatic autografts remained patent up to the end of the observation period at 24 weeks. Of 30 venous interpositional autografts, only 4 were patent after 1 week. None of the

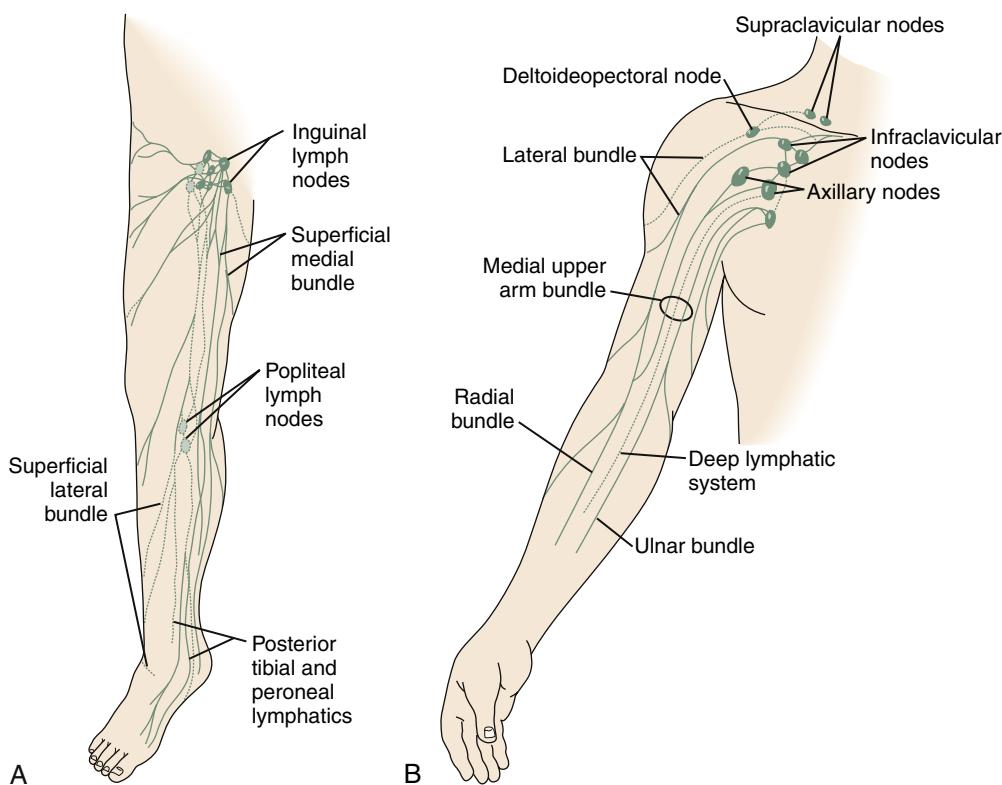


Figure 169.1 (A) Superficial lymphatic system of the lower extremity. (B) Lymphatic system of the upper extremity. (Courtesy Mayo Foundation.)

lympholymphatic anastomoses with silicone tubing showed patency at any time.⁵⁰

Acland and Smith were the first to attempt to anastomose lymphatic vessels.^{51–53} The first successful therapeutic lympholymphatic graft was performed in 1980 by Baumeister in a patient with unilateral lymphedema of the lower extremity.^{54–57} This followed extensive animal experiments on thoracic duct transplants in rats⁵⁸ and the treatment of experimental lymphedema in dogs using lymphatic autografts.⁵³

PREOPERATIVE PLANNING

Visualizing Lymphatic Vessels

Lymphography

Direct contrast lymphography, using oily contrast medium and invasive administration through dissected lymphatic vessels, was introduced by Kinmonth and greatly advanced our knowledge of the lymphatic system.⁵⁹ However, owing to the invasiveness of the procedure (and injury to the lymphatic vessels and lymph nodes), it was found to worsen lymphedema and is rarely used today. Indirect contrast lymphography, using a water-soluble contrast medium injected subepidermally, cannot visualize lymphatic vessels as successfully as direct lymphography and gained only limited use.⁶⁰

Magnetic Resonance Imaging

Attempts to visualize lymphatic vessels with magnetic resonance imaging (MRI) and subdermally administered contrast medium have been promising. This technique may be useful

in the future for preprocedure planning and postoperative assessment of the patency of lymphatic reconstructions.⁶¹ For the detection of vascular lymphatic malformations, MRI is extremely valuable both with and without contrast medium.

MR lymphangiography and lymphoscintigraphy show a clear concordance. Inguinal lymph nodes were better visualized using lymphoscintigraphy, whereas lymph vessels and their abnormalities were better depicted by MR lymphangiography.⁶²

Lymphoscintigraphy

The most important test to evaluate chronic lymphedema and to plan surgical treatment is lymphoscintigraphy. It can be repeated and used for treatment planning and follow-up. It not only evaluates function but also visualizes routes of lymphatic transport. The lymphatic transport index summarizes the findings derived from lymphoscintigraphic studies and allows a semiquantitative evaluation of lymphatic flow without the need for standardized physical movements by the patient. The transport index ranges from 0 for an optimal lymphatic outflow to 45 for no visible transport; normal values are less than 10. It also provides a good basis for follow-up studies and can show lymphatic transport along the route of lymphatic grafts.^{63,64} In measuring lymph transport at regions of interest, it is critical to standardize the dose of radiopharmaceutical and the physical activity of the patient during the procedure.⁶⁵

Dye Injection

Another diagnostic tool that can be used to identify lymphatic channels is the subepidermal injection of a vital dye (patent

blue dye in Europe; isosulfan blue [Lymphazurin] dye in the United States). Normally, lymphatic transport is visualized in the superficial lymphatic collecting system. In pathologic situations, dermal backflow leads to the pooling of contrast medium within the skin, resulting in a cloudlike appearance. Because allergic reactions have been reported, staining of lymphatic vessels with patent blue or isosulfan blue dye is generally performed during surgery under general anesthesia.

Lymphatic Donor Site Assessment

For lymphatic grafting, it is critical to choose and carefully evaluate the proper harvest site for lymphatic vessels to avoid the development of edema secondary to the procedure. Thus, the donor lower extremity must be evaluated by lymphoscintigraphy before harvesting. During the harvest, the narrowing lymphatic system at the medial aspect of the knee and the groin must be left untouched, and all stained lymphatic vessels other than those used as grafts should be left in place. A study including 80 patients with arm edema showed that when this method was used, the harvest site and the untouched leg were not different in size.⁵⁷

No pathologic values were detected after the harvest in a study of 19 consecutive patients, where the donor limb was examined pre- and postoperatively by lymphoscintigraphy. The scintigraphic follow-up was performed 48.6 months following harvest and transplantation. In all patients, the postoperative transport index was close to the preoperative baseline value and within the normal range.⁶⁶

Patient Risk Assessment

Because this type of surgery is performed in the subcutaneous tissue, the surgical risk is generally low, and the procedure is well tolerated. Peripheral lymphovenous shunting is often performed under local anesthesia and is unproblematic as long as the patient tolerates local anesthetics. Because the application of patent blue or isosulfan blue dye can lead to allergic reactions, it should be used only under general anesthesia. Excisional methods typically involve more surgical trauma and the possibility of greater blood loss. Therefore, it is sometimes advisable to perform large excisional operations in two stages. For surgical intervention within the abdomen and thorax, the usual preoperative risk assessment must be done (see Ch. 34, Preoperative Evaluation and Management).

SURGERY

① Autologous Lymphatic Grafting

Indications

Lymphatic vessel grafts can be attempted for the treatment of secondary lymphedema caused by localized obstruction or interruption of lymph vessels and lymph nodes, such as the lymphedema of the arm that develops after breast cancer surgery because of the excision of axillary lymph nodes and possible radiation treatment (see Fig. 169.1B). Patients with

unilateral lower limb lymphedema due to the excision of inguinal or pelvic lymph nodes or pelvic irradiation for malignant disease are also potential candidates for such procedures. Transplantation of lymphatic vessels can be attempted in patients with primary lymphedema if it is caused by localized lymphatic obstruction or atresia, such as unilateral atresia of the pelvic or inguinal lymphatic system.

Surgical intervention should be considered only after a trial of conservative therapy. Conservative treatment should be continued for at least 6 months because spontaneous regression has been reported. However, if conservative therapy is unsuccessful during this time frame, reconstruction should be attempted soon to avoid secondary tissue changes. Unfortunately, treatment is often delayed. In my experience, the mean time between the onset of edema and the patient's presentation for surgery is more than 7 years.

Surgical Technique

The lymphatic grafts are harvested from the patient's thigh (Fig. 169.2). The ventromedial lymphatic bundle contains up to 16 lymphatic vessels.⁶⁷ About one to four lymphatic collectors are dissected in the medial area of the thigh, and great care is taken to spare the lymphatic system where it narrows at the level of the knee and groin. Additional peripheral branches often exist, and these can be dissected as well to create a greater number of peripheral anastomoses.

For free transfer of the graft, a ligature is placed on the lymphatic vessel selected as a graft beneath the inguinal lymph nodes with 6-0 polyglactin 910. One thread is left long to facilitate handling of the graft thereafter. Proximal to the ligature, the lymphatic vessel is transected. At the distal end of the

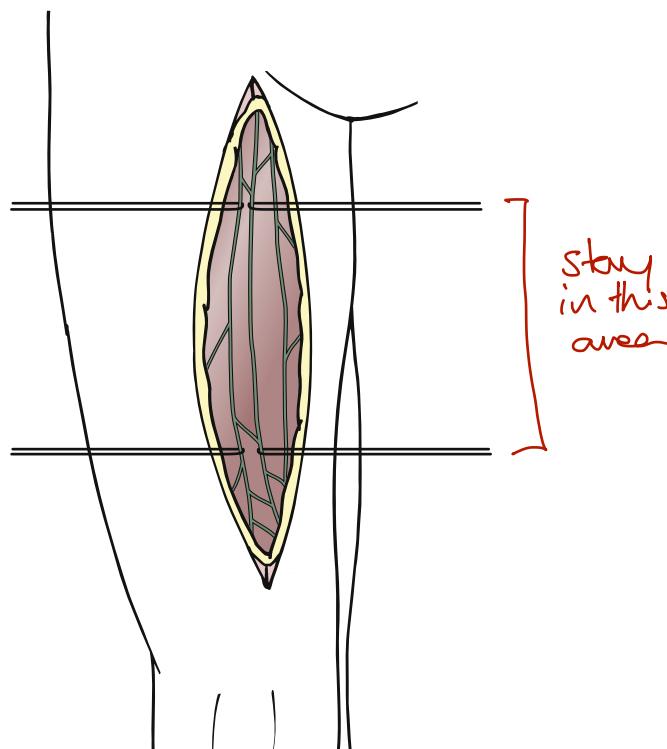


Figure 169.2 Harvesting of lymphatic grafts from the patient's thigh.

proposed graft, the lymphatic vessel is transected proximal to the level of the knee. The lymphatic vessel beneath the transection site is occluded by placing a suture or by using coagulation to avoid lymph leakage.

If a **transposition procedure** is performed, the grafts are transected distally after double ligation and tunneled subcutaneously superior to the pubic symphysis to the contralateral side, where **end-to-end lympholymphatic anastomoses** are performed. In free transfers and in transposition procedures, the graft has to be pulled from one incision to the other (e.g., from the upper arm to the neck or between inguinal regions). To **avoid any friction during tunneling**, tubes (suction catheters) are placed between the two incisions according to the proposed route of the grafts. Thereafter, the grafts themselves can be pulled through the tubes without tension. After removal of the tubes, the grafts remain undisturbed in place within the subcutaneous tissue.

Arm and neck

For arm edema as a result of interventions in the axilla, the grafts are interposed between ascending lymphatic vessels in the upper arm and lymphatic vessels or lymph nodes in the neck (Fig. 169.3). In the upper arm, lymphatic vessels are usually **epifascial** (if not, they may be located subfascially in proximity to the vessels) and are best sought from an **oblique incision** made medially and superior to the route of the brachial vessels. The search is performed under the microscope with a medium (3x to 10x) magnification. In the early stages of lymphedema, the lymphatic vessels have a gray, shiny appearance, and the lumen can be seen clearly after transection. As the lymphatic vessels undergo fibrosis in later stages of lymphedema, it becomes more difficult to discriminate between small nerves and fibrous cords. In this case, the final decision about the potential use of grafting can be made only after transection of the structure.

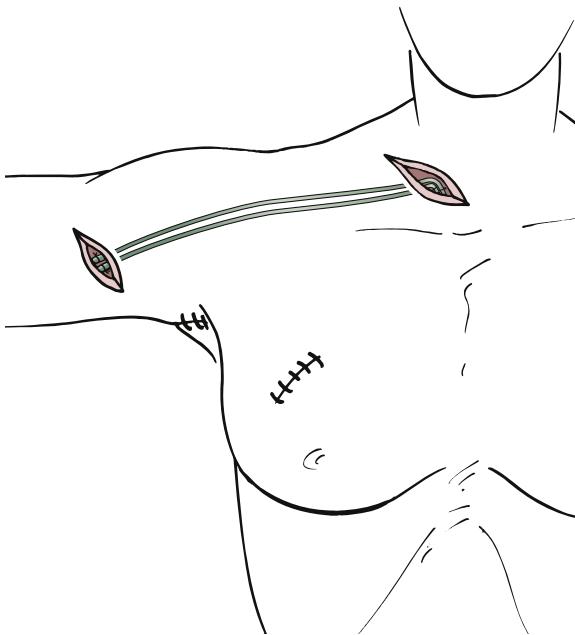


Figure 169.3 Lymphatic grafting in arm edema.

The walls of lymphatic vessels are thinner in the neck than in the arms and legs. Injection of a vital dye in the hair-bearing parietal area above the ear facilitates the search for appropriate vessels. If the lymphatic vessels stain appropriately, recognition is easy. However, suturing in this area is often difficult because of the collapsing, thin-walled vessels. If this is the case, it is also possible to suture the grafts to lymph nodes. A superficial incision is made in the capsule of the node, and the graft is connected with approximately three single interrupted sutures.

To position the grafts between the sites of anastomosis, tubing from a drain is placed in the subcutaneous tissue between the incisions in the upper arm and neck. Subsequently, the grafts are pulled through the wet drain gently and without friction. After removal of the tube, the grafts remain in the subcutaneous tissue free of tension.

Leg

For unilateral edema of the lower extremity, the grafts remain attached to the inguinal lymph nodes, and the distal ends of the grafts are transposed to the opposite thigh with the help of tubing from a drain, which is temporarily interposed between the two incisions at the thigh (Figs. 169.4 to 169.6).

The tension-free technique is used to anastomose the lymphatic vessels under the operating microscope with maximal magnification (Fig. 169.7). The **suture opposite the surgeon** should be performed first. Because of the fragility of the vessels, the vessels are not turned over. Only the back wall is lifted as far as necessary to place a dorsal stitch. One or two additional single stitches complete the anastomosis. In my experimental studies of suture material, absorbable polyglactin was superior to nonabsorbable material. Currently, 10-0 absorbable suture

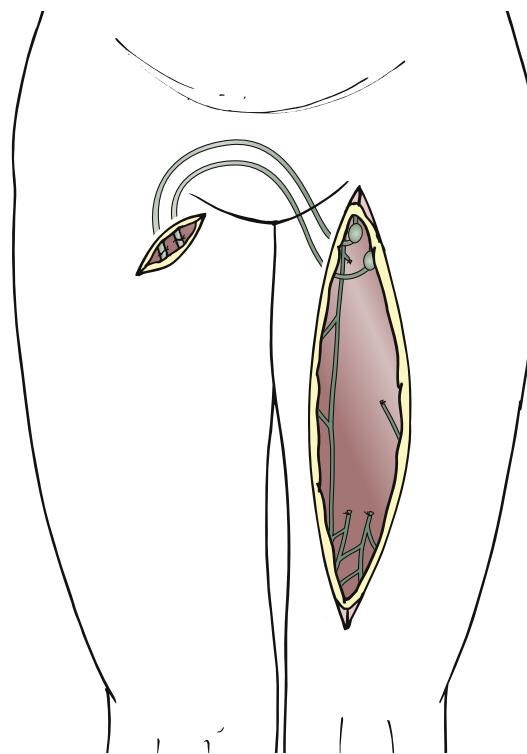


Figure 169.4 Lymphatic grafting in unilateral edema of the lower extremity.

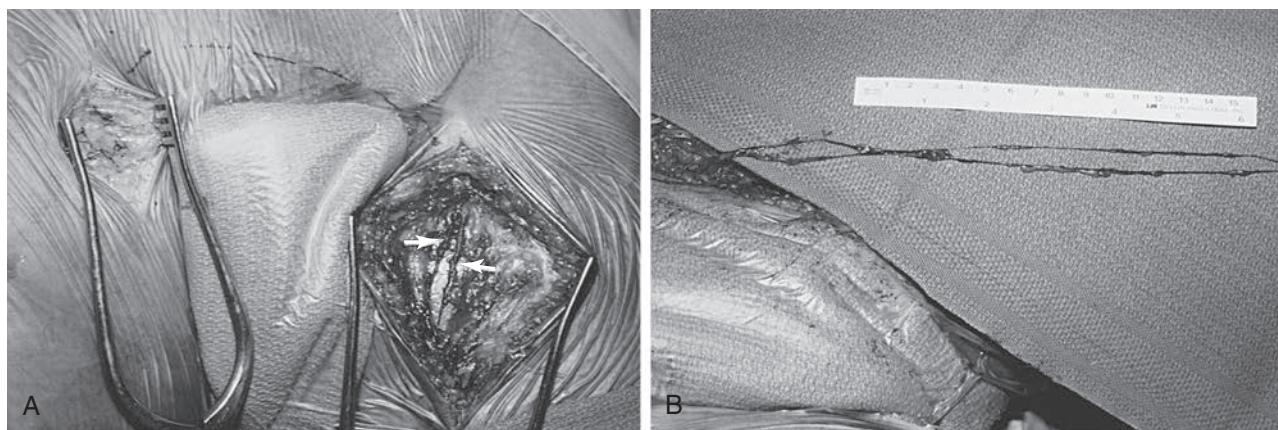


Figure 169.5 (A) Exposure of lymph vessels for suprapubic transposition. Note that two major lymph vessels of the left thigh will be used for grafting (arrows). (B) Two lymphatic grafts divided at the distal thigh are prepared for grafting. (Courtesy Mayo Foundation.)

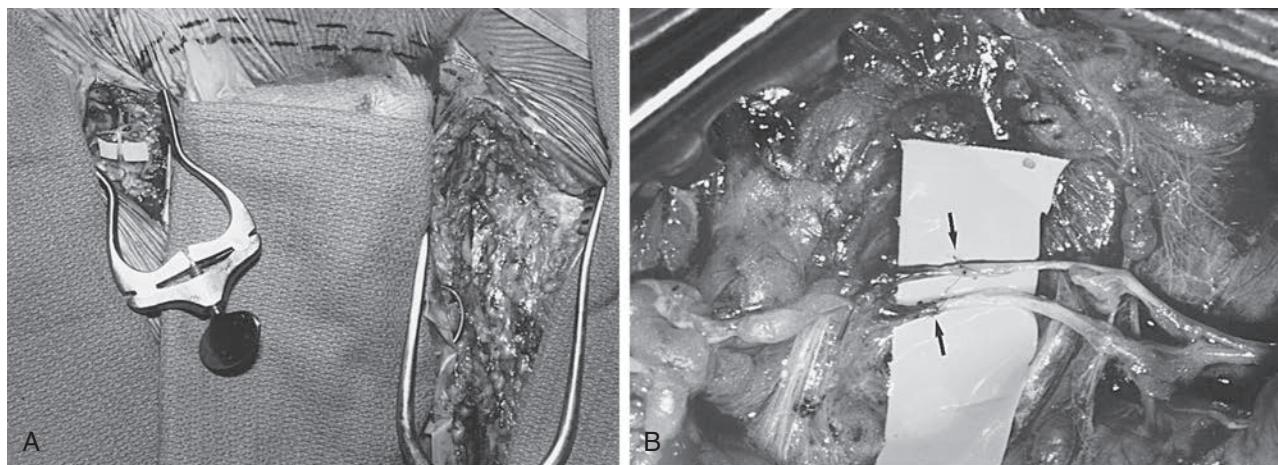


Figure 169.6 (A) Completed suprapubic lymph graft with two lympholymphatic anastomoses in the right groin. Dashed line indicates the position of the suprapubic lymphatic grafts. (B) Magnified photograph of two end-to-end lympholymphatic anastomoses (arrows) performed with 11-0 interrupted monofilament sutures. (Courtesy Mayo Foundation.)

(polyglactin 910) is the thinnest material available, used on a BV-75-4 needle.

Postoperative Treatment

After surgery, elastic bandages are applied, and an elastic compression garment is prescribed for 6 months, at which time discontinuation of the garment is considered. Antibiotics are given for about one week because of the reduced immunologic resistance in patients with lymphedema.

Results

Results were evaluated by volume estimation based on circumferential measurements along the limb in increments of 4 cm. Further, lymphatic outflow was measured semiquantitatively by the lymphatic transport index based on lymphoscintigraphic studies.⁶³ Direct visualization of the grafts is difficult because, with lymphangiography using water-soluble contrast medium, the lymphatic vessels can generally be visualized only over short distances. However, in several patients, patent grafts

could be demonstrated more than 10 years after grafting with this technique.⁶⁸

In a series of 214 patients with arm edema, a significant volume reduction was achieved, from a mean of 3288 cm³ preoperatively to a mean of 2561 cm³ after 8 to 10 days ($P < 0.001$). At a mean follow-up of 2.5 years, the mean volume was 2634 cm³ ($P < 0.001$).⁶⁹

In a group of eight patients with long-term follow-up of more than 10 years, the mean volume was reduced to 2273 cm³ from a mean preoperative volume of 3004 cm³ ($P < 0.001$).⁵⁷

In 145 adult patients with unilateral edema of the lower extremities, the mean preoperative volume of 12,784 cm³ was reduced to a mean of 10,404 cm³ at the time of hospital discharge ($P < 0.001$). After a mean follow-up period of 1.9 years, the volume reduction was sustained, with a mean volume of 10,987 cm³ ($P < 0.001$).⁶⁹ In a group of 12 patients observed for more than 4 years, the volume was reduced to 10,692 cm³ ($P < 0.001$).⁵⁷ The following complications were observed: two cases of erysipelas in the initial group of patients, one

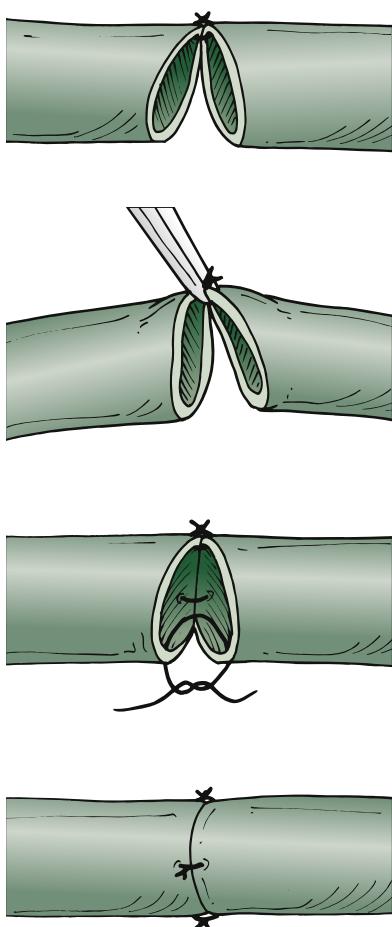


Figure 169.7 Tension-free technique for lympholymphatic anastomoses.

lymphocyst at the harvesting site, and swelling of the lower leg after thrombosis in one patient, and one patient showed a venous bleeding above the clavicle in the night after surgery.

Lymphoscintigraphic studies were performed during a follow-up period of 8 years in 20 patients (12 upper extremities, 8 lower extremities). Of the 20 patients, 17 showed improved lymphatic outflow. In five patients, patent grafts could be demonstrated directly by visualizing the routes of activity.⁷⁰ Figures 169.8 and 169.9 show lymphoscintigraphic studies along with the transport index for two patients with a follow-up period of 6 years. A quality-of-life study in 212 patients who underwent lymphatic grafting showed a significant improvement in the physiologic and the psychologic conditions as well.⁷¹

The functional outcome by dynamic imaging of lymph kinetics after autologous lymph vessel transplantation was studied recently in 177 patients suffering from upper limb lymphedemas. All patients underwent a preoperative scintigraphic baseline study and at least one scintigraphic follow-up. The patients were examined at four different time points after surgery: within 2 weeks (T1); between 6 and 12 months (T2); between 32 and 38 months (T3); and in 19 cases, at least 8 years (T4) after lymphatic grafting. Volume measurements were performed simultaneously.

At T1 the mean reduction in volume difference (RV) between the affected and normal extremity was 73%, and the mean improvement of the lymphatic transport index (ITI) was 28%.

At T2 the RV was 64% and the ITI was 23%, at T3 the RV was 63% and the ITI was 25%, and at T4 the RV was 68% and the ITI 25%. The mean overall correction was by a factor of 2.64.

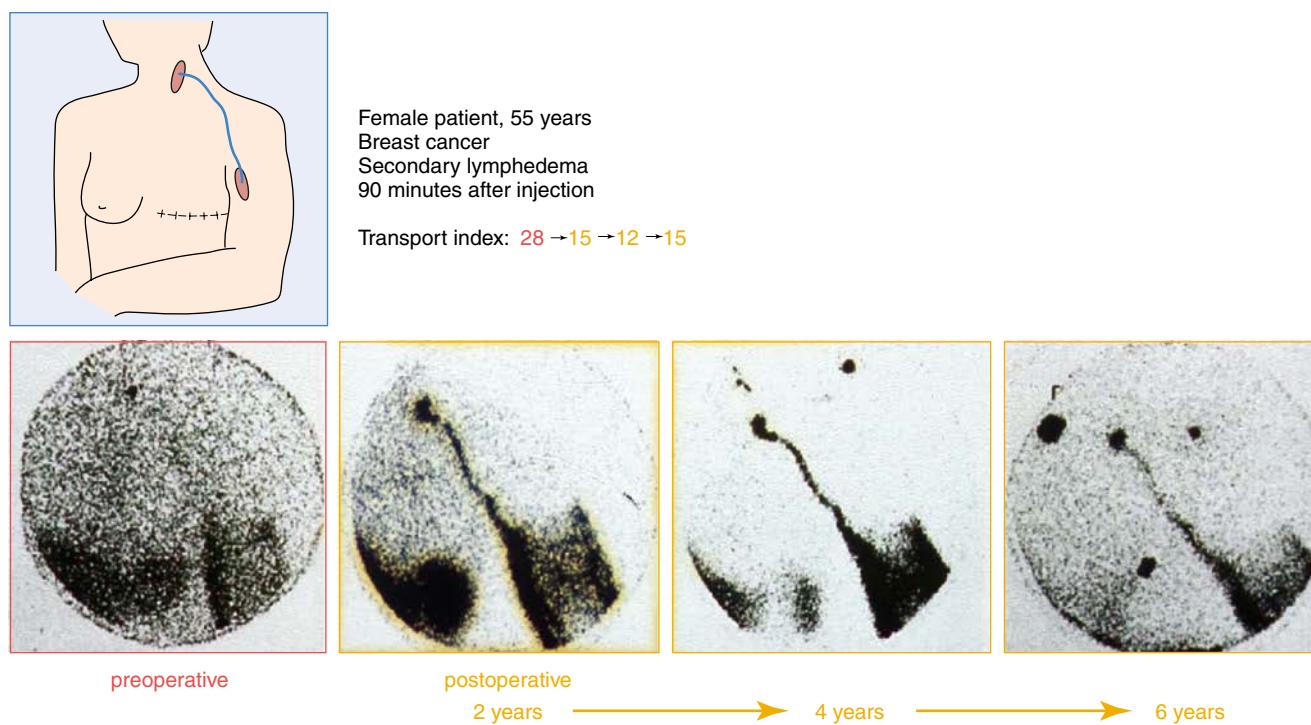


Figure 169.8 Lymphoscintigraphic long-term follow-up after lymphatic grafting in arm edema.

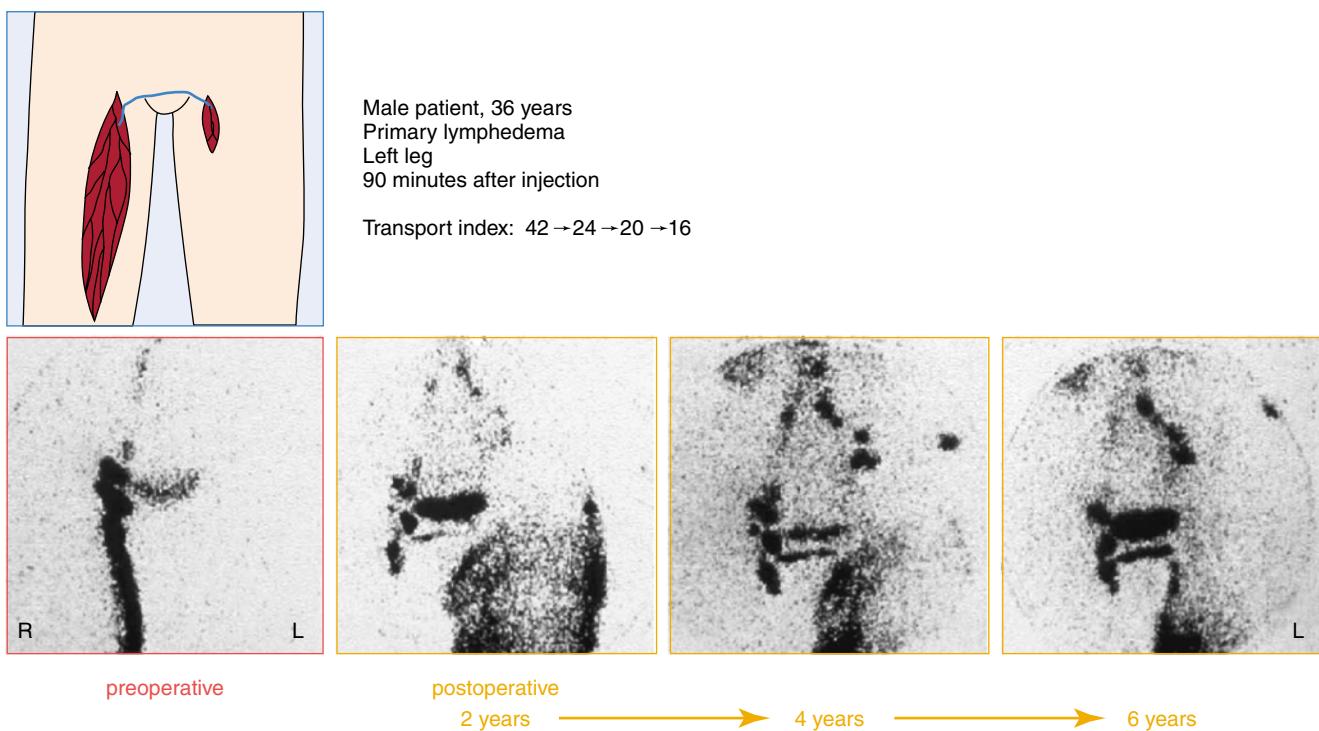


Figure 169.9 Lymphoscintigraphic long-term follow-up after lymphatic grafting in unilateral edema of the lower extremity.

The data confirmed the significantly improved lymph drainage after reconstruction by lymphatic autografts and showed a strong correlation between volumetric and scintigraphic findings.⁷²

Other Direct Reconstructive Methods

Trevidic and Cormier described a method of directly bridging a lymphatic defect with a free flap.⁴⁵ Li and colleagues isolated lymphatic vessels within the flap and created lympholymphatic anastomoses on both sides.⁴⁸ Ho and coworkers used the greater saphenous vein to invaginate the lymphatic vessels and also performed lympholymphatic anastomoses at the peripheral and central ends of the interposition tissue.⁷³ Another attempt to reconstruct a gap in the lymphatic system, described by Becker and associates, consists of free lymph node grafting with the goal of spreading lymphatic connections peripherally and centrally.⁴⁶

Different areas of implantation of the transplanted lymph nodes were reported besides the area of the original defect, such as the wrist and the elbow at the upper limb and distal areas of the lower limb.⁷⁴

However, reports of edema formation after the harvest have been published.^{75,76}

Different aspects of the effect of vascularized lymph node transfer are postulated and under discussion: a pumping force of lymph nodes via intranodal connections between the lymphatic and venous systems, which transports along the micro-surgical venous anastomoses and the enhanced presence of VEGF-C, stimulating the lymphatic network within the flaps around the lymph nodes.^{77,78}

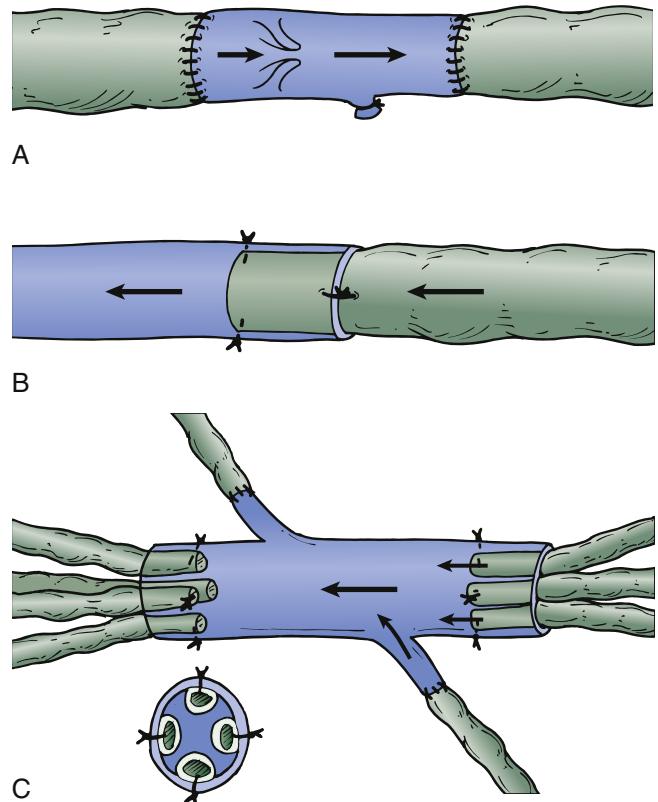


Figure 169.10 Techniques of lymphatic reconstruction with interposition vein graft (A) or lymphovenous anastomosis (B). Technique of invagination of multiple lymphatics into an interposition vein graft: lymphatic–venous–lymphatic anastomosis (C). (Courtesy Mayo Foundation.)

Another method of reconstructing an interrupted lymphatic system using veins was proposed by Mandl⁷⁹ and described in a series by Campisi and colleagues²⁷ (Fig. 169.10). The study included 64 patients, 59 with leg lymphedema and 5 with postmastectomy edema. Marked reduction was reported in 40 patients, moderate reduction in 18 patients, and mild reduction in 6 patients.

② Lymphovenous Anastomosis

Indications

Patients with secondary lymphedema of recent onset without previous episodes of cellulitis or lymphangitis are potential candidates for surgical treatment unless they can be managed easily with conservative measures. In the late stage of lymphedema, fibrosis and valvular incompetence of the main lymph vessels develop, the intrinsic contractility of the vessel wall is lost, and interstitial pressure decreases because of secondary changes in the subcutaneous tissue (see Ch. 10, Lymphatic Pathophysiology). The chance of successful lymphovenous anastomosis in such limbs is clearly diminished. Because venous hypertension impedes forward flow through the anastomosis, patients with chronic venous insufficiency are not candidates for this operation.

Preoperative Evaluation

Isotope lymphoscintigraphy is usually sufficient for preoperative imaging of the lymphatic system. In ideal candidates, it confirms the presence of dilated infrainguinal lymph vessels with proximal pelvic lymphatic obstruction. Although it does not differentiate between primary and secondary lymphedema, and even though it is primarily a functional study rather than an anatomic one, semiquantitative lymphoscintigraphy with technetium Tc-99m–antimony trisulfide colloid can reliably identify the pattern of lymphatic transport.⁸⁰ In selected patients, direct contrast lymphangiography can be performed to show the fine details of the lymphatic circulation.

Progress in visualizing superficial lymphatic vessels has been made with the use of indocyanine green fluorescence lymphography. Indocyanine green is injected intradermally. With the help of a near-infrared camera, the lymphatic vessels are detected as blurred linear images, whereas dermal backflow is seen as a spotty image. This facilitates the search for superficial lymphatic vessels appropriate for lymphovenous anastomoses.⁸¹

Other preoperative tests include noninvasive venous studies and duplex scanning of the deep veins. Computed tomography (CT) is used in most patients to exclude an underlying mass or malignant tumor. Once the decision to perform surgery is made, the patient is hospitalized for 24 to 48 hours to elevate the extremity in a lymphedema sling and to allow the use of intermittent compression with a pump to decrease the volume of the extremity.

Surgical Technique

Leg

For lower extremity lymphedema, a transverse incision at the midthigh or a longitudinal incision close to the saphenofemoral

junction is performed to allow dissection of the lymphatic of the superficial medial bundle. The greater saphenous vein and any tributaries are also dissected. An attempt is made to visualize the lymph vessels by injecting 5 mL of isosulfan blue dye subcutaneously; half this amount is directed toward the first interdigital space and half toward the area 10 to 15 cm distal to the incision site. Because of lymphatic obstruction, even lymph flow in patent lymphatics may be minimal, and the dye usually is not visible during dissection. With experience, the whitish fluid-filled lymphatics, frequently with vascularized adventitia, can be distinguished from small subcutaneous nerves or fibrotic bands.

If contrast lymphangiography is performed within 24 hours of the operation, the contrast-filled lymphatics are easily identifiable and can be located during the operation with an image intensifier and a C-arm. In some patients, contrast lymphangiography helps avoid many hours of unsuccessful searching for patent lymphatics in the groin. Once the lymphatic vessels and the veins are isolated, a standard microsurgical technique is used to perform an end-to-end anastomosis with six to eight interrupted 11-0 monofilament sutures. The operation is performed with a Zeiss operating microscope with 4x to 40x magnification.

Arm

For arm lymphedema, the lymphatics are dissected through a transverse incision at the wrist or in the midcubital fossa or through a longitudinal incision at the medial aspect of the arm, a few centimeters proximal to the elbow. Lymphatics of the superficial medial lymphatic bundle are usually used for anastomoses, which are performed with the midcubital, basilic, or brachial veins or their tributaries in an end-to-side or end-to-end fashion.

Postoperative Treatment

Postoperatively, the limb is wrapped with an elastic bandage and elevated 30 degrees. For the arm, this can be accomplished with two pillows; for the lower extremity, the foot of the bed can be elevated.

Results

Objective evaluation of the long-term effectiveness of lymphovenous anastomosis has been difficult. Decrease in the circumference or volume of the extremity, patient satisfaction, decrease in episodes of cellulitis, and improvement in lymphatic clearance as measured by lymphoscintigraphy have been used as the criteria of success. In a review of 14 patients who underwent lymphovenous anastomosis at the Mayo Clinic, only five limbs remained improved at a mean follow-up of 46 months after surgery.⁸² Improvement was observed in four of seven patients with secondary lymphedema but in only one of seven with primary lymphedema. Improvement in lymphatic clearance from the injection site was the only indirect sign of shunt patency. Therefore, the investigators were unable to provide objective evidence of late patency of the lymphovenous anastomoses in these patients.

A large experience with lymphovenous shunts was reported in Australia. O'Brien and colleagues published a well-documented report with long-term follow-up of 90 patients who

underwent lymphovenous anastomoses for chronic lymphedema.⁸³ Although a significant number of patients underwent additional excisional operations, improvement was documented even in those with only lymphovenous anastomoses. Of the latter, 73% had subjective improvement, and 42% had objective long-term improvement. Seventy-four percent of all patients discontinued the use of elastic stockings. However, objective imaging evidence that improvements were caused by patent and functioning lymphovenous anastomoses is still lacking.

The largest experience to date comes from Campisi and colleagues in Italy.^{84,85} This group treated 665 patients with obstructive lymphedema using microsurgical lymphovenous anastomoses and achieved subjective improvement in 87% of their patients. In the 446 patients available for long-term follow-up, the authors observed volume reduction in 69% and discontinuation of conservative measures in 85%. This is a remarkable result that has not yet been duplicated elsewhere. The authors concluded that microsurgical reconstruction early in the course of lymphedema is more effective because the intrinsic contractility of the lymphatic vessel is maintained and the chance of normalizing the lymph circulation is better before significant chronic inflammatory changes develop in the subcutaneous tissue.

Koshima and coworkers from Japan reported significant improvement of lymphedema at a mean of 3.3 years after lymphovenous anastomoses in 8 of 13 patients.⁸⁶ However, Vignes and associates failed to confirm the therapeutic benefit of lymphovenous anastomoses in a group of 13 patients (10 with primary and 3 with secondary lymphedema).⁸⁷ Global assessment of clinical outcome was very good or good in five patients and intermediate in another five, but the operation failed to improve the volume of lower limbs or to reduce the frequency of erysipelas. A follow-up study of 237 lymphaticovenous side-to-end anastomoses, performed in 57 patients with lymphedema, showed at least one patent anastomosis in 34 patients by use of indocyanine green fluorescence lymphography after a mean follow-up period of 14 months. In 23 patients, no patent anastomosis was seen. There was no significant difference in limb volume reduction between the two groups.⁸⁸

In one surgical technique, the so-called lymphaticovenous implantation, the lymph vessel is inserted into the lumen of a bigger vein together with the surrounding fat, including the lymphatic capillaries.⁸⁹ The same procedure is also used to improve lymphatic drainage of the dermal lymphatics.⁸¹

A large series of patients treated for secondary and primary lymphedema by supermicrosurgical lymphovenous anastomosis and lymphaticovenous implantation was published by Demirtas and colleagues.^{90,91} In 40 patients with unilateral primary lymphedema, a mean reduction of 56% of the surplus volume was seen after a follow-up period of 13.3 months. Although only 17% of the patients had complex physical therapy before surgery, all stage 4 patients and most stage 3 patients (according to Campisi's classification) used custom-made pressure garments after surgery. In 20 patients with unilateral secondary lymphedema, a mean reduction of 60% was seen after

a mean follow-up period of 12.8 months; 50% of the patients did not receive complex physical treatment before surgery, and continuous custom-made pressure garments were used in two of five stage 3 lymphedema patients and in all stage 4 lymphedema patients. There was no significant relationship between the number of microsurgical anastomoses or implantations and the mean reduction in volume.

A systematic review of 32 patient-reported outcome studies following lymphovenous bypasses and lymph node transplants showed an improved quality of life in most patients.⁹²

Resection

Resection involves the removal of the lymphedematous, fibrotic, and frequently sclerotic subcutaneous tissue of the limb. Liposuction is a more recent technique used to accomplish resection. Other open excisions are usually performed during staged procedures. If the skin is diseased and requires resection, coverage with skin grafts may be necessary.

Liposuction

Surgical technique

Brorson and Svensson advocate use of liposuction in patients with postmastectomy lymphedema to reduce the volume of the extremity.¹³ The rationale behind this treatment is that chronic lymphedema causes hypertrophy of the subcutaneous fat. Removal of the hypertrophied and edematous adipose tissue is performed through 3-mm-long incisions (20 to 30 incisions) with vacuum aspiration. During the postoperative course, controlled compression therapy (CCT) is administered to decrease bleeding complications and to help reduce the volume of the limb.

Results

In a report by Brorson and Svensson, preoperative and postoperative arm edema volumes were measured by the water-displacement technique, and lymph transport was assessed by lymphoscintigraphy.⁹³ Twenty-eight patients were prospectively matched and divided into two groups. One group received liposuction combined with CCT, and one group received CCT alone. Liposuction combined with CCT was more effective than CCT alone; the edema reduction figures after 1 year were 104% for liposuction with CCT and 47% for CCT alone ($P < 0.0001$). Continued use of compression garments is important to maintain the primary surgical outcome. Liposuction can be useful in patients with no functioning lymphatics, but in others, the destruction of functioning lymphatics and worsening of the edema are possible.

The need of continuing compression therapy can be reduced if secondary arm lymphedemas are initially treated by autologous lymphatic grafting to bypass the axilla and restore lymphatic flow. Liposuction is used thereafter as a secondary procedure in patients with excess of adipose tissue. Eighteen out of 28 consecutive patients did not need any supportive therapy beyond 6 months after the initial postoperative period of 6 months.⁹⁴

Staged Subcutaneous Excision Beneath Flaps

Surgical technique **Homans**

The technique described by Miller and colleagues is most popular in the United States.^{95–98} The excision is performed in two or sometimes three stages, starting medially during the first operation. A bloodless field is obtained with a pneumatic tourniquet. An incision is made along the ankle beginning 1 cm posterior to the medial malleolus and extending proximally into the midthigh. Flaps approximately 1.5-cm thick are elevated anteriorly and posteriorly to the midsagittal plane in the calf, with less extensive dissection in the thigh and ankle. All subcutaneous tissue beneath the flaps is then removed, but the sural nerve is preserved. The deep fascia of the calf is incised over the tibia and resected, sparing the fascia at the knee and ankle to preserve joint integrity. Redundant skin, about 4 to 10 cm wide, is then resected; suction catheters are placed, and the wound is closed in a single layer with 4-0 nylon. In suturing around the ankle and knee, portions of the deep fascia are included in the suture to fix the skin flaps deeply and to ensure contour. The extremity is immobilized with a posterior splint and elevated. The patient is kept on bed rest for 9 days and mobilized afterward wearing tightly wrapped elastic bandages to prevent seroma formation and to promote optimal healing and contour. This regimen is continued for 3 weeks postoperatively.

The second stage, consisting of lateral excision, is performed 3 months later in a similar fashion. During lateral excision, the sensory branches of the peroneal nerve are identified and carefully preserved.

Results

Staged excision underneath skin flaps offers the most reliable improvement of all debulking operations while minimizing the likelihood of postoperative complications. Miller and colleagues reported the long-term results in 38 patients with chronic lymphedema after staged subcutaneous excisions performed beneath skin flaps.⁹⁸ Thirty patients had marked and durable reduction in extremity size with improved function. Episodes of cellulitis were reduced or eliminated. No difference in long-term results was seen in patients with primary versus secondary lymphedema. This series had a remarkably low rate of skin complications (four patients) and a low rate of late disease progression (six patients).

The clinical benefit of excisional operations is directly related to the amount of subcutaneous tissue removed. Patients are susceptible to recurrences and should continue to wear elastic compression stockings. Although good volume reduction is achievable with most of these procedures, prolonged hospitalization, poor wound healing, long surgical scars, sensory nerve loss, and residual edema of the foot and ankle can be significant problems. Because of these potential complications, these procedures are generally offered only to patients with significant, disabling lymphedema that is not responding to medical measures.

PRIMARY CHYLOUS DISORDERS

Chylous disorders are characterized by an accumulation of chyle in abnormal areas of the body. Chylous ascites, chylothorax,

and chylocutaneous fistula may be caused by a malignant tumor (most frequently lymphoma) or by trauma to the mesenteric lymphatics or the thoracic duct, which may also occur during vascular surgical procedures. Primary chylous disorders are usually caused by congenital lymphangiectasia or megalymphatics, which in some patients are associated with obstruction of the thoracic duct. In patients with lymphangiectasia and lymphatic valvular incompetence, chyle may reflux into the lower extremities, perineum, or genitalia.^{93–101} Depending on the site of the dilated lymphatics and the site of the chylous leak, these patients may also have protein-losing enteropathy, chylous ascites, chylothorax, chylopericardium, or reflux of chyle into the lungs and tracheobronchial tree.^{93–111} In a series of primary chylous disorders at the Mayo Clinic, patients presented with lower limb edema (54%), dyspnea (49%), scrotal or labial edema (43%), and abdominal distention (37%).¹⁰³ The cause was primary lymphangiectasia in 66%, yellow nail syndrome in 11%, lymphangioleiomyomatosis in 9%, and other disorders in 18%.¹⁰³

Medical treatment is aimed at decreasing the production of chyle by means of a medium-chain triglyceride diet or occasionally by parenteral nutrition. Repletion of proteins and calcium lost with chyle is as important as strengthening of the body's defense mechanism because lymphocytes and important immunoglobulins are also wasted in these patients. Only surgical treatment can provide long-term improvement and occasionally cure by ligation of the incompetent retroperitoneal lymph vessels and oversewing of the site of the lymph leak. Attempts to reconstruct the obstructed thoracic duct by the creation of thoracic duct–azygos vein or internal jugular vein anastomoses have been reported.^{101,112–114}

Lower Extremity and Genitalia

Many patients with lymphangiectasia and reflux of chyle have unilateral lower extremity lymphedema. The main discomfort for these patients, however, is the intermittent or continuous discharge of chyle from cutaneous vesicles in the lower extremity or the genitalia. The first five patients known to have suffered from this rare condition were described in 1949 by Servelle and Deysson.¹⁰⁵

The preoperative evaluation of patients with chylous reflux into the lower extremity or genitalia should include lymphoscintigraphy (Fig. 169.11A). However, contrast lymphangiography is the definitive test to confirm the diagnosis and to localize the dilated retroperitoneal lymphatics and, frequently, the site of lymph leak. MRI with contrast enhancement may provide more precise information in the future.

Lymphography is increasingly used as a minimally invasive therapy for lymphatic injuries, sometimes combined with a lymphatic intervention, such as an embolization.¹¹⁵

Surgical Treatment

The only effective technique to control the reflux of chyle and its drainage through skin vesicles in the perineum, labia, scrotum, or lower extremity is radical excision and ligation of the incompetent retroperitoneal lymph vessels. Gloviczki and

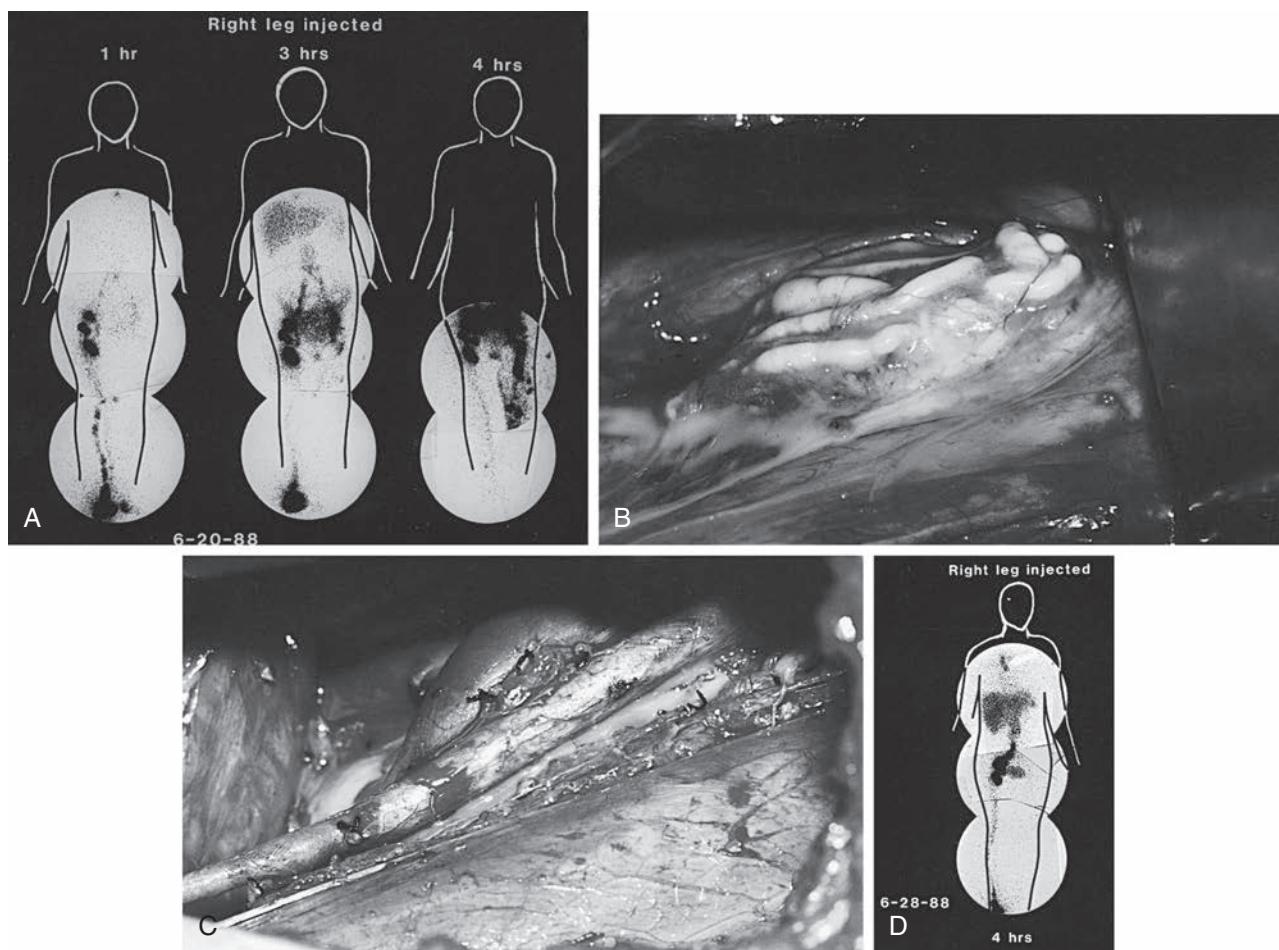


Figure 169.11 (A) Right lower extremity lymphoscintigram in a 16-year-old girl with lymphangiectasia and severe reflux of chyle into the genitalia and left lower extremity. Injection of the isotope into the right foot reveals reflux into the pelvis at 3 hours and into the left lower extremity at 4 hours. (B) Intraoperative photograph reveals dilated, incompetent retroperitoneal lymphatics in the left iliac fossa containing chyle. (C) Radical excision and ligation of the lymph vessels were performed. In addition, two lymphovenous anastomoses were created between two dilated lymphatics and two lumbar veins. (D) Postoperative lymphoscintigram reveals no evidence of reflux at 4 hours. The patient has no significant reflux 4 years after surgery. (From Gloviczki P, Calcagno D, Schirger A, et al. Noninvasive evaluation of the swollen extremity: experiences with 190 lymphoscintigraphic examinations. *J Vasc Surg*. 1989;9:683.)

coworkers used the technique of Servelle and performed the entire reflux operation in two stages through flank incisions by the retroperitoneal approach.¹⁰³ Four hours before the procedure, the patient ingested 60 g of butter and 8 oz of whipped cream. The fatty meal allowed ready visualization of the retroperitoneal lymphatics during exploration (see Fig. 169.11B–D). Ligation of the lymph vessels should be done with the utmost care to avoid tearing or avulsion of the lymphatics, resulting in residual leaks or rupture. In recent years, sclerotherapy of the dilated lymphatics has been added to ligation to increase the efficacy of the operation. Tetracycline solution, 500 to 1000 mg diluted in 20 mL of normal saline, is injected directly into the dilated retroperitoneal lymph vessels to provoke obstructive lymphangitis.

As reported by Molitch and associates, percutaneous CT- or MRI-guided cannulation of these dilated lymphatics may be possible, and sclerotherapy to decrease reflux can be performed repeatedly if necessary.¹⁰⁷ Lymphovenous anastomoses with the dilated lymphatics can also be performed. Reflux

of blood into the dilated and incompetent lymphatics can occur, however. A competent valve on the venous side completely avoids reflux and increases the chance of successful lymphatic drainage.^{108,112}

Results

The largest group of patients studied was reported by Servelle, who operated on 55 patients with chylous reflux into the lower extremity or genitalia and reported a durable benefit in most patients.¹⁰⁰ In Kinmonth and Cox's series of 19 patients who underwent ligation of the retroperitoneal lymphatics for chylous reflux to the limbs and genitalia, permanent cure was achieved in five patients, and alleviation of symptoms – frequently after several operations – occurred in 12 patients.¹⁰¹ No improvement or failure was noted in only two cases. Noel and coworkers reviewed the results of 35 patients with primary chylous disorders treated during a 24-year period.¹⁰⁸ Twenty-one patients (60%) underwent 27 surgical procedures. Nineteen procedures were performed for chylous ascites or reflux;

10 of these patients (53%) underwent resection of retroperitoneal lymphatics with or without sclerotherapy, 4 (21%) had lymphovenous anastomoses or saphenous vein interposition grafts, 4 (21%) had peritoneovenous shunts, and 1 (5%) had a hysterectomy for periuterine lymphangiectasia. All patients improved initially, but 29% had a recurrence of symptoms at a mean of 25 months (range, 1 to 43 months). Three patients with leg swelling had postoperative lymphoscintigraphy confirming improved lymphatic transport and diminished reflux.

Chylous Ascites

Chylous ascites usually results from intraperitoneal rupture of the mesenteric or retroperitoneal lymphatics or from exudation of chyle into the peritoneal cavity.¹⁰⁸ The evaluation of such patients should include CT or MRI to exclude abdominal malignant disease. The diagnosis of lymphangiectasia is confirmed by bipedal contrast lymphangiography. Paracentesis is both diagnostic and therapeutic.

Surgical Treatment

If conservative measures fail and ascites returns, abdominal exploration should be performed after a fatty meal, as described previously. If chylous ascites is due to primary lymphangiectasia, abdominal exploration may reveal ruptured lymphatics, which can be oversewn. Some patients develop large chylous cysts, which should be excised (see Fig. 169.11). If the condition is associated with protein-losing enteropathy and the disease is localized to a segment of the small bowel, the bowel segment should be resected. The outcome of the operation is usually good if a well-defined abdominal fistula is found. However, if the mesenteric lymphatic trunks are fibrosed, aplastic,

or hypoplastic, and exudation of chyle is the main source of the ascites, the prognosis is poor and recurrence is frequent.

Results

Browse and coworkers treated 45 patients with chylous ascites.¹⁰² The age at presentation ranged from 1 to 80 years (median, 12 years). Thirty-five patients had an abnormality of the lymphatics (primary chylous ascites); in the remaining 10, ascites was secondary to other conditions, principally non-Hodgkin lymphoma (six patients). Surgery (fistula closure, bowel resection, or insertion of a peritoneovenous shunt) was performed in 30 patients. Closure of a retroperitoneal or mesenteric fistula, when present, was the most successful operation, curing 7 of 12 patients. In those patients who develop chylous ascites from iatrogenic trauma, frequently after aortic reconstructions, a short period of conservative management is justified. If chylous ascites reaccumulates, reoperation with ligation of the fistula is the most effective treatment. Campisi et al. reported on 12 patients with a mean follow-up of 5 years; there was 1 death after 1 year, 3 mild recurrences, and 1 major recurrence that was treated.¹¹⁶

Results with peritoneovenous shunts have been mixed; patency is usually judged by the recurrence of ascites. In Browse and coworkers' experience with nine peritoneovenous shunt placements, all occluded within 3 to 6 months after insertion.¹⁰² Noel and colleagues used the LeVeen shunt with good results, although one of four patients developed symptomatic superior vena cava syndrome because of thrombosis around the shunt.¹⁰⁸

Chylothorax

As with chylous ascites, the most frequent cause of chylothorax is trauma or malignant disease.¹¹³ Primary lymphatic

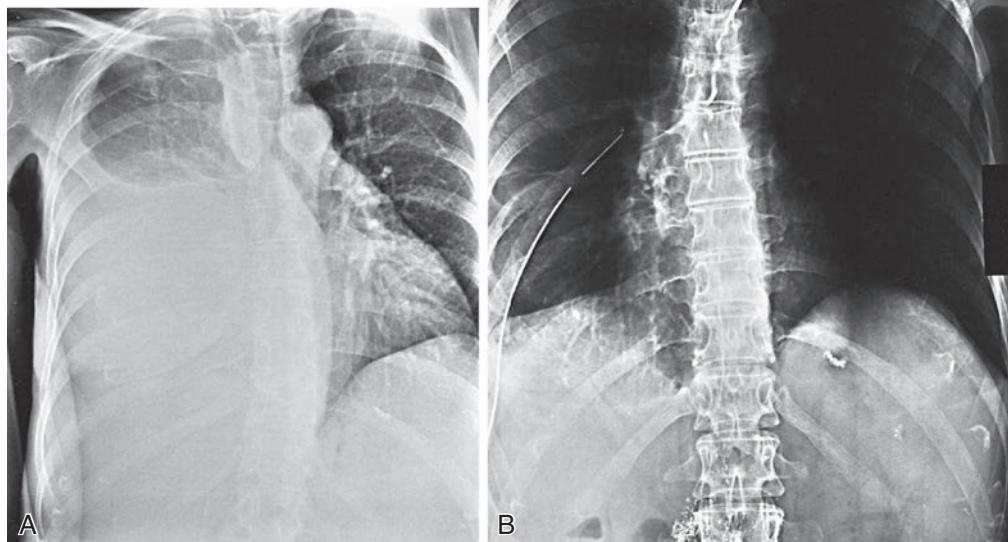


Figure 169.12 (A) Right chylothorax in a 63-year-old woman. (B) Bipedal lymphangiography confirms thoracic duct obstruction at the base of the neck. Note contrast medium in the supraclavicular and left axillary lymphatics (arrows).

disorders that cause chylothorax include lymphangiectasia with or without thoracic duct obstruction. However, chylothorax may also result from chylous ascites passing through the diaphragm. In these patients, the chylothorax is cured when the chylous ascites is controlled. Preoperative lymphangiography should be performed in these patients because it may localize the site of the chylous fistula or document occlusion of the thoracic duct (Fig. 169.12). Thoracentesis usually is not effective in curing the disease, and chyle that leaks from the thoracic duct or one of the large intercostal, mediastinal, or diaphragmatic collaterals reaccumulates. Injection of tetracycline is frequently ineffective because it is diluted by the leaking chyle.

Surgical Treatment

The best treatment of chylothorax is surgical pleurodesis with excision of the parietal pleura and prolonged pleural suction.^{109,113} After the patient has eaten a fatty meal, thoracotomy or video-assisted thoracoscopy is performed, and the leaking lymphatics are oversewn or clipped. This is followed by pleurodesis. In the Mayo Clinic series, eight procedures for chylothorax consisted of thoracotomy with decortication and pleurodesis (four patients), ligation of the thoracic duct (three patients), and resection of a thoracic duct cyst (one patient), with excellent early results in all patients.¹⁰⁸

Thoracic Duct Reconstruction

If occlusion of the cervical or upper thoracic duct (Fig. 169.13) is the cause of lymphangiectasia and reflux of chyle into the pleural or peritoneal cavity, thoracic duct–azygos vein anastomosis can be attempted to reconstruct the duct and improve lymphatic transport. Preoperative imaging of the duct with contrast pedal lymphangiography is important because occlusion of the entire duct precludes anastomoses.

The operation is performed through a right posterolateral thoracotomy, and the anastomosis between the lower thoracic duct and the azygos vein is performed in an end-to-end fashion with 8-0 or 10-0 nonabsorbable interrupted sutures and magnification with loupes or an operating microscope. Only a few patients undergoing this operation have been described.^{101,113} Both patients operated on by Gloviczki's group¹¹⁷ had good immediate patency, and excellent flow of chyle was observed through the anastomosis intraoperatively (Fig. 169.14). Although neither had postoperative contrast lymphangiography, recurrent chylothorax (the main indication for the procedure) ultimately resolved in both. Browne et al. reported two successes in three patients who underwent thoracic duct reconstruction.¹¹³ Kinmonth and Cox performed this procedure in two patients and concluded that the anastomosis alone is not effective for decompressing the thoracic duct; ligation of the abnormal mediastinal lymphatics and oversewing of the sites of lymphatic leak are also necessary.¹⁰¹

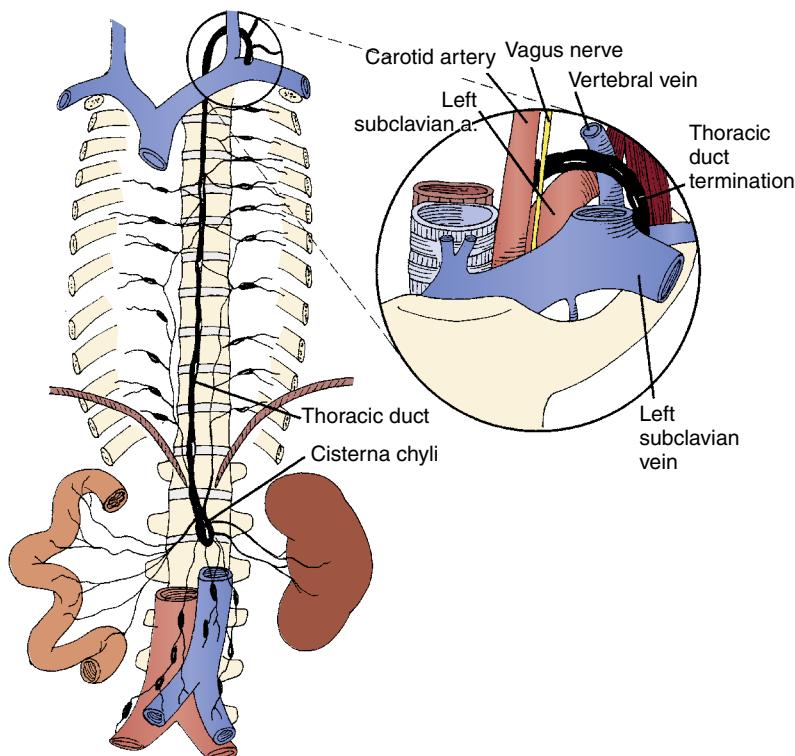


Figure 169.13 Cervical and thoracoabdominal anatomy of the thoracic duct.

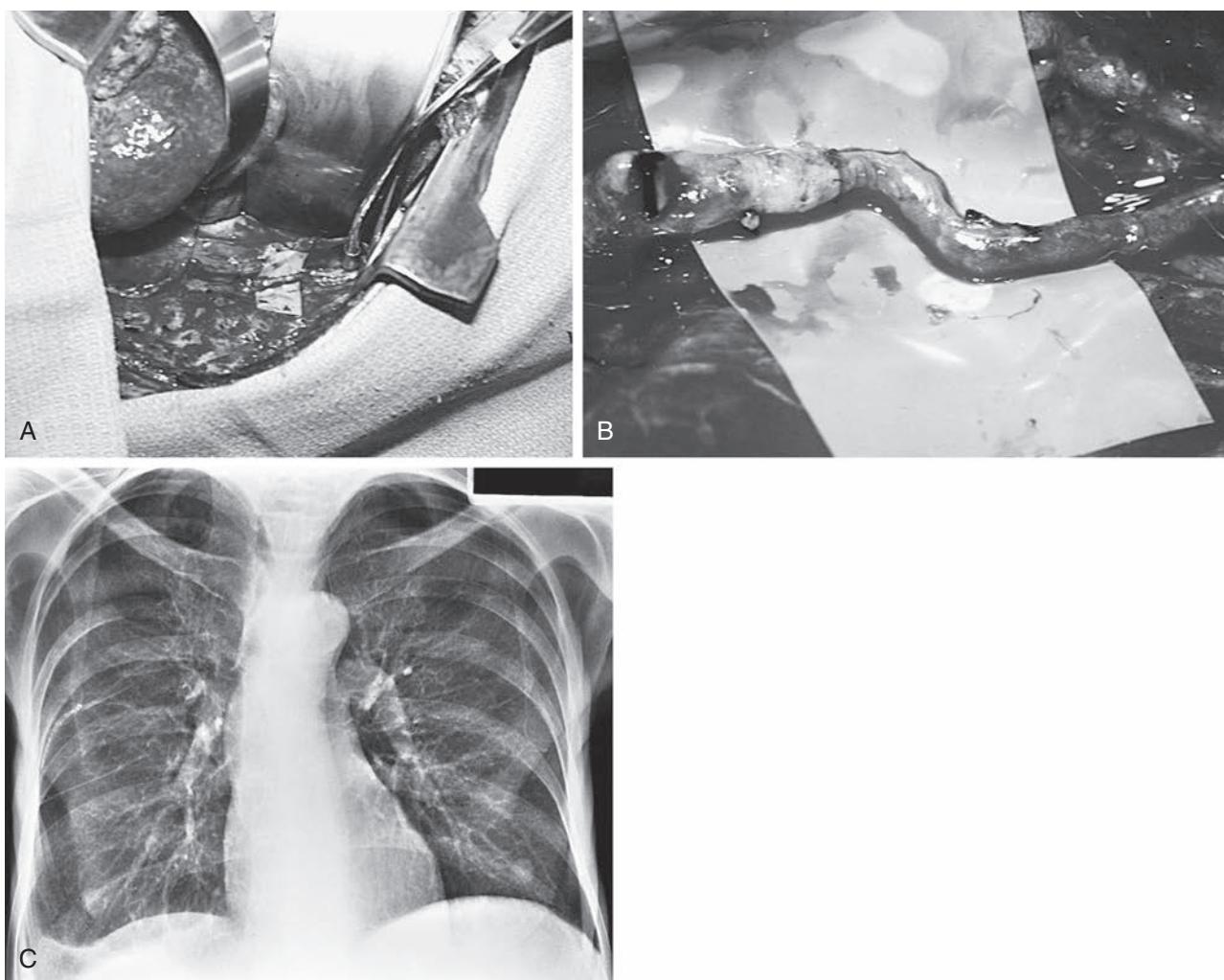


Figure 169.14 (A, B) Thoracic duct–azygos vein anastomosis performed through a right posterolateral thoracotomy in an end-to-end fashion with interrupted 8-0 polypropylene (Prolene) sutures. (C) Chest radiograph 2 years later confirms the absence of chylothorax.

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Congenital Vascular Malformations: General Considerations

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Based in part on a previous edition chapter by Byung-Boong Lee and J. Leonel Villavicencio

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Our understanding of why some children are born with imperfections while the majority are born with normal anatomy has made a tremendous improvement through the last half century.¹ These often disfiguring anomalies are commonly seen by both general practitioners and specialists but the spectrum of congenital vascular malformations (CVMs) is so wide and complicated that it often requires a wide range of specialists dedicated to their study and treatment as a challenging problem.

DEFINITIONS

The term “congenital vascular malformation” (CVM) is used to describe malformed vessels resulting from *arrested* development during various stages of embryogenesis.^{2,3} It is the outcome of a congenital defect in the vascular system and is therefore present at birth, although it is not always clearly identifiable immediately. CVMs may involve one or all three circulatory systems – arterial, venous, and lymphatic – either as a predominant form (e.g., venous malformation) or as a mixed condition (e.g., hemo-lymphatic malformation). The lesions originating from the “early” stage of embryogenesis keep the unique condition of continuing to grow regardless of type.

CVMs may be confused with a more common vascular anomaly, the infantile or neonatal hemangioma.^{4,5} Although both CVMs and hemangiomas are vascular anomalies, the conditions are fundamentally different not only in their anatomic, histologic, and pathophysiologic findings but also in their clinical course (Fig. 170.1).^{5,6} A true hemangioma is a vascular tumor that originates from endothelial cells. It usually appears in the early neonatal period as a rapidly growing tumor. It has a distinctive course characterized by a proliferation phase of early, rapid growth followed by an involutional phase of slow regression. Hemangiomas are therefore, “self-limited” to grow in general; involution is usually complete before age 12 years. In contrast, CVMs are “self-perpetuating” continuing to grow when stimulated and generally distinctive at birth as inborn errors, and they grow steadily in parallel with the child’s systemic growth. CVMs never disappear or regress.

NOMENCLATURE AND CLASSIFICATION

In the early 20th century, many physicians, including Maurice Klippel and Paul Trénaunay (1900), reported a congenital anomaly involving skin, soft tissue, bone, and blood vessels.^{7,8} Owing to limited anatomic and pathophysiologic knowledge and a lack of appropriate diagnostic studies, this condition was not properly understood and was simply named after the describing physicians, such as Klippel-Trénaunay syndrome (KTS)^{9,10} and Parkes Weber syndrome (PWS).^{11,12} These eponymous conditions included various clinical findings (e.g., soft tissue swelling, long-bone growth discrepancy), but the primary vascular lesion and secondary nonvascular lesion were not appropriately identified.¹³ This resulted in significant confusion about the true nature of the problem,¹⁴ as well as a lack of essential information about the cause, anatomy, and pathophysiology of these complex vascular anomalies.^{15,16} Modern

diagnostic and therapeutic modalities have provided valuable information on the cause and anatomo-pathophysiology of CVMs.^{17,18}

The Hamburg Classification was established to accommodate the contemporary understanding of CVMs based on anatomy and pathophysiology based on modern diagnostic criteria.^{2,14–16} However, it is still useful for understanding the combined forms of vascular malformations in particular. For example, the vascular components of KTS are now called hemo-lymphatic malformations (HLMs) in the Hamburg classification (a combination of venous, lymphatic, and capillary malformations), whereas the components of PWS consist of venous, lymphatic, capillary, and arteriovenous malformations (Fig. 170.2).^{9–12}

The term angiodyplasia has been replaced with the term congenital vascular malformation to minimize confusion.^{14,19} Finally, the term capillary or cavernous hemangioma²⁰ has erroneously been used to describe a venous malformation and should be removed.^{21,22} Finally, the term hemangioma is correctly used only to identify a genuine hemangioma (i.e., a vascular tumor), not a vascular malformation.²³

Hamburg Classification

The Hamburg classification (Box 170.1) appropriately classifies CVMs according to the underlying anatomic, histologic, pathophysiologic, and hemodynamic status derived from different embryonic stages.^{2,14,16} It is based on a consensus of CVM experts who met at the Seventh International Workshop on Vascular Malformations in Hamburg, Germany, in 1988. This classification has shown its excellent clinical applicability and has been well accepted as a modern classification system.²⁴ It originally divided CVMs into five types based on the predominant vascular component: arterial malformation (AM),^{25,26} venous malformation (VM),^{27,28} arteriovenous malformation (AVM),^{29,30} lymphatic malformation (LM),^{31,32} and combined vascular malformation represented by the HLM.^{33,34} The initial consensus did not include the capillary malformation (CM) because it was believed to lack the clinical significance of other CVMs. However, the addition of CMs was proposed and upheld at subsequent consensus meetings.^{35,36} The Hamburg classification with further modification to accommodate embryological subclassification has been accepted worldwide as a practical guideline for the CVM management, however it is far from perfect, and further improvements are necessary before it completely replaces the old terminology and classifications.

Each vascular malformation is subclassified into extratruncular and truncular forms, based on its embryologic stage of development (see Box 170.1).^{37,38} The clinical behavior of every vascular malformation is dependent on its embryologic characteristics, closely linked to the stage of embryogenesis when arrested development occurred. The varied embryologic characteristics result in a wide range of clinical presentations, unpredictable clinical courses, and erratic responses to treatment, along with potentially high rates of recurrence. The embryologic subclassification of CVMs into truncular and extratruncular allows clinicians to predict the clinical course,

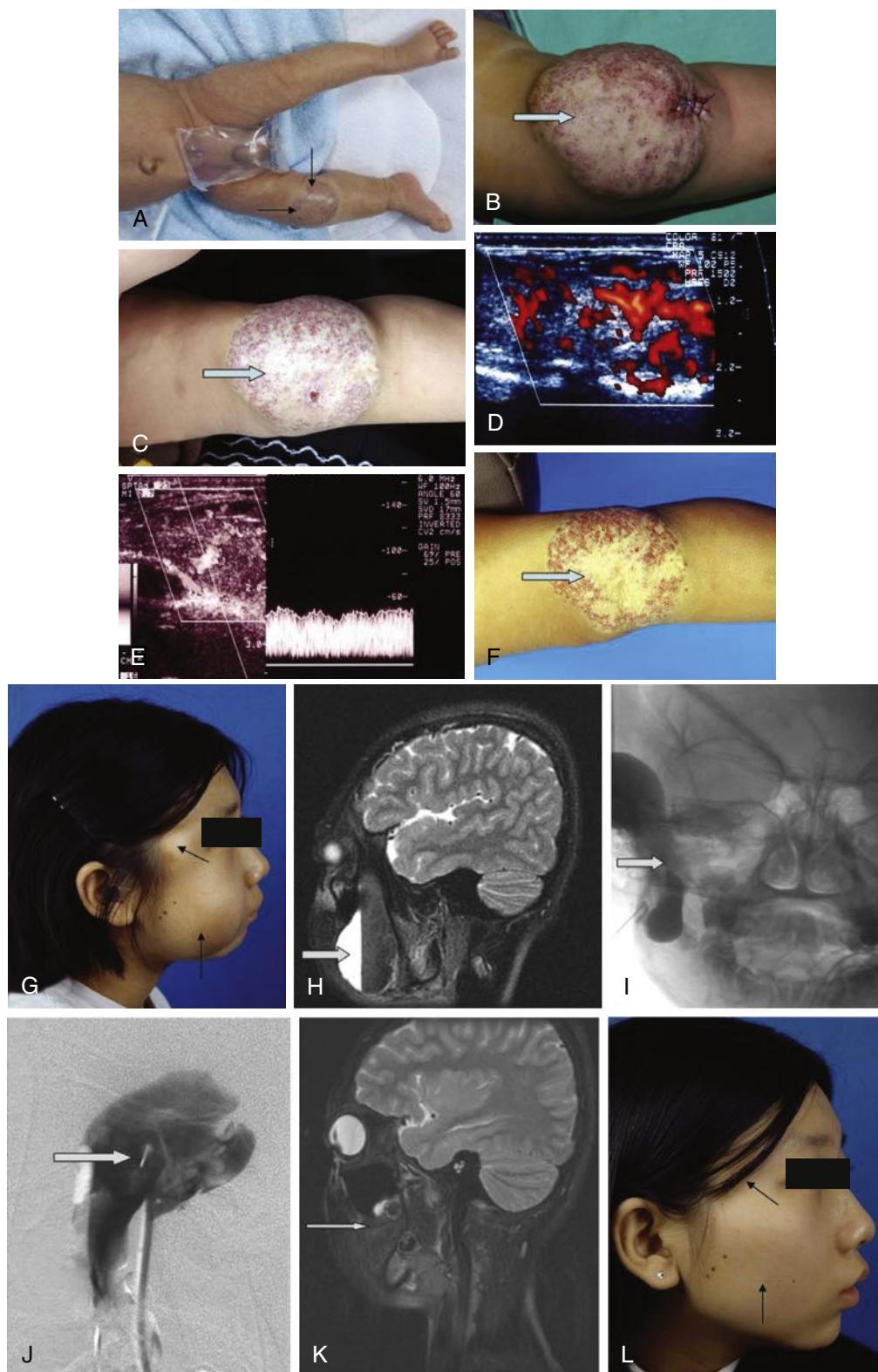


Figure 170.1 Hemangioma and Venous Malformation. (A–F) Hemangioma. In this infant, a hemangioma appeared 1 month after birth in a normal-looking area of the right lower thigh (arrows in A). The swelling grew quickly, reaching its peak size within a year (arrow in B). This was followed by a significant reduction in size during the second year (arrow in C). Duplex ultrasonography during the proliferative stage shows typical vascular hyperactivity along the tumor, with distinctly large feeding arteries (D and E). The lesion regressed almost completely, leaving only an area of skin discoloration, before the child reached 4 years of age (arrow in F). (G–L) Venous malformation (VM). This young girl was born with a swollen right cheek (arrows in G) – the site of a VM. The swelling was noticed at birth, but there was minimal change until menarche. Sagittal T2-weighted MRI depicts a large VM affecting the entire right cheek (arrow in H). Percutaneous direct-puncture angiography demonstrates a large cystic lesion (arrow in I). Percutaneous ethanol sclerotherapy resulted in complete control of the lesion (arrow in J), as shown by MRI (K) and a clinical photograph (L) taken at the 3-year follow-up visit.

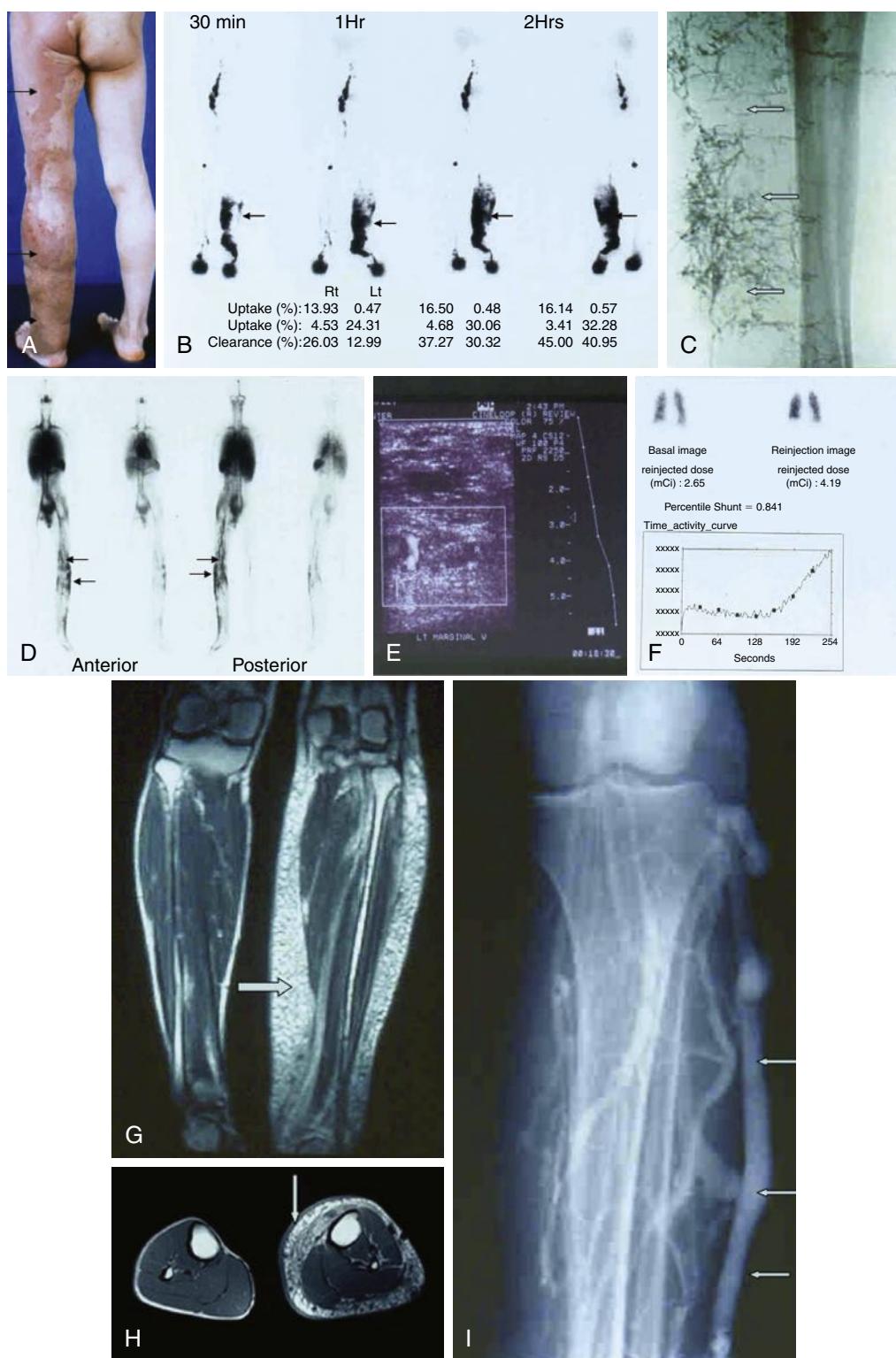


Figure 170.2 Hemo-lymphatic Malformations. (A–I) Klippel–Trénaunay syndrome (KTS). In a patient with typical KTS of the left lower extremity, a port-wine stain covers most of the leg (arrows in A); there is limb swelling as well as leg-length discrepancy. Radionuclide lymphoscintigraphy demonstrates severe dermal backflow (arrows in B) due to primary lymphedema secondary to a truncular lymphatic malformation (LM). Percutaneous direct-puncture lymphangiography reveals a typical lace-pattern appearance (arrows in C) of an infiltrating extratruncular LM. Whole-body blood pool scintigraphy (WBBPS) shows abnormal blood pooling in the entire left lower extremity (arrows in D), suggesting an extratruncular venous malformation (VM) as the third component of the vascular malformation. Further evaluation with duplex ultrasonography (E) reveals a marginal vein as a truncular VM; this lateral embryonic vein is the fourth and last vascular malformation component of KTS. Transarterial lung perfusion scintigraphy (TLPS) results (F) rule out a hidden arteriovenous malformation (AVM). Coronal (G) and sagittal (H) T2-weighted MRI scans demonstrate soft tissue swelling typical of lymphedema (arrows). Ascending phlebography, performed to provide a roadmap for treatment, shows a marginal vein running along the lateral aspect of the left lower leg (arrows in I). (J–P) Parkes Weber syndrome (PWS). The clinical features of PWS are localized to the left lower extremity.

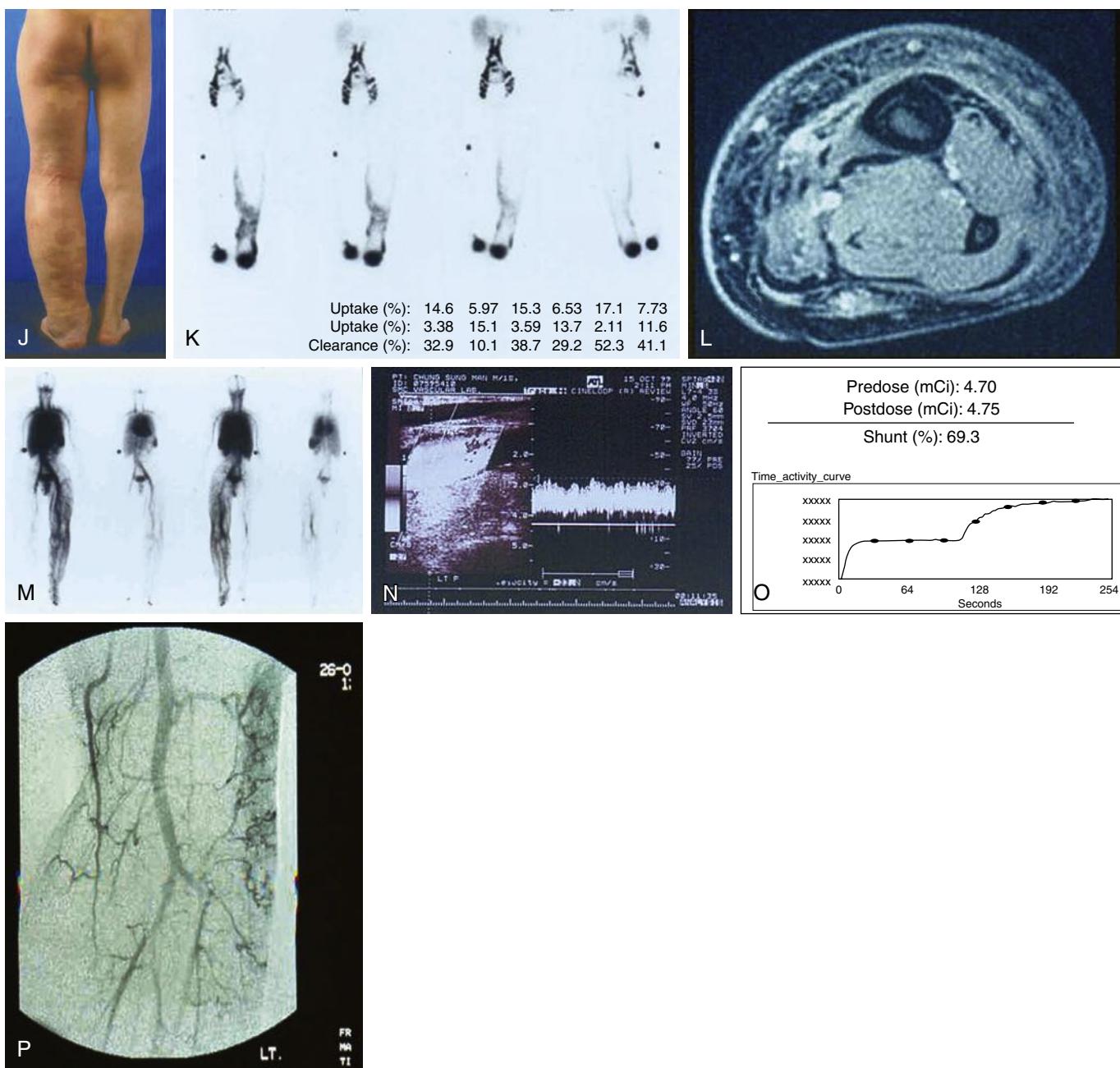


Figure 170.2 Cont'd. (J), similar to the findings in KTS (see A). Radionuclide lymphoscintigraphy (K) and MRI (L) reveal primary lymphedema caused by a truncular LM. WBBPS (M) shows diffuse, abnormal blood pooling throughout the limb due to an extratruncular VM. Duplex ultrasonography (N) depicts a hyperdynamic arterial condition secondary to an AVM. TLPS (O) reveals the precise shunting percentage (69.3%) through the hidden AVM shunts. Arteriography (P) demonstrates multiple superficially located microshunting AVMs scattered throughout the lower extremity. The clinical diagnosis of PWS was confirmed (with LM, VM, AVM, and capillary malformation components).

response to treatment, and likelihood of recurrence.^{39,40} Further information on their distinctive characteristics is included in subsequent sections.

ISSVA/Mulliken Classification⁶

Another classification system, introduced by Mulliken et al., is based on the hemodynamic status of the CVM and provides an

excellent guideline for clinical management.⁴⁻⁶ In the ISSVA (International Society for the Study of Vascular Anomalies)/Mulliken classification, all CVMs are divided into two groups, depending on blood flow: fast-flow lesions and slow-flow lesions. This helps in understanding the complex nature of the hemodynamic status of a CVM. It also accommodated old eponym/syndrome-based classification. Currently, many specialists have adopted parts of this classification system and

BOX 170.1**Hamburg Classification*****Congenital Vascular Malformations – Types**

- Arterial defects
- Venous defects
- Arteriovenous shunting defects
- Lymphatic defects
- Combined vascular defects – hemolymphatic defects
- Capillary defects

Congenital Vascular Malformations – Embryologic Subtypes†**Extratruncular Forms**

- Infiltrating, diffuse
- Limited, localized

Truncular Forms

- Stenosis or obstruction
 - Hypoplasia, aplasia, hyperplasia
 - Membrane; congenital spur
- Dilatation
 - Localized (aneurysm)
 - Diffuse (ectasia)

* Modified from the original classification based on the consensus reached at the international workshop in Hamburg, Germany, 1988.

† Represents arrested development at different stages of embryonic life, with extratruncular being an earlier stage and truncular a later stage. Both forms may coexist.

combined it with the Hamburg classification to enhance the efficacy of overall clinical implication.

INCIDENCE

Due to confusing nomenclatures and definitions in times past, epidemiologic data often misstate the true incidence and prevalence of CVMs.^{41–43} In a comprehensive study of the incidence and geographic distribution of congenital vascular anomalies, Kennedy published data based on 238 studies reporting more than 20 million births.⁴⁴ The overall incidence of CVM was 1.08%, ranging from 0.83% in data obtained from hospital records, birth certificates, and retrospective questionnaires to 4.5% in data from intensive examinations of children. This study highlighted the variability in reporting methods due to differences in terminology and inconsistent diagnostic criteria.

In a large study sponsored by the World Health Organization, Stevenson and colleagues surveyed 426,932 live and still-born births and reported an overall frequency of major and minor malformations of 12.7% in single births and 4.6% in multiple births.⁴⁵

Tasnadi et al. reported overall incidence of the CVM in 1.2% among 3573 3-year-old children they studied.⁴⁶ Among them, they found VM and/or AVM in 0.45%, CM (port-wine skin lesion) in 0.42%, LM/primary lymphedema in 0.14%, and mixed CVM showing phlebectasia, nevus and limb-length discrepancy in 0.34%.

CVMs have a male-to-female ratio of 1:1 and VMs are generally known as the most common type. Among VMs, the extratruncular type is the most frequent lesion, and presents in

either diffuse or localized forms.⁴² Eifert et al. reported on the prevalence of deep venous anomalies/truncular VMs among 257 VMs; phlebectasia was the most frequent (36%), followed by aplasia or hypoplasia of the deep venous trunks (8%) and venous aneurysms (8%).⁴⁷ However, more than 70% of the CVMs are mixed, and these complex forms can include arterial, capillary, venous, or lymphatic elements as well. When both extratruncular LM/lymphangiomas and truncular LMs/primary lymphedema are combined, the overall incidence is equal or higher to those of the VM.

ETIOLOGY

During the first half of the 20th century it was believed that all congenital malformations were inherited, and the terms congenital and inherited were used interchangeably. A remarkable step forward was the finding that chromosomal abnormalities can cause certain types and combinations of congenital malformations

A number of genetic and chromosomal abnormalities have been implicated in the development of CVMs. These have been associated with: (1) exposure to damaging chemical compounds during the first trimester of pregnancy; (2) infections such as rubella, cytomegalic inclusion disease, herpesvirus, and toxoplasmosis; (3) thalidomide and other drugs such as amionopterin, cyclophosphamide, quinine, anticonvulsant drugs, cortisone, and corticotropin; and (4) alcohol, tobacco, and cocaine abuse. Maternal diseases and exposures including goiter, diabetes mellitus, thyroid disease, tuberculosis, hypoxia, and carbon monoxide and lead poisoning have also been identified as potential causes of CVMs.^{35,36,39}

Genetic Background

Although most CVMs are sporadic, autosomal dominant inheritance has also been confirmed to cause various CVMs based on genetic study of families to identify mutated genes.^{48–52} These mutated genes that have an important role in angiogenesis encode tyrosine kinase receptors and intracellular signaling molecules in some patients.⁵² The endothelial-specific angiopoietin receptor TIE2/TEK, located on 9p21 was identified to cause familial mucocutaneous CVMs.⁵² Further studies have shown that somatic mutations in angiopoietin receptor gene TEK resulted in single or multiple VMs and led to loss of TIE2 receptor function⁵³ and upregulated expression of other vascular endothelial growth factors such as β TGF and β FGF, which exacerbated the severity of the lesion.⁵⁴

Vascular endothelial growth factor (VEGF) has also been found to induce penetration of capillary vessels into the avascular epidermis.⁵⁵ A defective response of endothelial cells to VEGF as the consequence of abnormal signaling of VEGF receptors results in CVMs if the differentiation is abnormal and there is an arrest in the development of normal vascular tissue. The persistence of the embryonic vascular system also causes additional abnormal development.

More recently a high susceptibility locus within the HLA locus on chromosome 6p21.32 has been identified with a

development of truncular VM. Due to deletion or duplication, the number of copy number variations is significantly associated with an increased chance of developing truncular VMs. The region contains 211 known genes.^{56–60} In addition, the increased expression of matrix metalloproteinase-9 in intramuscular VM lesions suggests that VMs have the ability for angiogenesis to provoke invasive growth while expanding slowly due to the increase in hydrostatic pressure.⁶¹ Progesterone receptors in VMs are also suspected to cause lesion progression when hormonal levels change.⁶²

Hereditary hemorrhagic telangiectasia (HHT)⁶³ is now confirmed as an autosomal dominant condition caused by a “loss-of-function mutation” in the genes encoding activin receptor-like kinase-1 (ACVRL1) and endoglin (ENG), specialized transforming growth factor-beta (TGF- β) superfamily receptors. Although these are CVMs, these lesions develop progressively in the brain, lungs, liver and intestine, and are generally diagnosed at a later age.

CM–AVM syndrome (combined capillary malformation and AV malformation)⁶⁴ is another autosomal dominant condition caused by RASA1 mutations with the AVM affecting the brain, spine, face and extremities. These familial/syndrome-based AVMs associated with RASA1 mutations behave differently from the sporadic type and remain relatively stable with minimal progression, although the symptomatology varies with anatomic location.

The AVM associated with Parkes Weber syndrome (PWS)⁶⁵ is also associated with the RASA1 mutation, but these AVM lesions generally have a slow progression as a part of PWS in comparison to the AVM belonging to sporadic type. Together with other vascular malformation components, VM and LM, it often results in marked tissue overgrowth of affected muscle, bone and subcutaneous fat. As a part of syndromes of tissue overgrowth (e.g., Cowden and Banyan–Riley–Ruvalcaba syndromes), PTEN mutations are also responsible for the focal tissue overgrowth in hamartomas that frequently contain AVMs.⁶⁶ AVMs caused by PTEN mutations are the most aggressive type of AVM, recurring rapidly following therapy with the tendency to develop new AVM lesions at different sites.⁶⁶

EMBRYOLOGY

When the embryo begins its exponential growth, an equivalent growth of the vascular system is necessary for the proper development of the fetus.^{67–69} If this growth does not occur there is a high risk of CVM. The long, complex process of angiogenesis increases the risk of developmental defects in comparison to other tissues from the same mesodermal origin, such as bone, muscle, and connective tissue.

Embryonic blood vessels originate from the blood island of Pander, which represents the masses of vasoformative cells that undergo a complicated process of evolution.³⁸ Undifferentiated capillary plexus becomes the initial primitive vasculature; subsequently, some capillaries undergo regression and coalescence with others to form a reticular structure. This reticular structure is efficient to meet the embryo's needs during the

early, rapid-growth stage of embryogenesis. This extratruncular stage occurs before the final truncular stage, during which formation of the actual artery, vein, and lymphatic trunks occurs to complete the differentiation. The characteristics of the embryonic cells change drastically between the extratruncular and truncular stages.^{2,14–16,39} The clinical behavior of the vascular defect depends on the stage at which arrested development occurs. Any defect occurring before the truncular stage maintains the embryonic characteristics of mesenchymal cells origin.

Extratruncular Lesions

Extratruncular CVMs represent arrested development during early embryonic life, while the vascular system is in the reticular stage.^{37,38} Therefore, these embryonic remnants of mesodermal origin retain the characteristics of mesenchymal cells (angioblasts). They have the potential to grow and proliferate when stimulated internally (e.g., by menarche, pregnancy, hormonal release) or externally (e.g., by trauma, surgery). Therefore, all extratruncular lesions, regardless of type, carry a significant risk of recurrence after inadequate treatment that provokes a dormant or silent lesion to grow rapidly.^{39,40} By nature, an extratruncular lesion behaves like an infiltrating process, invading the surrounding structures. Because bones, muscles, soft tissues, and blood vessels all originate from the same mesoderm, there is no plane of partition between them. Therefore, such a lesion, whether diffuse or circumscribed, produces a pressure effect on the surrounding tissues, in addition to the hemodynamic impact on the affected vascular system.

Truncular Lesions

Truncular CVMs arise when arrested development occurs later, during the vascular trunk formation stage of embryonic development.^{38,39} Truncular lesions have lost the embryonic characteristics of the mesenchymal cells, together with the potential to grow and proliferate. These lesions do not carry the same risk of recurrence as extratruncular lesions, but they are generally associated with more serious hemodynamic consequences than their extratruncular counterparts. Based on their pathoanatomic condition, truncular lesions are further divided into obstructive and dilated lesions.^{2,14–16} All truncular lesions appear as formed vessels with various degrees of developmental defects, ranging from incomplete or immature lesions (aplasia or hypoplasia) to overdeveloped lesions (hyperplasia). A truncular VM may present as a persistent fetal remnant (truncal) vessel that does not involute normally (e.g., sciatic vein, marginal or embryonic vein) or as a defective vessel trunk (e.g., vein web, venous aneurysm/ectasia) to result in various extents of stenosis to obstruction as well as dilatation.^{42,70,71}

PATOPHYSIOLOGY

In terms of pathophysiologic significance, CVMs can be divided into two types: those with a mechanical impact on surrounding structures, producing a compression effect, and those with a hemodynamic impact on the affected circulation. The

relative significance of these variants depends on the type of CVM as well as its embryologic subtype.

Extratruncular Lesions

In general, all extratruncular lesions have various degrees of mechanical and hemodynamic impact. The initial mechanical impact is generally of little significance, because compression is the result of steady growth of the infiltrating lesion. Rapid expansion of the lesion increases the mechanical impact by compressing surrounding tissues. A simple lesion can result in serious damage if it is located near vital structures (e.g., those involving breathing, sight, hearing, eating) and can even become life-threatening (e.g., airway obstruction). In general, the hemodynamic impact is usually far more serious than the mechanical impact. High flow CVMs (e.g., AVMs) have greater hemodynamic impact than low-flow lesions (e.g., VMs) because the pathoanatomic structure of arteriovenous shunting does not have the resistance of the normal capillary system.^{72–74}

Truncular Lesions

All truncular lesions, regardless of type, have a mainly hemodynamic impact. This hemodynamic impact is variable, depending on the type of CVM. For example, the impact of a truncular LM that manifests clinically as primary lymphedema remains limited to the lymphatic transportation system, seldom involving the accompanying venous system.^{75–78}

In contrast, a truncular VM affecting the lower extremity (e.g., femoral vein aplasia or hypoplasia) often presents with more serious hemodynamic impacts, resulting in chronic venous insufficiency.^{79–82} When venous insufficiency is combined with lymphatic insufficiency caused by coexisting truncular LM/primary lymphedema, its pathophysiologic impact (e.g., phlebolymphedema) is substantially increased.^{83–86}

Among truncular VMs,^{39,42,71} a venous aneurysm is a unique condition, defined as a segmental venous dilatation 1.5 to 2 times the normal vein size. This is potentially a source of venous thrombosis and pulmonary embolism, especially when the deep system is involved. The most common symptoms are a painful mass and localized swelling. In some cases, a massive pulmonary embolism is the first symptom. In children, venous dilatation is most common in the internal jugular vein and is most noticeable during crying or other physical effort. The incidence of venous aneurysms is similar in men and women. Gillespie et al.⁸⁷ reported on 39 venous aneurysms in 30 patients, the majority located in the deep venous system of the lower extremities, with five in the internal jugular vein and four in the superficial venous system. Diagnosis was made by phlebography, color-flow duplex scanning, and/or MRI. The size of the aneurysms ranged from 1.7 to 6 cm. Three patients had deep venous thrombosis, and three had pulmonary embolism.

Truncular AVMs, which are true fistulous “direct” connections between the arterial and venous system with no nidus interposed, have the most powerful impact on the vascular system although they are extremely rare. The shunting of arterial blood to the venous system may result in a substantial degree of

arterial steal from the distal arterial vessels, as well as overloading the proximal and distal venous system, especially when the lesion is located in the extremities.^{43,74,88,89} This may result in chronic venous hypertension distal to the lesion and high output cardiac failure due to the progressive increase in central venous overloading.⁴³

Secondary Organ Impact

The pathophysiologic impact of a CVM is not limited to the primary lesion. It may have a significant secondary impact on related tissues or organs. For example, an intraosseous CVM has an important effect on the musculoskeletal system by stimulating the epiphyseal plate and inducing abnormal long-bone growth, resulting in leg-length discrepancy.^{90–92} Compensatory scoliosis with or without pelvic tilt can have clinical consequences on several physiologic functions (e.g., abnormal gait, cardiopulmonary impingement). Other systems, such as the gastrointestinal, cardiopulmonary, and genitourinary systems, may also experience secondary pathophysiologic effects because of the location of the CVM (e.g., chylo-reflux).^{42,71}

CLINICAL PRESENTATION

The presentation of *extratruncular* CVMs depends on the vascular system involved, the location of the lesion, and whether the lesion is localized. They may affect the arterial, venous, lymphatic, or capillary system either as an independent lesion (CM, VM, LM, AM, AVM), or they may affect two or more of these vessel types (HLM). Each of these vascular systems may also be the site of *truncular* malformations, such as arterial aneurysms and ectasias, venous aneurysms and phlebectasias, and congenital/primary lymphedema when the defective development should occur in the *late* stage of embryogenesis. Hence, the variations in presentation are countless. An extratruncular CVM lesion may appear to be localized to one small area on initial assessment but, like the tip of an iceberg, it turns out to be an extensive malformation of the deep tissues revealed only by further diagnostic assessments. A complete clinical examination is usually sufficient to establish a diagnosis. However, diagnosis may be difficult in small children, and it may take some time for the lesion to become fully identifiable.^{42,43,71,93–95}

Capillary Malformations

A CM appears as a port-wine stain on the skin with a distinctive color; it is different from the common vascular birthmark known as nevus flammeus neonatorum. Birthmarks are pinkish discolorations affecting the nuchal region (“stork bite”) or the face along the eyelids, forehead, or lips (“angel’s kiss”). In contrast, CMs can present anywhere on the body and can range from small localized lesions to extensive lesions covering the skin in multiple areas. CMs are often accompanied by other abnormal physical findings beneath the skin, heralding other CVMs. For example, a CM in the face is a warning sign for an intracranial CVM known as Sturge–Weber syndrome, with

ipsilateral ocular and leptomeningeal vascular malformations.^{96–99}

Venous Malformations

VMs present at birth often as soft bluish swellings located near the skin surface, although some are not clinically distinctive at first glance.^{42,70,71} They are easily compressible and enlarge when the affected area is dependent or with a Valsalva maneuver. VMs in the extremity are easily collapsed when the extremity is elevated to allow venous drainage. VMs usually present as slowly growing solitary lesions, but there may be multiple lesions, either localized or extensively infiltrative. VMs are associated with various degrees of pain and stiffness, especially in the morning, but they are generally not tender. The symptoms respond to compression therapy. However, when the lesions involve underlying muscle, bone, abdominal viscera, or the central nervous system, they may be complicated by secondary symptoms.^{42,71,82} VMs in the head and neck region are usually unilateral, with a mass effect that causes significant distortion of the features and facial asymmetry. VMs involving the tongue, palate, and oropharynx often result in significant deformity, including dental malocclusion, and represent a potential life-threatening condition if they encroach on the upper airway together with laryngopharyngeal lesions. VMs affecting the limb are often associated with leg-length discrepancy caused by long-bone growth disturbance when they extend into muscle and bone, often resulting in compensatory pelvic tilt and scoliosis.

Intraosseous VMs in an extremity can cause structural damage to the bone shaft and pathologic fracture. VMs involving the synovial lining of the knee joint are vulnerable to trauma, and repeated hemarthrosis results in ankylosis or degenerative arthritis.^{42,71,100}

Thrombosis and pulmonary embolism are not rare with VMs. Clots originate in large venous dilatations (phlebectasias) or aneurysms, and the tendency for intravascular coagulation to progress to disseminated intravascular coagulation (DIC) and sometimes fatal embolism complicates these hematologic disorders.^{42,71,100}

VMs affecting the GI tract can cause chronic bleeding. The lesions can be located anywhere in the GI tract and can occur in various conditions involving polypoid, sessile, or nodular lesions affecting any or all layers of the bowel wall. Therefore, any GI bleeding in a VM patient warrants screening to rule out the VM as the cause.

Lymphatic Malformations

LMs present either as diffuse swelling of an extremity (primary lymphedema) or as localized swelling (lymphangioma).^{31,32} The swelling with lymphangioma ranges from a well-localized spongelike condition to a diffuse infiltrating condition affecting large areas and having a varying consistency, depending on the lesion's components (macrocystic or microcystic). LMAs are generally asymptomatic, neither tender nor painful, until complications develop (e.g., lymphatic leakage, intralesional

bleeding, infection). However, LMAs affecting the oral mucosa and tongue are often accompanied by pain, swelling, or bleeding, with mucosal vesicles.^{101–103}

Proptosis, amblyopia, strabismus, or even loss of vision can manifest with a periorbital LM. Difficulty chewing, talking, and breathing is infrequently caused by overgrowth of the mandible, maxilla, or tongue as a result of an LM affecting the face or cervical region. Skeletal overgrowth or pathologic fracture of a long bone can also be caused by an LM affecting the bone metabolism directly or indirectly (e.g., Gorham syndrome).^{101–103}

Arteriovenous Malformations

Small AVMs present at birth often remain obscure until they progress and become clinically evident as local swellings accompanied by various symptoms and signs of arteriovenous shunting.^{29,30,42,43} Local hyperthermia, a thrill, and bruit are the hallmarks of AVMs, often accompanying visibly dilated veins. Ischemic changes and ulceration of the skin can develop distal to the shunt, often with intractable pain and intermittent bleeding. Distal gangrene is likely if the arterial insufficiency is severe, and high-output cardiac failure is unavoidable if a large AVM is not treated.^{43,74}

Combined Vascular Malformations

Clinical findings of HLM, either as KTS^{104–107} or PWS,^{108–110} are a mixture of each type of CVM involved (e.g., CM, LM, VM, and/or AVM) – both the primary lesion and its secondary effects, as described separately below.^{33,42,71,111,112} Overgrowth of affected soft tissue and skeletal tissue as a secondary phenomenon induced by the CVM is more distinctive; the port-wine stain's characteristic geographic pattern over the lateral side of the involved extremity often extends to the buttock or thorax. Underlying LM infrequently accompanies various skin conditions consisting of vesicles, which often become symptomatic with leakage or infection.^{102,103}

Limb swelling caused by an HLM represents phlebolymphedema, a mixed condition with varying degrees of lymphatic and venous insufficiency.^{84–86} Chronic lymphatic insufficiency usually manifests as primary lymphedema, while chronic venous insufficiency relates to insufficiency of the marginal vein (MV) which is the most common truncular VM involved in KTS. The MV is an embryonic tissue remnant which failed to involute and is often visible or palpable as a large dilated vein along the lateral aspect of the lower extremity. Its distal portion often exhibits the physical findings of chronic venous insufficiency (e.g., stasis dermatitis, stasis ulcer) due to a lack of venous valves, a condition known as avalvulosis.^{42,72,113} Therefore all venous disorders, including varicose veins, thrombophlebitis, and pulmonary embolism, are major clinical signs of a VM involved with an HLM. In addition, the existence of the marginal vein often heralds coexisting deep venous anomalies (e.g., iliac vein aplasia, femoral vein hypoplasia, popliteal vein aneurysm) and warrants proper investigation.

Soft tissue and skeletal hypertrophy or hypotrophy (“vascular bone syndrome”) are secondary effects of the primary lesion in the affected limb. They are often obvious at birth and can be progressive.^{90,92} HLMs affecting the extremity carry a higher risk of involvement of other intraperitoneal, retroperitoneal, intrathoracic, and mediastinal organs. Depending on the CVM, the clinical findings may include cardiopulmonary, musculoskeletal, GI, genitourinary, or gynecologic symptoms. Infrequently, the lesion presents with a distinctive condition such as hematuria, hematochezia, chyluria, chylorrhea, chylothorax, or pleural effusion. Occasionally, it presents with vague symptoms such as constipation, malabsorption syndrome, bladder outlet obstruction, or recurrent infection.

DIAGNOSIS

General Principles

The majority of CVMs can be detected in early childhood based on a heightened clinical suspicion when a child presents with abnormal swelling and disfigurement. A careful history and physical examination often provide enough clues to make a presumptive clinical diagnosis. By nature, a CVM may appear anywhere in the body in various numbers, shapes, extents, degrees, and conditions, either as a predominant lesion or as a mixed anomaly. To further confuse the clinician, these lesions may change due to internal or external stimulations (e.g., menarche, pregnancy, trauma). One clinically detectable CVM might suggest other hidden lesions scattered throughout the body, so the diagnostic workup should include a full-body investigation.^{17,95}

The initial diagnostic workup should start by ruling out infantile hemangioma and then identifying the exact nature, type, and subtype of CVM.^{17,18} Following a careful history and physical examination, the appropriate combination of noninvasive to minimally invasive tests should be carried out to confirm or exclude the clinical impression (Box 170.2). This often results in a diagnosis. Invasive tests (arteriography) can generally be deferred to a later time if the diagnosis needs refinement, if surgical or other invasive therapeutic measures are being considered, or if the symptoms merit further investigation.^{42,43} However, because AVMs are potentially limb- or life-threatening, a full assessment of their status is recommended as early as possible, including arteriography if indicated, regardless of the patient's age. Other CVMs do not require such extensive initial diagnostic testing, and their investigation should be limited to the minimum basic noninvasive tests sufficient for a consensus decision by a multidisciplinary team.^{114,115}

In general, children younger than 2 years should have only those procedures that are necessary for diagnosis. However, when the child has a condition that warrants earlier intervention (e.g., abnormal long-bone growth with leg-length discrepancy) or the lesion is located in a limb- or life-threatening area or compromises vital functions, invasive tests should be included as indicated to start treatment.^{17,116}

BOX 170.2

Diagnostic Tests for Congenital Vascular Malformations

Noninvasive to Minimally Invasive Studies

- Duplex ultrasonography
- Magnetic resonance imaging – T2-weighted study
- Radioisotope lymphoscintigraphy
- Computed tomography with contrast and three-dimensional reconstruction
- Bone length scanogram
- Whole-body blood pool scintigraphy (transvenous angioscan using radioisotope-tagged red blood cells)
- Transarterial lung perfusion scintigraphy (transarterial angioscan using radioisotope-tagged microsphere albumin)
- Air plethysmography
- Magnetic resonance venography or arteriography
- Magnetic resonance lymphangiography
- Indocyanine green lymphangiography
- Ultrasound lymphangiography

Selective Invasive Studies

- Standard, selective, or superselective arteriography
- Ascending, descending, or segmental phlebography
- Percutaneous direct-puncture angiography: arteriography, phlebography, or lymphography
- Contrast (classic) lymphangiography

Physical Examination

Complete inspection and palpation of all skin surfaces, including the genitalia, should be performed in a well-lit environment. Although the majority of VMs and LMs present as single lesions, a physical evaluation for both conditions should be made to assess their relative significance (e.g., leg swelling, varicose veins). Auscultation (for bruit) and palpation (for thrills and pulse character) are helpful to assess the presence and extent of an AVM.

The examination should be done with the patient in the standing and lying positions, and posture and gait should be evaluated to assess the dynamic impact of the lesion. Involvement of the skin, soft tissue, and bone should be assessed so that positive findings will not be missed.⁹² The limb elevation test should be performed in all extremity CVMs. With this test, VMs may demonstrate dramatic emptying of the venous lakes or veins during leg elevation.¹⁷ In VMs, the findings of acute (e.g., superficial or deep venous thrombosis) and chronic (e.g., chronic venous insufficiency) complications and their sequelae should be investigated.

The evaluation of an AVM should include not only its hemodynamic impact on the distal and proximal arterial and venous systems (e.g., arterial steal with arterial insufficiency, chronic venous insufficiency) but also its effects on the central cardiovascular system (e.g., cardiac failure), in addition to secondary involvement of the lymphatic system.^{40,42,43}

Imaging

The imaging evaluation aims not only to identify the type and subtype (extratruncular or truncular) of CVM but also to

confirm or rule out the presence of other CVMs. In most cases the diagnosis of CVM can safely be made with noninvasive or minimally invasive studies alone.¹⁷ These studies can distinguish CVM from infantile hemangioma. Invasive studies such as phlebography and arteriography are generally reserved for therapeutic planning or for the diagnosis of aggressive AVMs or other lesions for differential diagnosis (e.g., sarcoma).

Minimally Invasive Studies

Basic imaging for CVM assessment includes magnetic resonance imaging (MRI),^{117,118} duplex ultrasonography,^{42,71,82,93,119} and preferably whole-body blood pool scintigraphy (WBBPS) if feasible.¹²⁰ If LM/primary lymphedema is suspected, radionuclide lymphoscintigraphy is added to these basic tests.^{121,122} For an AVM, transarterial lung perfusion scintigraphy (TLPS)¹²³ may be added if feasible but contrast computed tomography¹²⁴ is essential with 3-D reconstruction. T2-weighted MRI remains the “gold standard” for VMs, and when it is used together with duplex ultrasonography, most other CVMs (e.g., LMs) can be distinguished. WBBPS (a transvenous angioscintigraphy using radioisotope-tagged red blood cells) can detect small amounts of abnormal blood pooling throughout the body. WBBPS is valuable not only to confirm the presence of a VM but also to exclude an LM by the absence of abnormal blood pooling. This test is also widely used in the follow-up assessment of multisession treatments not only for the VM but also the AVM (Fig. 170.3).

TLPS is a transarterial angioscintigraphy with radioisotope-tagged microsphere albumin. It measures the percentage of blood volume shunted by AVM lesions preferably located in the extremities. TLPS is extremely valuable to detect the microshunting AVM lesions common in PWS. Seldom is it capable of identifying small AVMs missed by conventional arteriography, however (Fig. 170.4). TLPS has a further unique role to assess the response/outcome of therapy and also for follow-up assessment of AVM lesions instead of arteriography.⁴³

In addition to these basic tests, others can be performed when a more precise assessment is needed. These include air plethysmography, magnetic resonance venography or arteriography, and computed tomography with contrast and three-dimensional reconstruction. Ultrasonographic lymphangiography and magnetic resonance lymphangiography have limited but special value in candidates for lymphovenous reconstruction^{17,42,93} among truncular LM patients with primary lymphedema together with indocyanine green lymphangiography when the lesion is limited to the lymph nodes (lymphadenodysplasia).^{125–130}

Invasive Studies

The role of invasive studies in CVM evaluation is limited because the majority of CVMs can be safely diagnosed by noninvasive tests. Nonetheless, invasive studies remain the gold standard in the diagnosis of all CVMs, especially AVMs.^{17,72} In the case of VMs, ascending, descending, or segmental phlebography is an important study; together with percutaneous direct-puncture phlebography, it serves as a roadmap for diagnosis and a guide to treatment. Standard or selective arteriography is mandatory for the definitive diagnosis of AVMs and as a roadmap for surgical

or endovascular treatment. In contrast, in patients with LMs, percutaneous direct-puncture lymphangiography is infrequently needed but is occasionally performed to evaluate the extent of an extratruncular lesion.^{34,121,131} In general, traditional lymphangiography is no longer used as a diagnostic test for the lymphatic dysfunction assessment owing to its potential to damage the lymphatic vessels induced by the inflammation produced by the oil-based contrast unless indicated specifically for reconstructive surgery.

Evaluation of Affected Systems

Leg-length discrepancy secondary to abnormal long-bone growth should be evaluated by appropriate radiographic studies (e.g., bone scanogram) as described below under Congenital Vascular Bone Syndrome in the Special Treatment Issues section. Coagulation studies are not routinely included in the evaluation of CVMs, and not all phleboliths of a VM are an indication for a *full* coagulation study. However, as recommended below under Coagulopathy, in the same Special Treatment Issues section, extensive extratruncular VM, either large or multiple, is considered as an indication for the coagulation studies together with marginal veins. This is especially true when venous thrombosis is suspected. The findings of consumptive thrombocytopenia (e.g., elevated D-dimer) also merit blood coagulation studies. This is in contrast to the coagulopathy observed in patients with hemangioma (e.g., Kasabach–Merritt coagulopathy).^{23,42,71,100}

Differential Diagnosis

CVM Versus Infantile or Neonatal Hemangioma

Even though the overall incidence of CVM is much lower than that of hemangioma (2% to 3% in newborns, and 10% by the end of the first year of life),^{5,46,131} differentiating CVM from hemangioma should be the first step in the diagnosis of CVMs.^{6,14,42,71,132,133} As mentioned earlier, a CVM is a birth defect that develops within the peripheral vascular systems and manifests as a malformed vessel as the outcome of defective development, whereas a hemangioma is a newly rising vascular tumor mostly after birth as “infantile” type (cf., congenital hemangioma). Infantile hemangioma, therefore, is not present at birth and appears suddenly during the neonatal period as a rapidly growing tumor and its growth is usually self-limited.^{4–6} Typically, it exhibits a rapid growth rate during the early proliferative stages, followed by slow, gradual tumor regression during a long involutional stage. Hemangioma also has a higher incidence in females (3:1 to 5:1 female–male ratio).

In contrast, a CVM is always present at birth, even though it might not be apparent. It carries an equal gender distribution and grows commensurate with body growth. In most cases a careful history and physical examination allow one to distinguish a VM from a hemangioma. Distinction between the two entities is confirmed by noninvasive studies (e.g., duplex ultrasonography, MRI). These studies are especially useful in the case of a deep-seated hemangioma mimicking a VM. Tissue

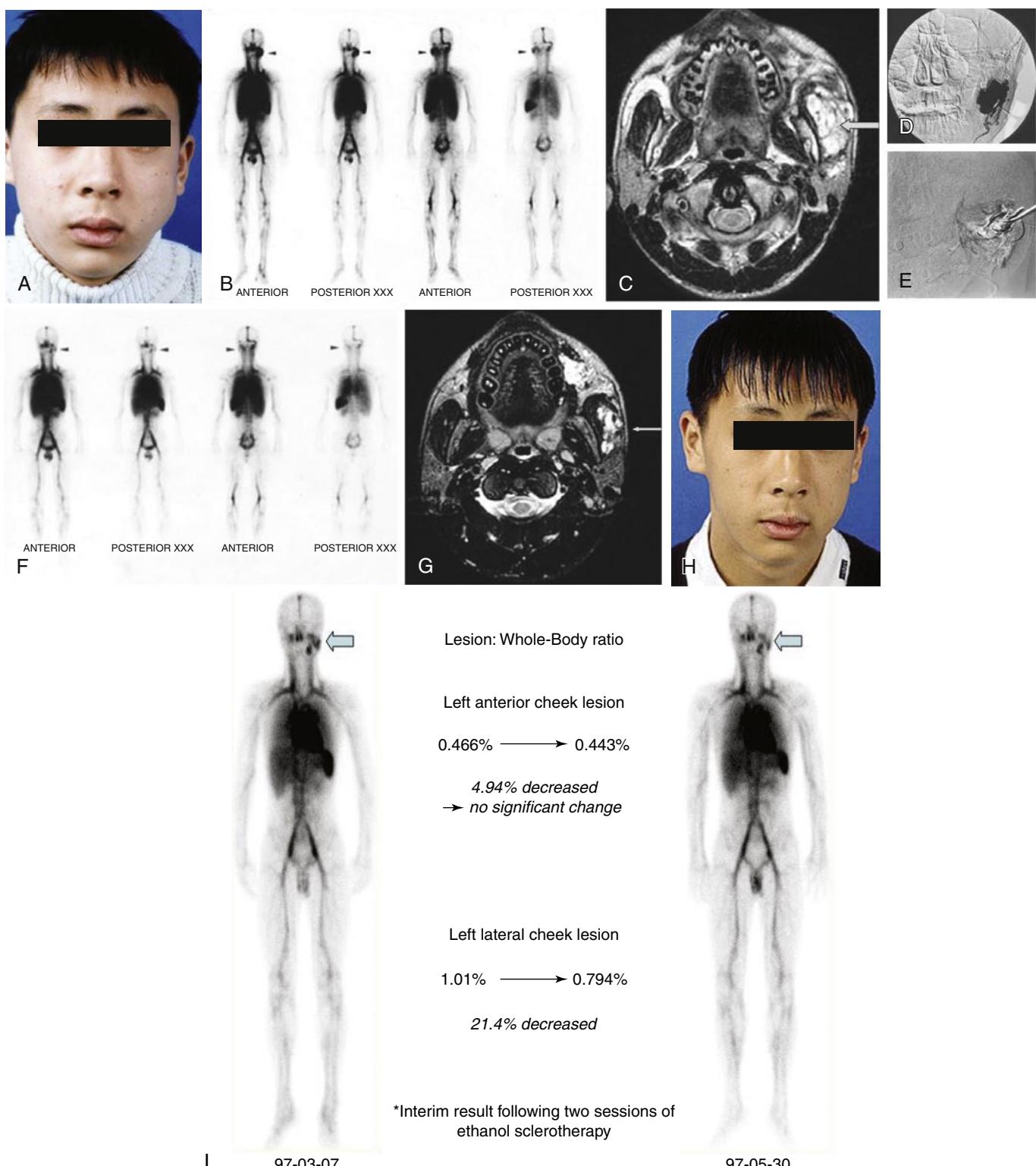


Figure 170.3 Role of Whole-Body Blood Pool Scintigraphy (WBBPS). (A–I) Qualitative and quantitative analysis of a venous malformation (VM). Photograph (A) demonstrates a VM affecting the left cheek and presenting as diffuse swelling. WBBPS (B) delineates abnormal blood pooling along the left cheek (*arrows*). T2-weighted MRI (C) reveals a large VM (*arrow*), compatible with other test findings. Based on the findings of percutaneous direct-puncture angiography (D), ethanol sclerotherapy (E) was carried out successfully. Both WBBPS (F) and MRI (G) findings demonstrate an excellent response (*arrows*) at interim follow-up. The swelling along the left cheek has completely disappeared (H). The quantitative measurement of the efficacy of therapy (I) is compatible with the qualitative findings (F).

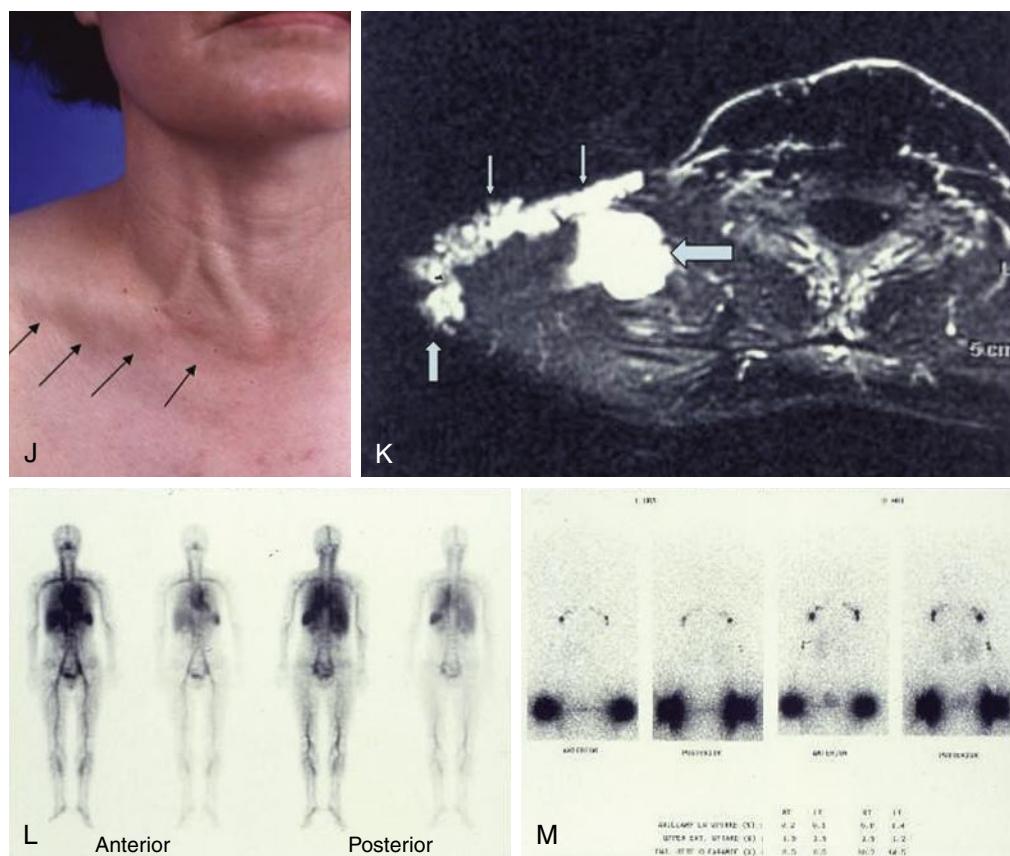


Figure 170.3 Cont'd. (J–M) Differential diagnosis of VM and lymphatic malformation (LM). Photograph depicts diffuse swelling over the right clavicular region (*arrows* in J), with vague but steady pain extending to the root of the neck and to the right shoulder. Clinically, this was considered a VM, based on an increase in size during the Valsalva maneuver. T2-weighted MRI shows findings typical of a VM (*arrows* in K). However, there was a strong clinical suspicion of an LM owing to its location in the common site of infiltrating, extratruncular LMs. WBBPS (L) does not show pooling in these areas, ruling out a VM. Radionuclide lymphoscintigraphy findings (M) illustrate a completely normal lymph transporting system. (From Lee BB, Kim DI, Huh S, et al. New experiences with absolute ethanol sclerotherapy in the management of a complex form of congenital venous malformation. *J Vasc Surg*. 2001;33(4):764–772.)

biopsy is rarely needed. Once, by misunderstanding, VM was erroneously called cavernous/capillary hemangioma but CVMs are not vascular tumors/hemangiomas and this misnomer should be corrected.^{14,80–82}

Differentiating the Type of CVM

Once hemangioma is excluded and a diagnosis of CVM is confirmed, further characterization is necessary because the embryologic and hemodynamic behavior of the various CVM types can be different. VM is the most common type of CVM. It appears clinically as a pure VM or as a mixed lesion.^{134,135} Approximately 15% to 20% of VMs are mixed lesions (venous and lymphatic, as in KTS; or venous, lymphatic, and arterial, as in PWS). The presence of an occult AVM must be identified owing to the aggressive nature of this lesion, and every effort should be made to confirm or exclude an AVM, regardless of its magnitude. The micro-shunting status of an AVM located in the extremity should be investigated by TLPS if feasible, although computed tomographic angiography or arteriography should be able to establish a precise diagnosis.^{42,43,74}

Diagnosing the presence of an LM as a component of a CVM is not as critical as identifying an AVM. However, an

LM cannot always be accurately distinguished from a VM by MRI without contrast. In these cases, WBBPS is extremely helpful for differentiating the two entities. However, the combination of T2-weighted MRI and WBBPS allows a precise diagnosis of combined VM and LM lesions in general. When the diagnosis is still in question, percutaneous aspiration (using ultrasound guidance or direct puncture) and fluid analysis of a mixed VM and LM lesion can determine its true nature unless percutaneous direct puncture lymphangiography is further included.

TREATMENT

General Principles

During the last century, limited knowledge about the natural history and biologic behavior of CVMs often contributed to poor outcomes following an overaggressive surgical approach.^{136,137} In retrospect, these poor outcomes were largely related to excessive surgery performed on extensive, surgically unresectable lesions. The view that surgical therapy had a very limited role in the treatment of CVMs then prevailed for many

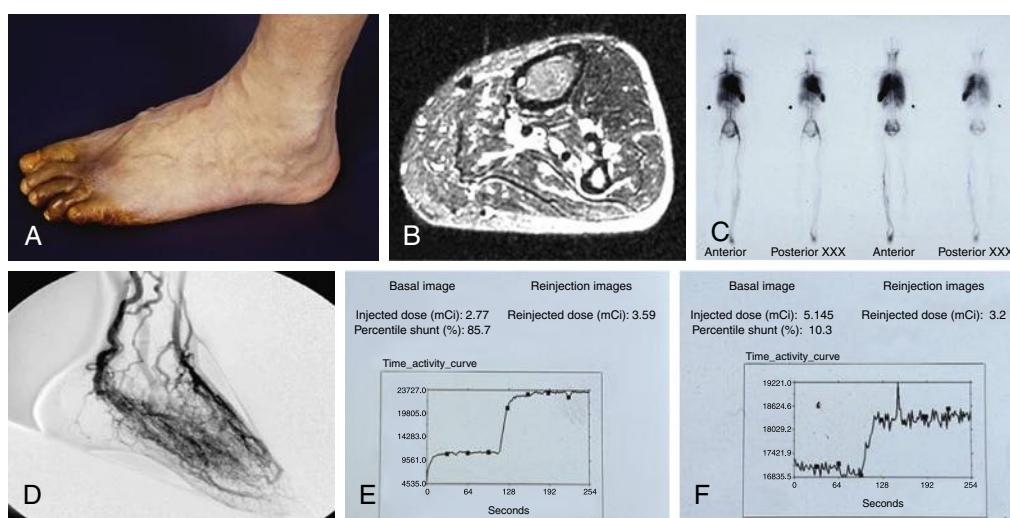


Figure 170.4 Role of Transarterial Lung Perfusion Scintigraphy (TLPS). (A) Ischemic left foot with impending necrosis of two toes. The local condition deteriorated rapidly after arteriovenous malformations (AVMs) affecting the pedal arterial arch were treated with coil embolization of the feeding artery. (B) MRI findings in the lower leg are compatible with an AVM affecting the foot only. (C) Whole-body blood pool scintigraphy shows the hyperdynamic status of the arterial system originating from the AVM in the foot. (D) Arteriography reveals massive shunting through the AVM. (E) Before treatment, the shunting percentage of blood measured with TLPS is 85.7%. (F) After multisession ethanol sclerotherapy, the shunting is effectively reduced to 10.3% on repeat TLPS. TLPS is a reliable test not only to assess the severity of AVMs but also to follow the response to therapy. It is also useful to find hidden micro-AVMs, often exceeding the reliability of arteriography. (From Lee BB, Bergan JJ. Advanced management of congenital vascular malformations: a multidisciplinary approach. *J Cardiovasc Surg.* 2002;10(6):523-33, Fig. 7.)

decades.¹³⁸ During that time, surgical resection was strictly limited to clinical situations in which palliative surgery was the only option (e.g., for bleeding control). This dramatic reversal caused a major setback in the treatment of CVMs for many decades. However, new concepts based on sound knowledge and a new classification system developed over the last 2 decades have provided a better understanding of the pathophysiology, anatomy, and embryology of CVMs, and recognition of the fundamental differences between extratruncular and truncular lesions has led to better management principles. Now, based on the new concept of a multidisciplinary approach, traditional excisional surgery can provide the best outcome to “surgically accessible” lesions as an independent therapy or combined with embolo-sclerotherapy perioperatively while the endovascular treatment with various modalities of embolo-sclerotherapy also provide the best outcome to “surgically inaccessible” lesions as independent therapy.^{40,43,71,114}

Extratruncular Lesions^{39,116}

All extratruncular lesions recur sooner or later owing to the unique characteristics of the mesenchymal cells, unless the lesion nidus is completely destroyed. Incomplete control of the lesion (e.g., ligation of the feeding arteries in an AVM) only stimulates the nidus to grow through neovascular recruitment. When formulating a treatment plan for an extratruncular lesion, a controlled, aggressive approach should be coupled with a realistic assessment of the risks and benefits of the treatment regimen. This is especially true for life- and limb-threatening situations (e.g., hemorrhage). Recurrence following treatment remains a significant problem for all embryologically immature extratruncular lesions, and the potential for recurrence should

never be underestimated. A diffusely infiltrating lesion requires special attention owing to its tendency to progress, its associated high morbidity and complications, and the high likelihood of recurrence.

Truncular Lesions^{39,116}

In contrast, truncular CVMs do not exhibit embryonic characteristics, and they lack the potential for proliferation. Therefore, the same aggressive approach is not justified in these cases. In addition, not all truncular lesions need treatment; some can be handled conservatively until they become hemodynamically significant. Intervention in these cases should be done only to manage specific hemodynamic situations such as deep venous thrombosis or thromboembolism, chronic venous insufficiency, and stasis ulceration.

Among the various truncular VMs (e.g., popliteal venous aneurysm or ectasia, femoral vein hypoplasia, iliac vein agenesis), only symptomatic lesions associated with hemodynamic consequences require carefully considered surgical reconstruction (e.g., venous bypass, venous aneurysmorrhaphy) or ablative (excisional) surgery (e.g., removal of the marginal vein) and the cautious use of endovascular ablation and/or sclerotherapy.^{70,71,79,82,113}

As previously noted, the lateral embryonic or marginal vein deserves special attention.^{91,92,139} Its resection is often indicated not only to prevent long-term hemodynamic consequences to the venous system (e.g., pulmonary embolism, chronic venous hypertension or insufficiency, leg ulceration) but also to prevent the aggravation of coexisting LMs (e.g., lymphatic leakage, sepsis) resulting in the unique condition of phlebolymphedema.⁸⁴⁻⁸⁶ Additionally, when the lesion is suspected to

BOX 170.3	Indications for Treatment of Extratruncular Congenital Vascular Malformations	BOX 170.4	Components of a Multidisciplinary Team for the Management of Congenital Vascular Malformations
<ul style="list-style-type: none"> • Hemorrhage • High-output heart failure (arteriovenous shunting malformation) • Secondary ischemic complications (arteriovenous shunting malformation) • Secondary complications of chronic venous hypertension (venous malformation) • Lesions located in life-threatening (e.g., proximity to airway) or vital function-threatening (e.g., seeing, eating, hearing) region • Disabling pain • Functional impairment • Cosmetically severe deformity • Vascular-bone syndrome • Lesions located in a region with a potentially high risk of complications (e.g., hemarthrosis, deep venous thrombosis, pulmonary embolism) • Lymph leak with or without infection • Recurrent sepsis (local or general). 		<ul style="list-style-type: none"> • Vascular surgery • Pediatric surgery • Plastic and reconstructive surgery • Orthopedic surgery • Anesthesiology • Pathology • Physical medicine and rehabilitation • Otolaryngology • Head and neck surgery • Cardiovascular medicine • Psychiatry • General medicine • Interventional radiology • Diagnostic radiology • Nuclear medicine • Dermatology 	

be the stimulus for abnormal long-bone growth, its early, aggressive control should be considered to minimize leg-length discrepancy. However, to avoid doing more harm than good, it is always prudent to verify the integrity of the deep venous system before treating.^{71,93,106,139}

Treatment Guidelines and Indications

Considering the hemodynamic and clinical characteristics of extratruncular CVMs, the primary rules in terms of management are that not every lesion should be treated, and no routine treatment can be applied in all cases.^{18,35,36,116} For bests results an individualized treatment plan should be derived by multidisciplinary team consensus following an appropriate diagnostic workup.^{114,116} This team approach results in selection of the best treatment modality based on appropriate indications (Box 170.3). This approach requires the active coordination of as many as 15 highly specialized disciplines (Box 170.4). Treatment should be considered only when the patient or lesion meets one or more indications for treatment and the benefit of the therapy is expected to exceed/compensate for the risk.^{43,71,102,116}

Arteriovenous and Venous Malformations

All AVMs should be considered potentially life- or limb-threatening lesions necessitating an early, aggressive approach (Fig. 170.5).^{29,30,43,74} However, a “controlled” aggressive approach is favored with every effort to minimize collateral damage during treatment. The benefit of treatment should always exceed the associated risk and a palliative approach should be considered when treatment morbidity and mortality are exceedingly high. In limb- and life-threatening situations, sacrificing limb over life may be necessary.^{43,74} In contrast, a VM usually does not carry the same risk. Therefore, not all VMs require treatment. Although extratruncular VM lesions tend to be more serious than truncular lesions, an overzealous approach sometimes does more harm than good.^{36,70,82,116,135} When the benefit of treatment outweighs the risk of complications and

morbidity, less risky treatment options (e.g. foam/liquid sclerotherapy) should be first-line therapy. An early, aggressive approach should be limited to VMs that threaten vital life-sustaining functions or lesions that produce the vascular bone syndrome, resulting in abnormal long-bone growth and subsequent leg-length discrepancy, scoliosis, or thromboembolism.^{18,22,70,71} In pediatric patients, a common VM without bone involvement can usually be monitored until the child reaches age 6 years or is mature enough to tolerate the various diagnostic and treatment procedures.^{17,116}

Order of Treatment

The treatment strategy should focus on the primary malformation first, followed by treatment of secondary disorders associated with the vascular, musculoskeletal, and integumentary systems. Correction of various hemodynamic derangements secondary to the primary lesion should be given priority. This can involve either reconstructive surgery (e.g., venous bypass, free lymph node transplant surgery) or ablative or excisional surgery (e.g., removal of the marginal vein, removal of aneurysms). Corrective surgery for the sequelae of secondary hemodynamic consequences may follow (e.g., orthopedic surgery, Achilles tendon lengthening, plastic and reconstructive surgery to correct cosmetic facial or limb deformities). When severe CVMs result in a nonfunctional limb with significant growth discrepancy, early amputation should be considered as a practical option; this allows early rehabilitation after the child has been fitted with a proper prosthesis.^{43,71}

Treatment Types – Endovascular Therapy

Endovascular therapy, primarily embolization and sclerotherapy, is well accepted as the treatment of choice for surgically *inaccessible* extratruncular lesions. It is the primary mode of therapy for poor surgical candidates with extensive lesions beyond the deep fascia and involvement of muscle, tendon, and bone – the diffuse, infiltrating type of extratruncular lesion.^{43,71,116}

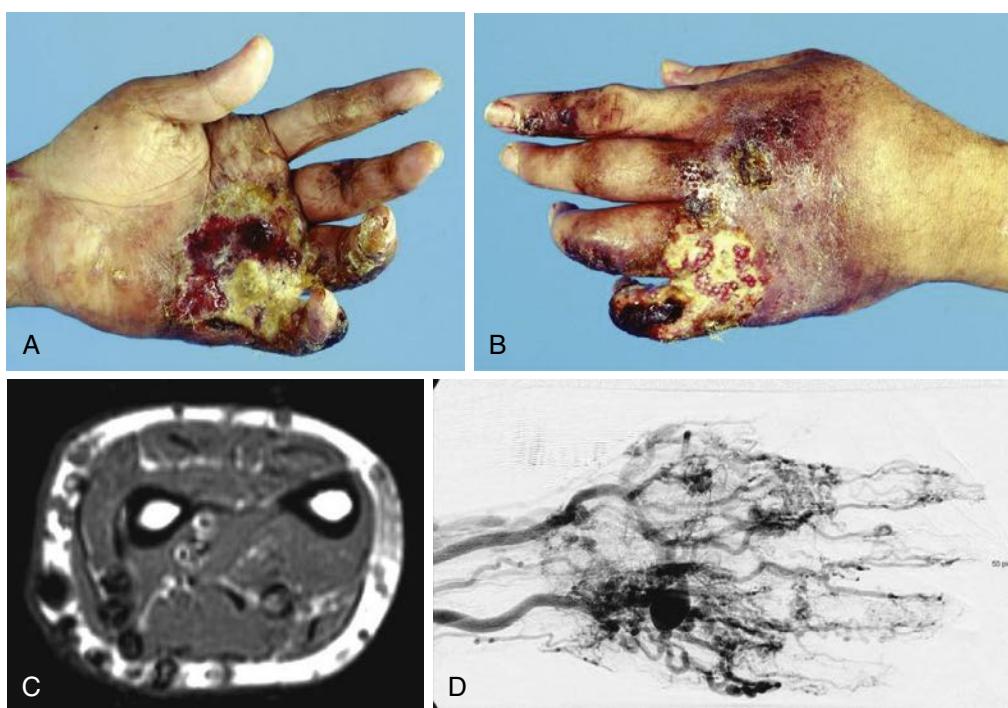


Figure 170.5 Natural course of arteriovenous malformation (AVM), with impending limb loss. (A, B) Ultimate outcome of a neglected AVM affecting the left hand and fingers. Stealing of arterial blood from the distal arterial trees by the AVM eventually leads to chronic arterial insufficiency and subsequent ischemia and gangrene. The hand and fingers are now in jeopardy, with great risk of major tissue loss. MRI (C) and arteriography (D) show evidence of massive shunting, making treatment more difficult.

The active incorporation of pre- and postoperative embolization or sclerotherapy has also expanded the traditional role of surgical therapy to previously surgically inaccessible lesions to deliver excellent results with minimal complications and limited morbidity. Adjunctive endovascular therapy, therefore, should be actively performed pre- and postoperatively in surgical candidates to improve the safety and effectiveness of surgery.^{116,140} Postoperative supplemental embolization and sclerotherapy can improve overall efficacy of surgical therapy, especially for the residual lesions after “limited” excision.

Sclerotherapy

Various liquid sclerosants are used as a major therapeutic tool for the treatment of CVMs to destroy the endothelial cell layer of the lesions. Each liquid agent has own unique properties and side effects, and proper sclerosant selection is critical, particularly for lesions with higher risk of complications and morbidity, such as superficially located VM lesions (e.g. hand/palm, feet/sole, mucosas).^{70,71,141}

Ethanol

Absolute ethanol is a powerful sclerosant that works by precipitating the protoplasm of the endothelial cells, permanently eliminating the “chemotactic cellular factor” and “angiogenesis factor” so that it has curative potential. Hence, ethanol can deliver excellent long-term results when done properly. However, it also carries the highest risk of cardiopulmonary complications (including pulmonary arterial spasm/hypertension) among the available

sclerosing agents.^{27,28} Close cardiopulmonary monitoring is warranted, with a Swan–Ganz catheter under general anesthesia, because pulmonary artery pressure increases when ethanol reaches the pulmonary circulation¹⁴² and pulmonary hypertension is potentially fatal when it progresses to pulmonary spasm and cardio-pulmonary arrest. To decrease the risk of complications, the minimally effective dose of ethanol should be administered over multiple treatment sessions. Less than 1 mL/kg as total dose of ethanol is the maximum volume that can be safely given during one session. We find that the risk of ethanol flowing to the pulmonary circulation becomes negligible when ethanol dose is limited to 0.14 mL of ethanol/kg ideal body weight every 10 minutes when anticipating large injections of ethanol to control large lesions.

This cautious approach minimizes the potential for collateral damage to surrounding tissues (nerve, vessel, cartilage, skin, soft tissue). The morbidity of the CVM should be weighed against the risks associated with ethanol sclerotherapy as, in certain situations, a reasonable degree of collateral damage is an acceptable outcome to control a life-threatening lesion. Thus, in spite of its risks, ethanol remains the primary sclerotherapy agent of choice in the management of severe CVMs, particularly AVMs.^{143,144}

Other sclerosing agents

For less aggressive lesions, such as VMs or LMs (versus AVMs), the risks involved with the use of ethanol can seldom be justified. In these cases, safer agents such as ethibloc, polidocanol, and sodium tetradecyl sulfate should be tried first

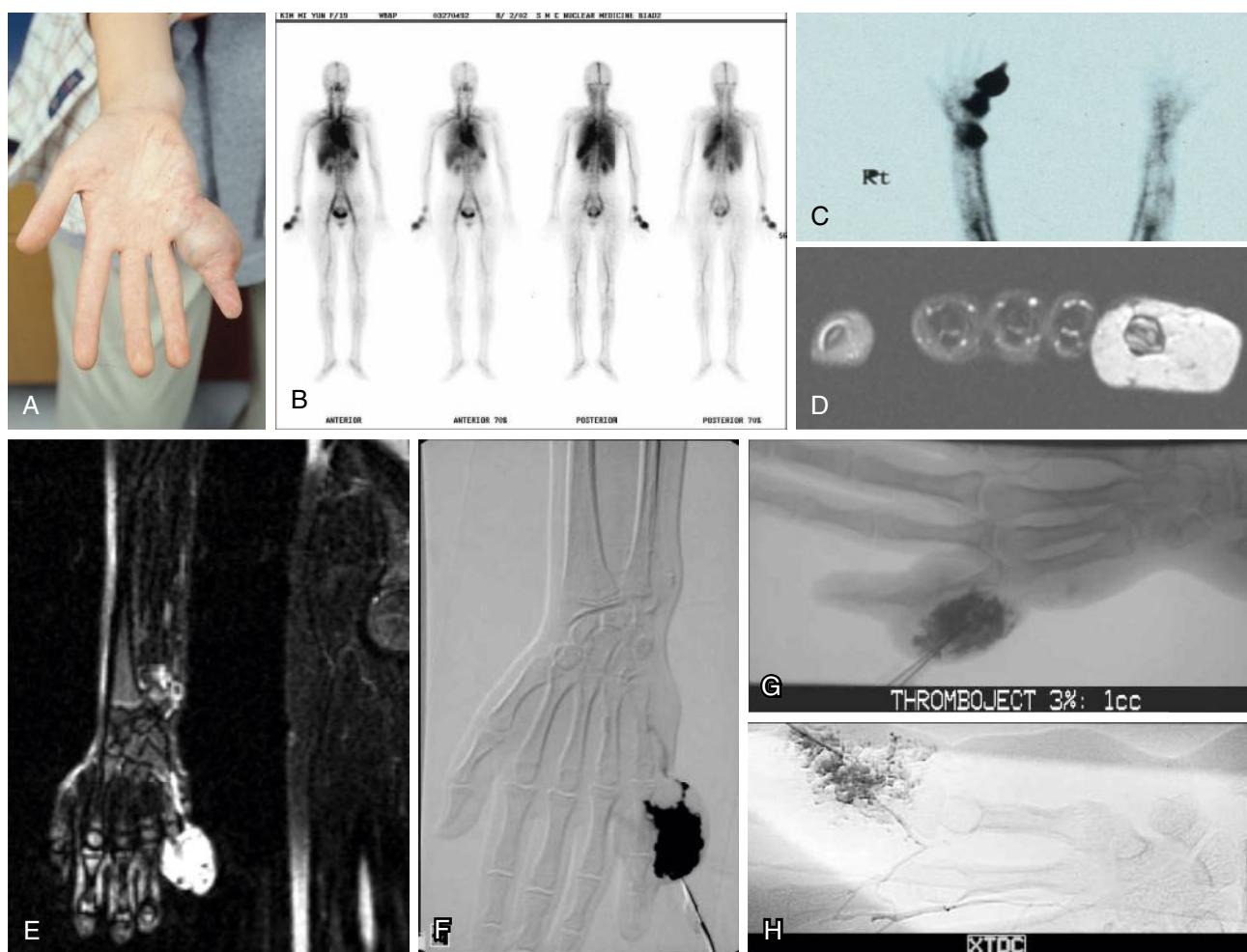


Figure 170.6 Endovascular Sclerotherapy with Sodium Tetradecyl Sulfate. (A) Localized venous malformation affecting the entire right fifth finger and extending to the palm. (B, C) Whole-body blood pool scintigraphy displays intense abnormal blood pooling of a much larger magnitude than is evident clinically. (D, E) MRI demonstrates a similar condition within close proximity to the skin. This finding suggests a higher risk of necrosis if ethanol is used. (F–H) Based on percutaneous direct-puncture phlebography findings (F), 3% sodium tetradecyl sulfate was used as a sclerosing agent (G), with an excellent response (H). Despite repeated sessions, the skin did not slough.

(Fig. 170.6).^{42,145,146} In cases where a VM involves skin and mucous membranes (e.g., face, palm or fingers, sole or toes, tongue), there is an increased risk of morbidity with the use of ethanol, and “foam” sclerotherapy is now considered a better option.^{147,148} However, the risk of paradoxical air embolism through a patent foramen ovale needs to be considered and its existence ruled out if foam is used.¹⁴⁹

Embolotherapy^{43,71,74,150–154}

Currently available embolization agents such as N-butyl-cyanoacrylate/NBCA,^{151,152} Onyx,¹⁵³ coils,¹⁵⁴ and/or contour particles^{43,74} are not suitable as an independent therapy with limited value since they all do NOT have the ability to penetrate the lesion nidus like liquid agents. These agents function by mechanical occlusion of the vessel lumen only, with cessation of flow and thrombosis. Since they are not able to cause a complete destruction of the vessel endothelium, embolization alone carries a significant risk of lesion recurrence.^{43,71,72,74}

Indeed, NBCA appears to be “resorbed” over time to cause recurrence of the lesions. Onyx, consisting of ethylene copolymer and vinyl alcohol (EVOH) dissolved in dimethyl sulfoxide (DMSO), has several advantages over NBCA as a new “less adhesive” liquid polymerizing embolic agent, including a much lower risk of pulmonary embolism, but onyx is also a palliative agent like NBCA.

Hence, long-term results of NBCA and Onyx, the two most commonly used polymerizing agents, as an independent therapy remain controversial when used as single agent therapy because the inability to induce complete destruction of the embryonic component increases the risk of recurrence.^{43,70,74} Hence, many consider NBCA and Onyx to be “palliative at best,” and rather ideal as a supplemental preoperative embolic agent for subsequent surgical excision either for peripheral AVM or VM to enhance the efficacy of surgical dissection (Fig. 170.7). These embolic agents can be utilized in various combinations either simultaneously or in multiple separate stages.

Coils also generate only a mechanical effect to occlude flow and induce thrombosis. They have no direct effect on the

endothelium. Coil embolotherapy is therefore not appropriate as an independent therapy for extratruncular CVM lesions, and additional permanent therapy is warranted to control the nidus completely either with absolute ethanol or surgical excision.^{43,74,154}

Coil embolotherapy is most effective to control a large multifistulous AVM lesion with extremely large volume and fast blood flow; initial coil embolization can convert a high-flow to a lower-flow lesion and make the lesion more amenable to ethanol sclerotherapy or NBCA glue embolotherapy for subsequent surgical excision with a reduced risk of complication and morbidity.¹⁵⁴

Treatment Types – Surgical Therapy

Resective Surgical Therapy

Surgical excision remains the only proven option for the chance of “cure” when the lesion is completely excised, but this generally requires extensive surgery (radical resection) with high morbidity to remove the entire lesion. Incomplete resection of the lesion nidus often results in recurrence, which can make the condition worse. Therefore, surgical excision is suited mostly for limited, localized lesions. Because CVMs rarely become life- or limb-threatening except AVMs, the majority do not require radical resection.^{43,74}

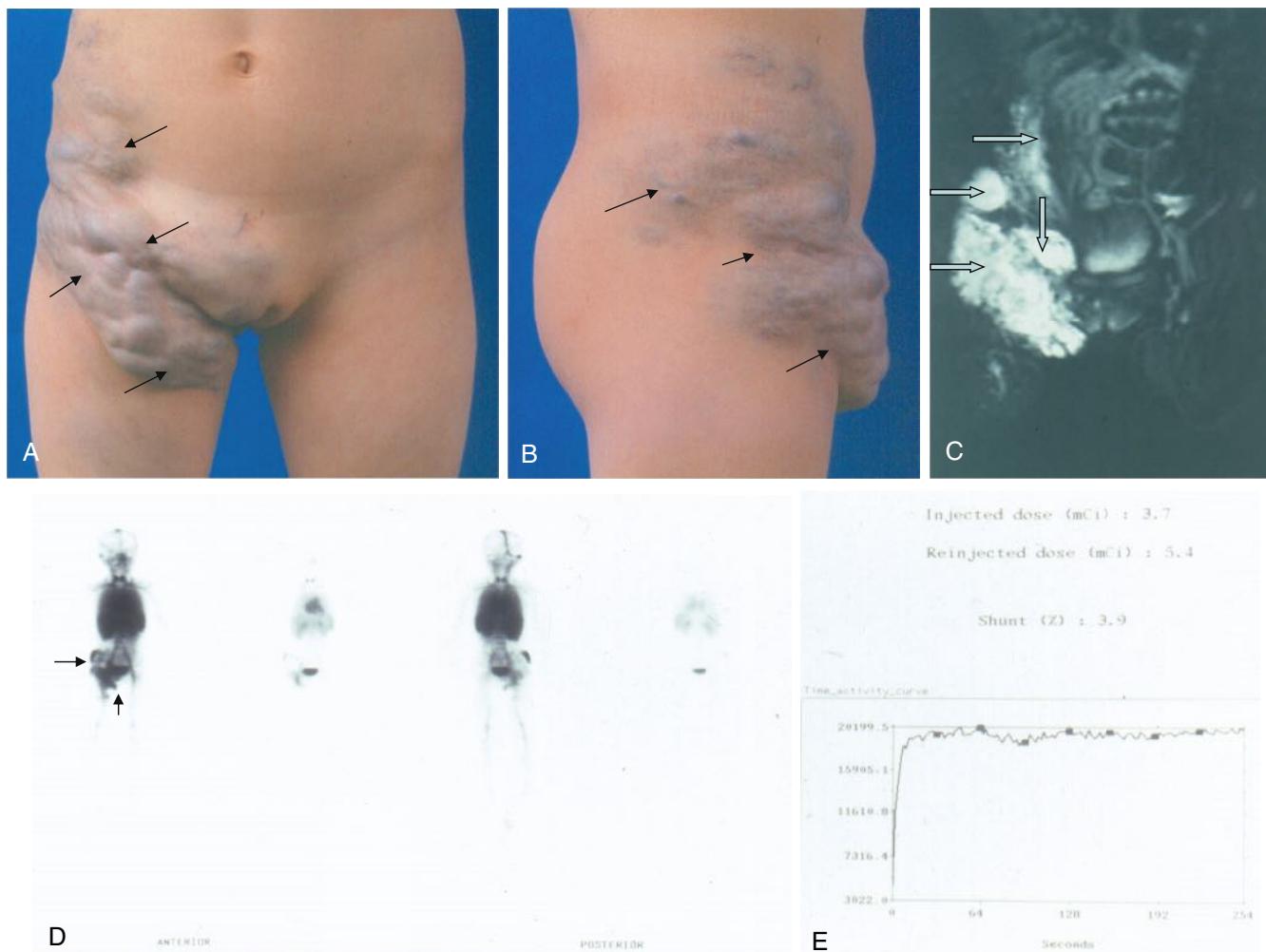


Figure 170.7 Preoperative Embolotherapy with N-Butyl Cyanoacrylate (NBCA). (A, B) This 4-year-old girl has a large venous malformation (VM) involving the skin along the entire right groin and extending to the upper thigh, lower flank, and pubis (arrows). (C) MRI shows a large infiltrating VM that is extremely vulnerable to trauma and bleeding (arrows). (D) Whole-body blood pool scintigraphy depicts the magnitude of the lesion affecting the entire right pelvic region (arrows). (E) Transarterial lung perfusion scintigraphy rules out a hidden arteriovenous malformation as a source of abnormally increased blood flow along the right lower extremity. There is no evidence of shunting – 3.9% is within the normal range.

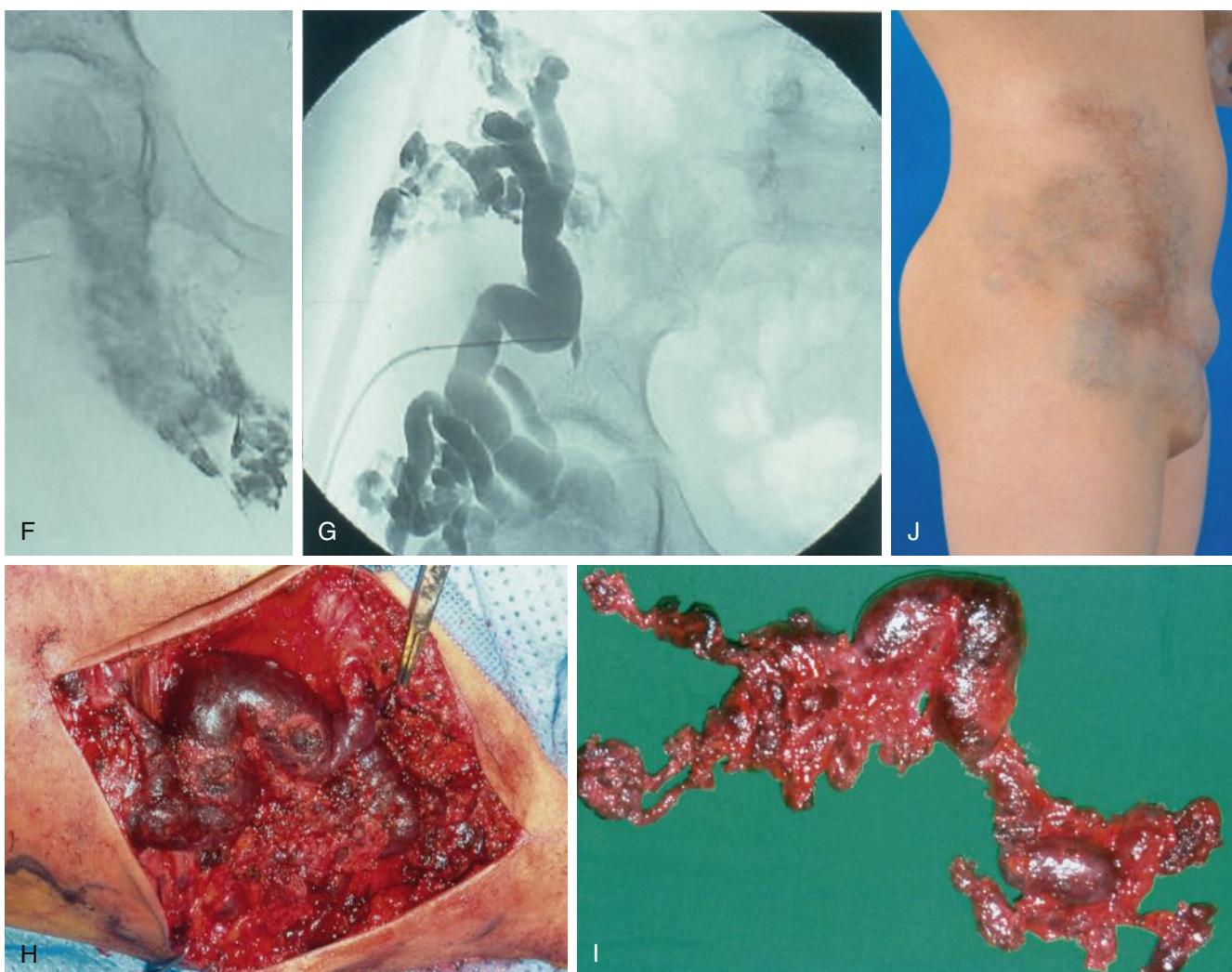


Figure 170.7 Cont'd. (F, G) Percutaneous direct-puncture phlebography demonstrates one large, infiltrating, extratruncular VM that is amenable to embolotherapy, before (F) and after (G) the preoperative embolotherapy. This step makes subsequent surgical excision safer. (H) Operative findings include an NBCA glue-filled lesion, done preoperatively to minimize bleeding during excision. The glue-filled lesion provides an excellent guide for resection, resulting in minimal damage to the surrounding tissue, as shown by the surgical specimen (I). Preoperative embolotherapy facilitates complete removal of the lesion with reduced morbidity. (J) Clinical photograph 2 years later shows no evidence of recurrence.

Reconstructive Surgical Therapy

Various truncular VM lesions with direct involvement of the named veins (e.g., the iliac vein, IVC) can be managed successfully by open reconstructive management. From a simple excision of the intravenous web/membrane to segmental resection of the involved vein combined with various reconstruction techniques can provide excellent long-term results.^{70,71,155,156}

Among various truncular VMs, venous aneurysms of main veins (e.g., aneurysm of popliteal or superficial femoral vein) can be managed either with a total resection and bypass/transposition, or partial tangential resection and suture aneurysmorrhaphy. According to the experiences by Gillespie et al.⁸⁷ with 39 venous aneurysms, the aneurysms in the lower extremity deep veins and internal jugular veins required tangential excision in 5, total excision in 23, and observation in 7. Because of the potential morbidity, treatment of venous aneurysms should be surgical in the majority of cases.^{70,71}

Valve function restoration is also technically feasible with vein valve transplant or transposition of the vein with normal valves into deep femoral vein as an anti-reflux measurement for the deep vein dysplasia of the lower limb with extensive reflux.¹⁵⁷⁻¹⁵⁹ But the experiences are all anecdotal and its long-term efficacy remained to be assessed.⁷¹

Endovenous reconstruction to restore the venous flow with angioplasty and stenting is the treatment modality of choice for obstructive iliac vein and vena caval lesions to restore the venous flow. Such an endovascular approach is also useful to manage various stenosing truncular VM lesions: webs, septum, and stenosis of the iliac vein, IVC, jugular vein, and azygous vein.¹⁶⁰⁻¹⁶³ However, when truncular VM lesions fail to respond to the endovascular therapy, excisional surgical therapy with/without bypass reconstruction would become the treatment of choice.⁷¹

SPECIAL TREATMENT ISSUES

Congenital Vascular Bone Syndrome: Angio-osteodystrophy

Congenital Vascular Bone Syndrome (CVBS) represents a group of abnormalities of long-bone growth caused by CVMs in childhood. Abnormal circulation around and/or inside the bone by CVMs would result in an angio-osteohypertrophy or angio-osteohypotrophy.^{90–92} The marginal vein (MV) has been well known to cause angio-osteodystrophy, mainly as hypertrophy, among VM. Limb overgrowth is always due to hypervasculization,¹⁶⁴ but undergrowth with bone shortening may be induced by local bone compression of abnormal vascular masses. Another rare cause of hypotrophy of the limb is a global reduction of blood inflow because of a congenital local hypoplasia of arteries. However, several tissue and bone growth factors may be involved in the phenomenon besides the hemodynamic factors.¹⁶⁵

Incidence of long-bone lengthening by CVBS was found in 19% and shortening in 7% among the VM groups while the incidence among AVMs is 49% elongation and 4% shortening.⁹⁰ Clinical recognition of limb length difference together with the CVM, mostly as a VM, can be confirmed with plain X-rays to demonstrate bone changes and a precise measurement can be obtained with bone scanogram. Duplex ultrasonography (DUS) is the next test to assess specific condition of the CVM lesions involved and further study with MR or CT examinations can confirm intraosseous localization of CVM.¹⁶⁶ Such assessment of the CVM lesion to cause the abnormal long-bone growth should be carried out expeditiously so that aggressive control of the lesion(s) itself can be started whenever feasible regardless of age before the epiphyseal plate is closed to complete bone growth at an average age of 16 to 18.^{71,82}

Removal of the CVM lesion in early childhood would give a sufficient time available for the natural compensation to stop the growing effect on the bone to get a spontaneous correction of limb length discrepancy. However, adjunctive orthopedic procedures (e.g., the application of staples) may be considered to the “affected” bone itself in case of a significant length difference. Such procedures are typically undertaken *after* the bone growth is completed since the outcome of the epiphyseal stapling is unpredictable. Any orthopedic procedures to the healthy contralateral “non-affected” limb to correct a leg length discrepancy should be discouraged during this bone-growing age in particular.^{90–92,167,168}

Coagulopathy: Thrombosis and Fibrinolysis

Extratruncular VM has been known for inherent risk of coagulopathy by blood stagnation within the cluster of embryological venous tissue with abnormal structures, which leads to the activation of the coagulation cascade with subsequent thrombin production and the conversion of fibrinogen into

fibrin.^{169,170} This unique condition known as localized intravascular coagulopathy (LIC) is followed by fibrinolysis, which is reflected by elevated levels of fibrin degradation products including plasmin derived D-dimer epitopes.^{171,172} Newly formed microthrombi in LIC form stone-like structures called “phleboliths,” which can be detected by palpation when the VM is located superficially or visualized on plain X-ray when located in deep VM.^{171,173}

LIC has the potential to lead to more serious thromboembolic events, including deep vein thrombosis (DVT), pulmonary embolism (PE), and subsequent chronic pulmonary hypertension. Further, this relatively benign local condition could progress to disseminated intravascular coagulation (DIC) with life-threatening hemorrhage related to consumption of coagulation factors and multiorgan failure by disseminated microvascular thrombosis. Events known to trigger the conversion of the LIC to DIC include sclerotherapy, surgical resection, bone fracture, prolonged immobilization and pregnancy or menstruation.^{173–177} The presence of phleboliths *may*, therefore, represent an indication for anti-coagulation, especially when the accompanying lesion is large and extensive.^{23,178}

However LIC is different from Kasabach–Merritt syndrome (KMS), although it is often erroneously labeled as the same condition. KMS is a different clinical entity associated with vascular tumors, characterized by DIC and profound thrombocytopenia,^{169–171} whereas the platelet count in LIC is minimally diminished as the outcome of consumptive coagulopathy (in the 100–150 × 10³/mL range).^{178,179}

Therefore, a thrombotic risk profile to evaluate a hypercoagulable state is highly recommended for all VM patients as a routine part of the diagnostic evaluation. A detailed coagulation profile is needed to identify those with increased risk of hemorrhage prior to surgery or sclerotherapy. Large VMs as well as multifocal VMs with significant elevation of D-dimer levels are associated with coagulation disorders with strong positive statistical correlation.

Extensive VM affecting an extremity with low fibrinogen level reflects an increased risk for bleeding due to consumptive coagulopathy, and requires preventive management with low-molecular-weight heparin (LMWH).^{180,181}

SYNDROMIC VASCULAR MALFORMATIONS

Klippel–Trénaunay Syndrome

Much has been written about KTS since its initial description at the beginning of the 1900s. Even though several variations are possible, the typical patient with KTS has the following clinical features: (1) port-wine stain that may be localized to a relatively small area or involve the lateral aspect of one or more extremities; (2) limb hypertrophy or gigantism; (3) presence of large clusters of varicose veins extending throughout the entire extremity; and (4) a large lateral venous

collector called the vena marginalis lateralis/marginal vein (MV), which typically drains into the pelvic veins. Nevertheless, by definition, all patients diagnosed with KTS should have three CVM components: VM, LM and CM. VM and LM are the major components in various combinations of extratruncular VM, truncular VM, extratruncular LM known as lymphangioma, and truncular LM as primary lymphedema.^{13,85,93,104,107,112}

The large majority of KTS patients can be managed with conservative measures such as compression (gradient elastic stockings with 35- to 45-mm pressure) and sclerotherapy. However, some patients have pain, venous ulceration, venous thrombosis, and pulmonary embolism often caused by MV. Excision of the large varicose clusters has been condemned by some authors in the past, who observed an aggravation of symptoms after excision of the superficial venous plexuses. We have learned that 8% of patients with KTS have either atresia or hypoplasia of the deep venous system, and in these cases surgical excision of the superficial plexuses does more harm than good.

However, when symptoms merit and the deep venous system is patent, surgery may bring a great deal of relief to these patients. In these cases, extensive surgery is often necessary. We recommend surgery in two or three stages and the use of a tourniquet to eliminate or decrease bleeding, which may be copious in these patients. In cases with multiple and large varicosities, surgery under controlled ischemia with two teams of surgeons dramatically shortens the procedure. Beginning 2 months after surgery, sclerotherapy in either liquid or foam form should be used to eliminate residual varicosities.^{70,71,113}

A large MV should be considered to be excised in its entirety when the deep system is patent. We avoid blind stripping and prefer segmental resection through several incisions. The reason for this technique is that there are large perforators, often 8 to 10 mm in diameter, that may bleed profusely if the vein is stripped. These may be the origin of large hematomas after releasing the tourniquet.^{104-107,182}

Owing to the presence of venous aneurysms or large phlebectasias in the deep venous systems of patients with KTS, steps must be taken to prevent deep venous thrombosis and pulmonary embolism. KTS patients should have a duplex ultrasound and a contrast MR or CT venogram to detect aneurysms or phlebectasia together with other coexisting VM as well as LM lesions.^{42,71,93}

The growth discrepancy of the extremities may lead to disabling skeletal sequelae in early adolescence. For this reason, children with KTS must have an orthopedic evaluation and the proper measures taken to prevent scoliosis.

Additionally, in some patients the lymphatic component may be the most important source of problems. Swelling leading to deformity, repeated episodes of lymphangitis and sepsis, lymph leakage through the perineum, or lymph blisters, as well as cosmetic concerns, may have a tremendous negative impact on the lifestyles of these patients.

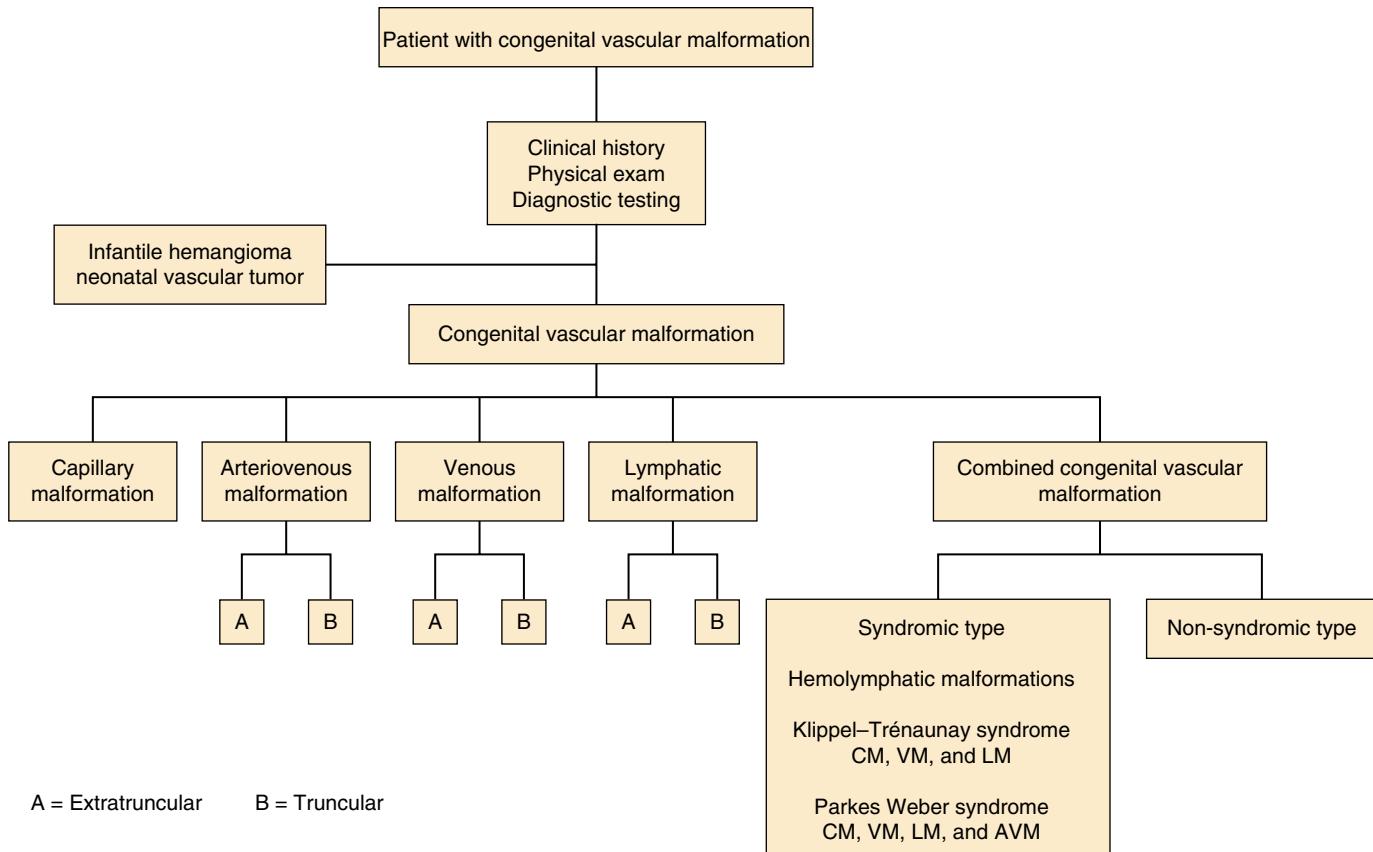
Parkes Weber Syndrome

PWS is a condition first described in 1907 with clinical features similar to those of KTS. As initially described, the syndrome consisted of varicose veins, limb hypertrophy, and a port-wine stain, but with a clearly detectable pulsation and thrill. The difference between PWS and KTS is primarily the presence of an AVM in PWS. Therefore PWS has a different clinical course with a different prognosis.¹⁰⁸⁻¹¹⁰ However, using TLPS¹²³ some investigators have been able to detect the presence of subclinical AV shunting among patients previously diagnosed with KTS, blurring the difference between the two syndromes. However, by definition, KTS does not include an AVM, regardless of the degree of AV shunting. The presence of significant AV shunting in a symptomatic patient with PWS warrants proper treatment.^{42,93} In PWS, the main focus of treatment is control of the arteriovenous shunting by therapeutic embolization.⁴³

LONG-TERM FOLLOW-UP ASSESSMENT

The clinical behavior of every vascular malformation depends on the stage of embryogenesis at which developmental arrest occurs. Therefore, as mentioned previously, the entire extratruncular lesion is destined to grow whenever there is adequate stimulation. All CVMs affecting the extremity should be closely observed during the child's growth until the epiphyseal plate has closed. Female patients have much higher risk of deterioration or revival of the lesion owing to menarche, pregnancy, or hormonal therapy.⁹⁰ A dormant lesion (e.g., microshunting AVM) may become clinically active, changing its clinical characteristics in this setting. Trauma or surgery can also trigger activity in a previously quiet lesion, stimulating it to grow rapidly. Hence, lifetime follow-up at regular intervals is necessary in all *treated or untreated* lesions, especially after pregnancy. Periodic follow-up evaluation, including radiographic studies and various noninvasive studies, is essential for proper long-term care.^{43,71}

CHAPTER ALGORITHM



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INTRODUCTION

The proper diagnosis and treatment of vascular anomalies has long been impeded by misused terminology. Advances in our understanding of these disorders led to the creation of a biological classification system, formally adopted by the International Society for the Study of Vascular Anomalies in 1996 and updated in 2018.^{1–4} This classification scheme divides these anomalies into vascular tumors and vascular malformations based on physical characteristics, natural history, cellular features, and genetic abnormalities. Vascular tumors are true neoplasms that arise from cellular hyperplasia, while vascular malformations are congenital lesions originating from errors of embryonic development of blood vessels. Vascular tumors include infantile hemangioma, Kaposiform hemangioendothelioma, and tufted angioma. Vascular malformations can be further subdivided based on vascular channel type (capillary, lymphatic, venous, arterial, or combinations thereof) or by flow (slow vs. fast). Slow flow lesions include capillary malformations (CM), lymphatic malformations (LM), and venous malformations (VM). Examples of fast flow lesions include arteriovenous fistulas (AVF) and arteriovenous malformations (AVM). Combined malformations (such as Klippel–Trénaunay and CLOVES [congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and skeletal abnormalities] syndromes) consist of two or more

types of vascular malformations and can be associated with other anomalies.^{1,4} A general overview of vascular malformations can be found in Chapter 170 (Congenital Vascular Malformations: General Considerations).

Correct identification of the type of anomaly present in a vascular malformation is paramount to appropriate treatment selection. Consequently, lesions must be properly imaged prior to procedural planning. Ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are the most common modalities used to determine the extent of the malformation. Angiography can also be useful for delineation of AVM, demonstrating the nidus and its feeding vessels, along with flow characteristics.^{5,6} For those with lymphatic anomalies, lymphoscintigraphy may be useful for demonstration of lymphedema, while digital subtraction lymphangiography and magnetic resonance lymphangiography can best delineate the alternate anatomy and dysfunction of the central conducting lymphatics.^{7–9}

Vascular malformations are treated with several modalities. Conservative treatment such as compression garments can help control symptoms of bulky disease and lymphedema. Sirolimus, an mTOR inhibitor, has been used to successfully treat several types of vascular anomalies, including LM, venous lymphatic malformations (VLM), and capillary lymphatic/venous malformations (CLVM).¹⁰ It can also be given before

sclerotherapy or surgery for more complicated lesions to help decrease volume and make these procedures more feasible.¹¹

Preoperative sclerotherapy or embolization may decrease intraoperative blood loss and increase the likelihood of achieving a safe and successful surgical procedure.^{12–16} Endovascular treatments, including sclerotherapy, are addressed in Chapter 172 (Congenital Vascular Malformations: Endovascular Management). General principles for resection have been well described.¹⁷ One should avoid the creation of a large scar that may be as unaesthetically pleasing as the original malformation. Tourniquets should be used for extremity lesions to limit blood loss. Vital structures should also be tagged and avoided to prevent functional loss. Limiting administration of paralytics allows for the use of intraoperative nerve monitoring. Incisions should be closed without tension and drains used to prevent accumulation of fluid postoperatively.

Complete surgical resection may not be achievable, and lesions may require multiple or staged procedures. Resection is generally performed to improve contour and mobility, decrease infectious risk, and for pain relief rather than purely for cosmetic purposes.

SURGICAL TREATMENT OF LOW-FLOW MALFORMATIONS

Capillary Malformations

Capillary malformations are present at birth and typically appear as flat, pink-red cutaneous lesions. They can be associated with underlying soft tissue and skeletal overgrowth, other internal abnormalities, or as part of combined malformations. Resection is not usually necessary for isolated CM, and treatment consists primarily of flashlamp pulse-dye laser or the neodymium-doped:yttrium-aluminum-garnet laser therapy for cosmetic purposes. They may be partially resected during debulking procedures for underlying venous or lymphatic malformations. Those with underlying soft tissue hypertrophy can be surgically excised using a staged zonal approach.¹⁸

Lymphatic Malformations

Lymphatic malformations are often classified as macrocystic (diameter >1 cm), microcystic (diameter <1 cm), or a combination of both. This description of the type of LM, along with its location and extent, is useful when determining treatment options.¹⁹ Presentation can vary from a localized mass to a diffuse anomaly. LM are unique among vascular anomalies in that they not only can serve as a source of infection, causing cellulitis or bacteremia, but they also are affected by illness occurring elsewhere in the body, increasing in size in response to infection. Cervicofacial LM in the head and neck region are common and can present with breathing and swallowing difficulties. Congenital anomalies of the central lymphatics can present with chylothorax or chylous ascites, respiratory compromise, malnutrition and hypoproteinemia, lymphopenia, and bony erosion.²⁰ Intralesional bleeding may also occur secondary to trauma or an abnormal venous connection. Cutaneous involvement of LM manifests as reddish-purple to black vesicles, which can leak serosanguinous fluid.

In general, LM that are predominantly macrocystic are more amenable to sclerotherapy, while those that are microcystic in nature often require resection. Lesions with poor response to sclerotherapy can also be resected. Massive LM, even when predominantly macrocystic, are often best treated with resection since shrinkage after sclerotherapy may not be sufficiently satisfying. Asymptomatic lesions can be observed. Indications for treatment include deformity, dysfunction, leakage into body cavities or from the skin, and recurrent infections. Since these procedures may be lengthy, operative intervention should be delayed until 6 months of age unless the airway is threatened.

Operative Treatment

Subcutaneous LM can cause considerable tissue expansion, and thus for larger lesions, a lenticular excision should be made. As much involved skin as possible (i.e., with creases, dimpling, or vesicles) should be included in the excision to prevent rupture of lymphatic cutaneous vesicles at a later time. The remaining overlying skin and subcutaneous tissue is then dissected off the underlying LM as flaps. The appearance of an LM is similar to fat but has a distinguishable texture. In situations where there is no normal subcutaneous tissue and the LM extends into the dermis, a deep subdermal dissection plane can be created to ensure sufficient vascularity. An intraoperative nerve stimulator is helpful, particularly when the LM encompasses neurovascular structures. Since LM are not malignant lesions, the entirety of the lesion need not be removed, and care should be taken to preserve any vital structures. Subsequent operations may be necessary to remove residual LM or re-contour areas following the initial resection (Fig. 171.1A–C). However, re-operations can be much more difficult because of scar tissue and loss of planes, so every effort should be made to be as thorough as possible at the initial operation. Moreover, depending on how much LM is left behind, any residual lesion may re-expand in the months following surgery. Closed suction drains are placed in the wound to absorb lymphatic leakage, and excision of redundant skin may be required to close the skin in a cosmetic fashion. Complex flaps may be required to provide adequate tissue coverage and cosmetic reconstruction.²¹

Treatment of symptomatic abdominal and pelvic LM can be challenging as they can be quite large and involve multiple viscera. Sclerotherapy is effective for treatment, while surgery can be reserved for refractory lesions.²² Figure 171.2 demonstrates an abdominal LM that was able to be excised laparoscopically. Removal of major associated viscera should be avoided; however, this may not be possible with extensive involvement. Splenectomy may be necessary for patients who develop massive or symptomatic splenomegaly or hypersplenism.²³ LM of the gastrointestinal (GI) tract can cause pain and obstruction, and bowel resection may be required for symptomatic relief.

LM can occur in the subcutaneous tissue of the penis, and lymphedematous swelling of the penis not controlled by wrapping can be excised. The entire thickness of the subcutaneous tissue should be removed to minimize recurrent swelling.

Management of leakage from lymphatic anomalies can be difficult. Chylous pleural effusions from thoracic LM can sometimes be treated with chemical or mechanical pleurodesis.

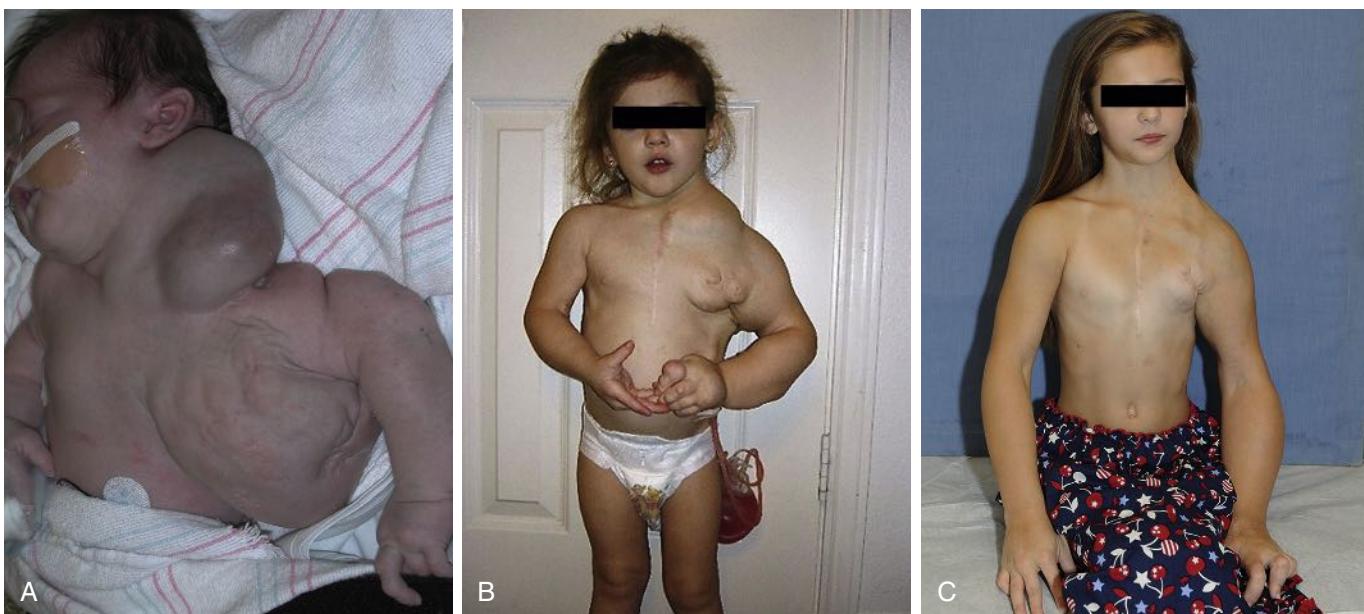


Figure 171.1 (A) Lymphatic malformation of left neck, axilla, mediastinum, and upper extremity in baby girl, shortly after birth. (B) Girl, age 3, following multiple sclerotherapy and debulking procedures. (C) Girl, now age 10, active in dance and other activities.

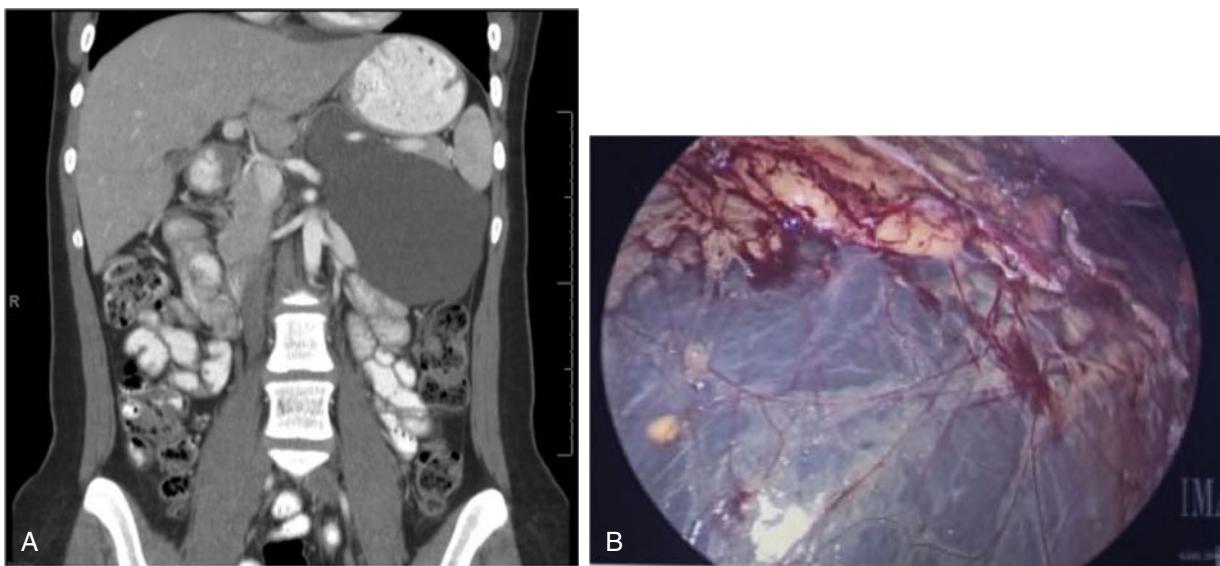


Figure 171.2 (A) CT scan of a 15-year-old girl who had left upper quadrant pain and was noted to have a $10.7 \times 11.3 \times 8.4$ cm cyst in the left side of the abdomen. The cyst was medial to the spleen, posterior to the pancreas and splenic artery and vein, and anterior to the left kidney. (B) Intraoperative view of the cyst on laparoscopy. Final pathology was consistent with a lymphatic malformation.

LM of the pericardium causing pericardial fluid accumulation can be treated by pericardial window or repeated pericardiocentesis by needle or indwelling catheter. Nonoperative management, including octreotide, low-fat diets, total parental nutrition, or sirolimus, may reduce thoracic duct flow and the volume of lymphatic fluid.²⁴ Ligation or embolization of the thoracic duct can be useful, but this should be done with caution in those with diffuse lymphatic anomalies, as outflow obstruction may exacerbate symptoms. In some rare cases, shunt procedures or drainage catheters can provide palliation.

For those with central conducting lymphatic anomalies, lymphaticovenous bypass may provide therapeutic benefit.²⁵ Patients should be carefully selected based on cross-sectional

imaging studies showing delayed emptying of the thoracic duct into the venous system. High-fat meals are given the night before and day of operation to improve visualization of the lymphatics perioperatively. The thoracic duct is exposed in the left neck and divided proximally; an anastomosis is then created between it and a nearby bypass vein (typically the external jugular vein).

Postoperative Management

Closed suction drains are left until output is minimal to prevent seromas and hematomas that may delay healing and induce wound disruption. These can remain in place for weeks to months, so patients should be warned preoperatively regarding the duration of drainage. Patients with abdominal lymphatic



Figure 171.3 (A) Two-year-old boy with large venous malformation of lower back. (B) Resection of venous malformation demonstrating creation of flaps. (C) Venous malformation following resection. (D) Child at 2-month follow-up.

malformations may develop a postoperative ileus and require nasogastric decompression.

Cutaneous vesicles from unexcised lymphatic channels may occur within the surgical scar following resection, but they can be controlled by local intravesicular sclerotherapy or CO₂ laser treatment. They can be resected, but due to their extensive nature, recurrence is common. Consequently, to prevent development of vesicles, the uninolved dermis should be advanced over the resection bed and any involved skin excised during the procedure.

Venous Malformations

Venous malformations may be present at birth and typically grow with the patient, although symptoms may not arise for some time. They may expand with dependent position and Valsalva maneuver. Stasis in VM can lead to phlebothrombosis, causing pain and swelling. In addition, VM of the bone and joints can lead to fractures and hemarthroses. VM involving the muscle can also present with pain and swelling, which are exacerbated by the dependent position and exertion, and can cause associated skeletal problems, including fracture, overgrowth, deformation, or undergrowth.²⁶

VM can be managed conservatively with compressive garments to minimize thrombotic episodes. Some patients,

particularly those with abnormal D-dimer and fibrinogen levels, may show improvement in symptoms with daily low-dose aspirin or low-molecular-weight heparin. Surgery is reserved for symptomatic lesions, cosmesis, or functional impairment, but prior to any operation, coagulation studies should be obtained, as localized intravascular coagulation can occur.²⁷ Those VM that are well-localized are most amenable to surgical excision (Fig. 171.3). Large lesions can be debulked if they are causing uncontrolled pain, significant limb length discrepancy, bleeding, severe cosmetic problems, impairment in function, or limitation of range of motion. Lesions that cannot be entirely resected may be treated with sclerotherapy, and preoperative sclerotherapy can also be performed to decrease blood loss and shrink the lesion.

VM of the GI tract can occur anywhere from mouth to anus. Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by multifocal venous malformations, most commonly involving the skin and GI tract (Fig. 171.4).²⁸ Skin lesions have the appearance of tiny “blue rubber nipples” and can be numerous. Lesions in the GI tract can cause intussusception, which is manifested by intermittent abdominal discomfort. Some lesions may never cause symptoms and require no intervention, and moderate fecal blood loss can often be managed conservatively with iron supplementation. Severity and frequency of bleeding can be decreased with stool softeners and



Figure 171.4 (A) Patient with blue rubber bleb nevus syndrome, with multiple venous malformations (VMs) of the foot. (B) Multiple VM in the intestine. (C) Densely populated VM in resected bowel.

avoidance of constipation. Exsanguinating hemorrhage is rare. However, those with significant anemia, particularly requiring blood transfusions, or an acute small bowel obstruction may warrant an operation. A study of four patients with BRBNS demonstrated that sirolimus was effective in decreasing pain and improving quality of life.²⁹

Operative Treatment

For extremity VM, the use of a tourniquet can decrease intraoperative blood loss. VM have fragile, dysplastic vessels and permeate into surrounding tissues, which can result in significant blood loss with dissection.³⁰ Cutting through a VM produces a surface resembling a sponge, and bleeding is difficult to control with cautery, clamps, or sutures. Hemostatic devices such as bipolar sealers, electrocautery, and ultrasonic scalpels can be useful. Involved skin should be incorporated in the incision as much as possible. VM can also act as a tissue expander, leading to redundant skin once excised, and a large amount of involved skin can be removed with the specimen. Flaps are raised in all directions from the incision (see Fig. 171.3B). When lesions involve the dermis or are just below the dermis, flaps should be made as thinly as possible without devascularization of the skin. Care should be taken to preserve nerves, tendons, and joint cavities; and closed-suction drains are placed in the flap. Large resection areas can be covered by local or distant flaps, or by the use of skin grafts.

For those with blue rubber bleb nevus syndrome affecting the GI tract, VM can be removed with a combination of wedge bowel resection, band ligation, polypectomy, suture-ligation of narrow-based polypoid lesions, and segmental bowel resection (see Fig. 171.4B–C). It is preferable to remove individual lesions rather than sections of intestine, since lesions are distributed throughout the gut. Intraoperative endoscopy, from mouth to anus, identifies lesions that may not be seen



Figure 171.5 A 9-year-old boy presented with left upper quadrant pain. Work-up included an MRI, which demonstrated a 5 × 3.6 × 4.4 cm soft tissue mass at the superior aspect of the spleen, concerning for venous malformation (VM). He underwent laparoscopic splenectomy and pathology confirmed presence of VM.

externally or palpable. Serosal sutures or dye stain can be used to mark these lesions. Diffuse and densely located VM, involving large continuous segments of bowel, require more than simple excision, and can be managed by colectomy, anorectal mucosectomy, and coloanal pull-through.³¹

Anorectal VM can be associated with an ectatic inferior mesenteric vein, which can siphon blood flow from the portal vein.³² This causes stagnation of blood resulting in portomesenteric thrombosis and resultant portal hypertension. Patients with rectal VM should be screened for this anomaly, and if found, it can be ligated proximally to prevent thrombosis.

Symptomatic VM of solid organs may require removal. This can potentially be done with partial resection or complete removal of the organ, if necessary. Figure 171.5 shows a VM of

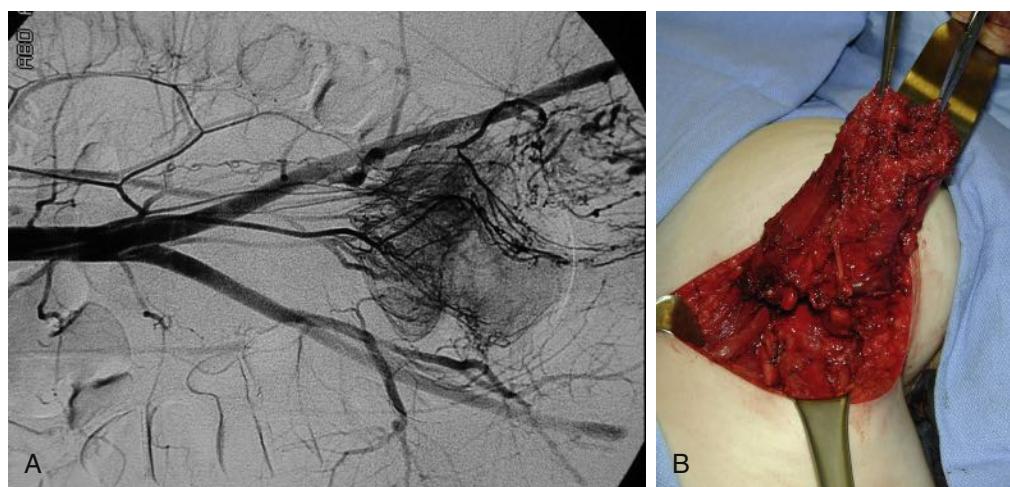


Figure 171.6 (A) Angiogram of diffuse arteriovenous malformation (AVM) of the gluteus maximus muscle, prior to pre-operative embolization. (B) Excision of AVM.

the upper pole of spleen in a child with abdominal pain who eventually underwent splenectomy.

While bulky VM of the scrotum may be amenable to sclerotherapy, repeated sessions should be avoided to minimize radiation, and thus surgical resection is preferable. Sclerotherapy of labial VM can be performed as long as female gonads are shielded. Debulking is best undertaken after puberty, although massive lesions can be debulked earlier. Sclerotherapy of the clitoris should be avoided; clitoral VM can be resected, but care should be taken to avoid neurovascular injury.

Postoperative Management

Lesions not completely excised can re-canalize and enlarge, requiring additional procedures or sclerotherapy.³³ Postoperative complications include hematoma, partial skin necrosis, and persistent edema. Drains are left in place until fluid outflow is minimal.

SURGICAL TREATMENT OF HIGH-FLOW MALFORMATIONS

Arteriovenous Malformations

Arteriovenous malformations are characterized by abnormal connections between feeding arteries and draining veins. They may begin as only a pink stain, but they can expand during pregnancy or puberty or secondary to local trauma. Expansion can lead to skin ischemia and local steal phenomenon, resulting in pain, ulceration, functional impairment, nerve compression, soft tissue and bony destruction, and bleeding. These symptoms necessitate treatment.^{14,34} Large AVM can also cause high output cardiac failure, which requires early intervention. Asymptomatic lesions can be observed, although it is preferable to treat before the AVM progresses.

Operative Treatment

Management of AVM includes embolization alone or in combination with surgical excision. Preoperative embolization of the nidus is followed by surgical resection in 2 to 3 days, since

rapid expansion can occur during the period between embolization and resection (Fig. 171.6).¹⁴ Unless the surgeon is sure that the entire AVM has been removed, the proximal feeding arteries should not be embolized or ligated, as these provide the only avenue to reach the nidus of the AVM for subsequent embolization. Occlusion of the primary vessels will result in recruitment by the nidus of other nearby arteries, allowing the AVM to recur and progress. Embolization can also be used for palliation in persistent AVM.

The goal of the operation is complete excision to normal margins with removal of both the nidus of the AVM and involved skin. Focal AVM can be excised with good long-term control.³⁵ In addition, diffuse lesions have higher recurrence rates and are more difficult to treat, as residual tissue can form collaterals and re-expand.³⁶ Intraoperative Doppler examination and recognition of the bleeding pattern at the margin are also useful guidelines for resection. Intraoperative frozen sections have not proven useful in determining the extent of resection.¹⁴ Reconstruction immediately following resection may require skin grafts or local, regional, or microvascular free flaps.^{14,35–37} Large excisions that do not allow for primary closure can be managed with vacuum-assisted closure devices or tissue transfer techniques. For difficult extremity AVM, particularly those with loss of function, amputation can be performed.

AVM of the thoracic and abdominal cavity are managed with a combination of sclerotherapy and open resection. Most AVM of the chest are intrapulmonary and can be associated with hereditary hemorrhagic telangiectasia. They can be managed with partial pulmonary resection or embolization. AVM of the GI tract are rare.^{38,39} Most patients present with GI bleeding. Bleeding may be temporized with embolization, but recurrent or serious bleeding requires a formal resection. Splenic hilum or parenchymal lesions are uncommon, but they can be managed with splenectomy.^{40,41} Pancreatic AVM can cause portal hypertension and eventual GI bleeding. Straightforward cases can be controlled with embolization, but permanent control may require complete resection, such as a pancreaticoduodenectomy.^{42–46} More complex hepatic AVM may require hepatectomy or hepatic transplantation. Congenital

arterioportal fistulae can cause ascites, abdominal pain, GI bleeding, or malabsorption.⁴⁷ Hepatectomy or surgical ligation of the fistula can be performed if transcatheter embolization fails.^{48–51}

Urinary tract AVM can cause hematuria, hypertension, and flank pain.⁵¹ Localized lesions can be resected.^{52,53} AVM of the genitals can be managed with embolization and resection. AVM of the buttock often involves the gluteal muscles. These can be resected if embolization fails to control symptoms.

Postoperative Management

Patients should be followed long-term since lesions can recur. Reported rates of recurrence range from 8% to 81%, depending on how diffuse the AVM is.^{36,37} Early signs of recurrence include erythema, superficial telangiectasias, swelling, pulsation, bleeding, or Suen sign (rapid soft tissue rebound upon palpation).

SURGICAL TREATMENT OF COMBINED VASCULAR MALFORMATIONS

Diseases with combined vascular malformations include Klippel-Trenaunay syndrome (KTS), Parkes Weber syndrome (PWS), and CLOVES syndrome and present within a wide-ranging spectrum. KTS is a slow-flow combined capillary-lymphatico-venous malformation associated with prominent soft tissue and bony hypertrophy of one or more extremities.^{54–56} Capillary malformations may be large, multiple, or develop lymphatic vesicles, which may weep or bleed. Lymphedema is a common complaint. The deep venous system can be absent or hypoplastic, and often anomalous superficial veins will develop in the extremity, including the primitive lateral embryonic vein of Servelle. These

anomalous veins can cause cellulitis, pain, edema, and bleeding and are at risk for thrombophlebitis and as a source of pulmonary emboli.⁵⁷ These veins should be imaged prior to treatment.

Parkes Weber syndrome is a fast-flow lesion characterized as a capillary arteriovenous malformation (CAVM) or capillary arteriovenous fistulae (CAVF) and involves the upper and lower extremities.⁵⁸ Congestive heart failure can develop secondary to the AVM and fistulae and may necessitate embolization of these.

CLOVES syndrome is characterized by congenital lipomatous overgrowth, vascular malformations, epidermal nevi, seizures, scoliosis, and skeletal/spinal anomalies.^{59,60} Lipomatous masses on the trunk and flank can be present at birth, and extend into the mediastinum, pleural cavity, retroperitoneum, and paraspinal-intraspinal space. These can cause physical deformity and functional impairment (Fig. 171.7A). For example, large hands, macrodactyly, widened triangular feet, and “sandal gap” toes are extremity abnormalities found in these patients. Anomalous veins are also present in the extremities and along the thoracic wall and have been shown to cause pulmonary embolism.⁶¹

Nonoperative management with compression therapy can improve symptoms of pain, swelling, and heaviness from chronic venous insufficiency and lymphedema. Routine use of compression garments is started around age 4 to 5 years. Pneumatic compression devices can be used while sleeping or recumbent, but they are expensive. Anomalous veins were historically managed with resection, but endovenous laser ablation is now the more common therapeutic modality.

Operative Management

Soft tissue overgrowth can be managed by debulking and contour resections, which are typically done as staged procedures

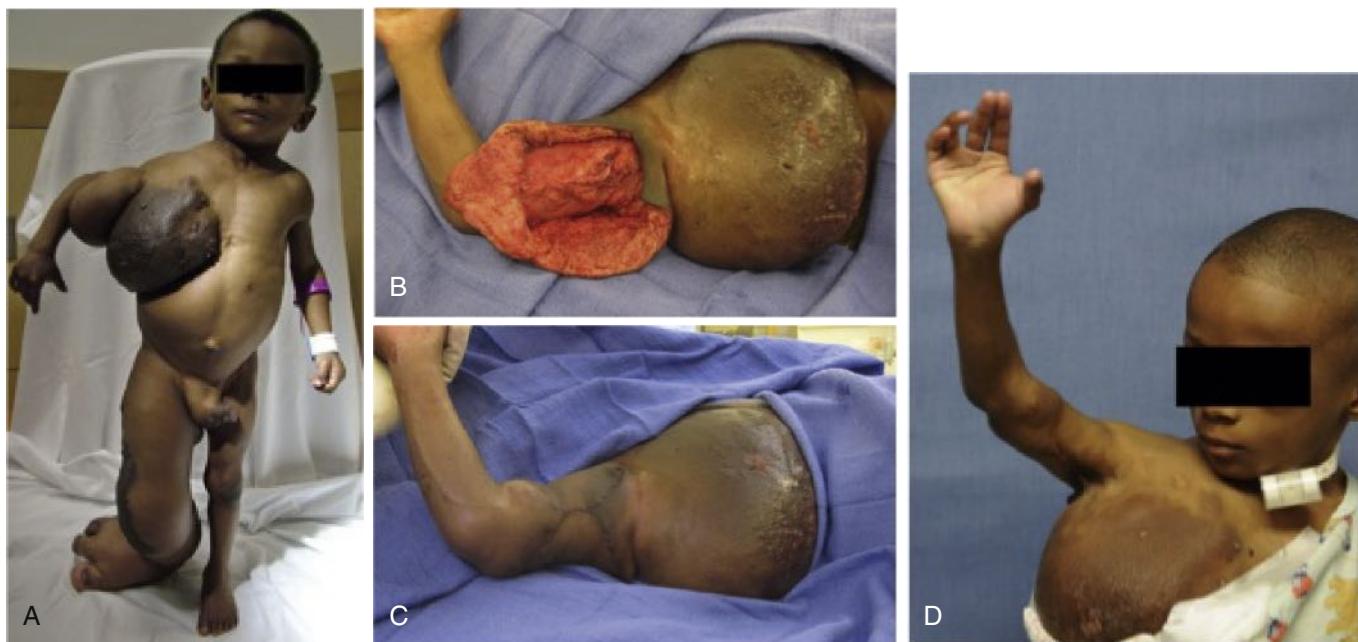


Figure 171.7 (A) Patient with congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and skeletal abnormalities (CLOVES) syndrome, with mixed malformation of right upper extremity and chest wall, limiting range of motion. (B) Lenticular incision was created and malformation removed off muscle fascia. Note that the incision does not cross the axilla or elbow joint. (C) Closure of incision by adjacent tissue advancement technique. (D) At 14 months' follow-up, patient now has improved mobility in upper extremity.

(see Fig. 171.7B–D).^{62,63} The most common areas of debulking are the trunk, genitalia, perineum, buttock, and lower extremity. Debulking should be considered in those with multiple soft tissue infections. Asymptomatic lesions extending into the mediastinum or thoracic cavity are managed conservatively. Because of the risk of thromboembolism, patients should be considered for preoperative and postoperative anticoagulation and temporary inferior vena cava filter placement. Preoperative imaging is critical to determine if overgrowth is extrafascial or intrafascial, because injury to major neurovascular structures and immobility can occur with debulking of intrafascial overgrowth. Hypertrophy of the extremity can result in limb-length discrepancy that may require epiphysiodesis.

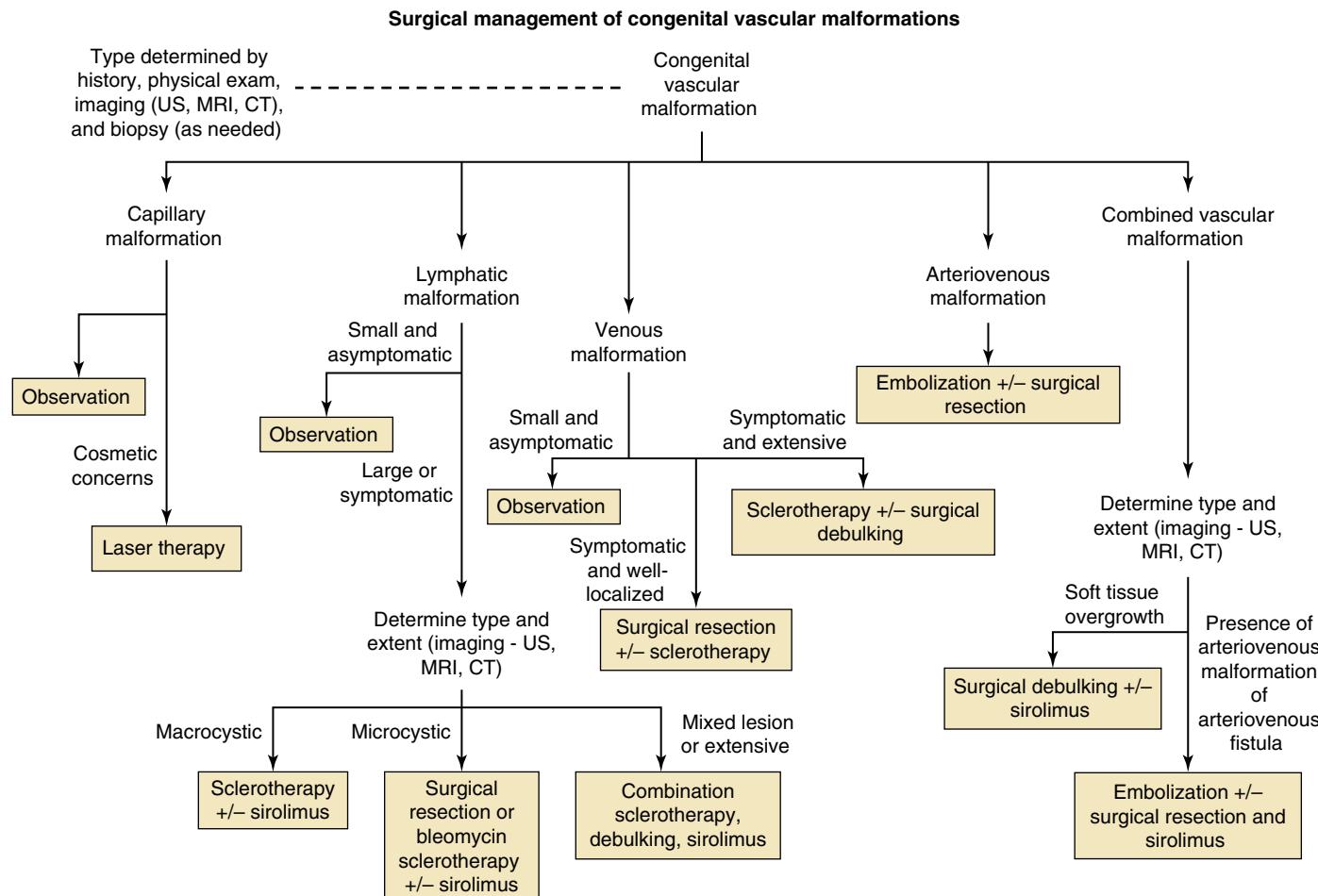
Debulking should be tailored to address the specific problematic areas of each patient and to remove as much excess bulk and weight as possible. The most extensive areas are usually addressed first. Blood loss and transfusions can be minimized by using tourniquets and intraoperative cell saver machines. A lenticular excision is used when excess tissue is present and should incorporate cutaneous lesions as anatomic options allow. The skin is incised down to the subcutaneous tissue and then skin flaps are raised. Areas with malformation

that involves or is adjacent to the dermis require cautious dissection of flaps to avoid devascularization. The flap dissection should be limited to a maximum circumference of 180 degrees to enhance flap viability and minimize postoperative wound complications. Once flaps are raised, the abnormal tissue between the muscle fascia and skin is removed. Drains are then placed in the wound bed, and skin flaps are reapproximated. The overgrowth acts as a tissue expander and often allows a large amount of excess skin to be removed. Amputation of an extremity may be necessary for palliation for unrelenting symptoms or destroyed fixed joints.

Postoperative Management

Patients should be counseled prior to resection regarding delayed postoperative healing and the protracted use of closed-suction drains. Because of altered circulation and poor lymphatic drainage, tissue in these patients makes for poor flaps, and wound healing can take several weeks to months. Drains are removed once output decreases to approximately 10 to 15 mL/day. Lymphatic vesicles may appear in and around the scar postoperatively and can be treated by laser therapy.

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A complete reference list can be found online at www.expertconsult.com.

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Congenital Vascular Malformations: Endovascular Management

CHRISTOPHER R. BAILEY and CLIFFORD R. WEISS

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INTRODUCTION

Vascular anomalies comprise a collection of disorders characterized by abnormal, non-neoplastic blood vessel growth. The need for accurate characterization of these lesions has led to the development of a classification system based on biologic behavior which is approved by the International Society for the Study of Vascular Anomalies (ISSVA).^{1,2} This classification system was most recently updated in 2018.¹ It broadly divides vascular anomalies into vascular malformations and vascular tumors (Table 172.1).

Vascular malformations are the more common anomaly, comprising approximately two-thirds of all vascular anomalies; they are congenital, non-neoplastic lesions that develop secondary to defects in different molecular pathways of

vasculoneogenesis.^{3,4} Vascular malformations are further subdivided into low- and high-flow lesions based on their hemodynamic characteristics. Low-flow vascular malformations are composed of capillaries (capillary malformation), veins (venous malformation), lymphatics (lymphatic malformation [LM]), or a combination (venolymphatic malformation). High-flow vascular malformations are characterized by a direct communication between arterial and venous vessels without an intervening capillary bed (arteriovenous malformations [AVMs] and arteriovenous fistulas [AVFs]).

Vascular tumors are neoplastic vascular anomalies defined by the presence of abnormal endothelial proliferation. Overall, the most common vascular tumor is the infantile hemangioma, which is benign and characteristically involutes over time.⁵ Angiosarcoma and epithelioid hemangioendothelioma

TABLE 172.1

Classification of Vascular Anomalies by the International Society for the Study of Vascular Anomalies – Overview

Vascular Anomalies

VASCULAR MALFORMATIONS				
Vascular Tumors	Simple	Combined	Of Major Named Vessels	Associated with Other Anomalies
<ul style="list-style-type: none"> • Benign • Locally aggressive or borderline • Malignant 	<ul style="list-style-type: none"> • Capillary malformations • Lymphatic malformations • Venous malformations • Arteriovenous malformations • Arteriovenous fistula 	<ul style="list-style-type: none"> • CVM, CLM, LVM, CLVM, CAVM, CLAVM, other 	<ul style="list-style-type: none"> • Channel type or truncal malformations • See ISSVA for complete list 	<ul style="list-style-type: none"> • Klippel–Trénaunay • Parkes–Weber • Servelle–Martorell • Sturge–Weber • CLOVES • See ISSVA for complete list

CVM, capillary–venous malformation; CLM, capillary–lymphatic malformation; LVM, lymphatic–venous malformation; CLVM, capillary–lymphatic–venous malformation; CAVM, capillary–arteriovenous malformation; CLAVM, capillary–lymphatic–arteriovenous malformation.

ISSVA. International Society for the Study of Vascular Anomalies Classification of Vascular Anomalies. <http://issva.org/classification>; 2018.



Figure 172.1 (A) An 11-year-old female with LVM of the tongue, status post-tongue reduction surgery and prior laser treatment. Recurrence of numerous small blue-black cystic lesions on her tongue. They weep clear lymphatic and bloody fluid. (B–C) Sagittal T2-weighted image of the tongue shows increased T2 signal in the intrinsic tongue muscles, which are mildly enhanced in the contrast-enhanced T1-weighted sagittal image (C). Magnetic resonance imaging (MRI) is helpful for identifying the depth of infiltration in this superficial lesion. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol*. 2014;69(5):443–457, Fig. 11.)

are examples of malignant vascular tumors and require oncologic evaluation and treatment.⁵

This chapter focuses on the diagnosis and treatment of vascular anomalies most commonly treated by endovascular specialists.

DIAGNOSIS OF VASCULAR MALFORMATIONS

The diagnosis of vascular malformations can be confusing due to their relative rarity and overlapping clinical and imaging features. Because of this confusion, suspected vascular malformations are often referred to centers with a dedicated multidisciplinary vascular anomaly team for diagnostic workup and treatment.⁶ It is common to seek multidisciplinary consultation from dermatology, plastic surgery, neurosurgery, vascular

surgery, and diagnostic and interventional radiology. At our institution, the vascular anomaly team classifies vascular malformations according to an established visual pathway, known as the S.E. Mitchell vascular anomalies flowchart (SEMVAFC),⁶ which combines clinical and imaging findings to accurately identify lesions. In some cases, syndromes associated with vascular malformations, such as Parkes–Weber syndrome and Klippel–Trénaunay syndrome (KTS), can be identified with SEMVAFC.

Vascular malformations can be imaged with duplex ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), and conventional angiography. Patients are often first evaluated with US, which has the advantages of wide availability, lack of ionizing radiation, patient comfort, and real-time hemodynamic characterization. However, US is limited by a small field of view that may exclude portions of large or deep vascular malformations. MRI is the preferred

examination for most lesions, given its wide field of view, excellent soft tissue resolution, and ability to assess enhancement characteristics (Fig. 172.1).⁷ Accurate classification is assisted by the addition of dynamic contrast-enhanced magnetic resonance angiography (DCE-MRA), which produces imaging of

the lesion in the arterial, capillary, venous, and delayed venous phases.⁸ MRI is also useful after treatment to judge changes in size and flow characteristics.

At our institution, the MRI protocol for vascular anomalies includes multiplanar fat-saturated T2-weighted, T1-weighted,

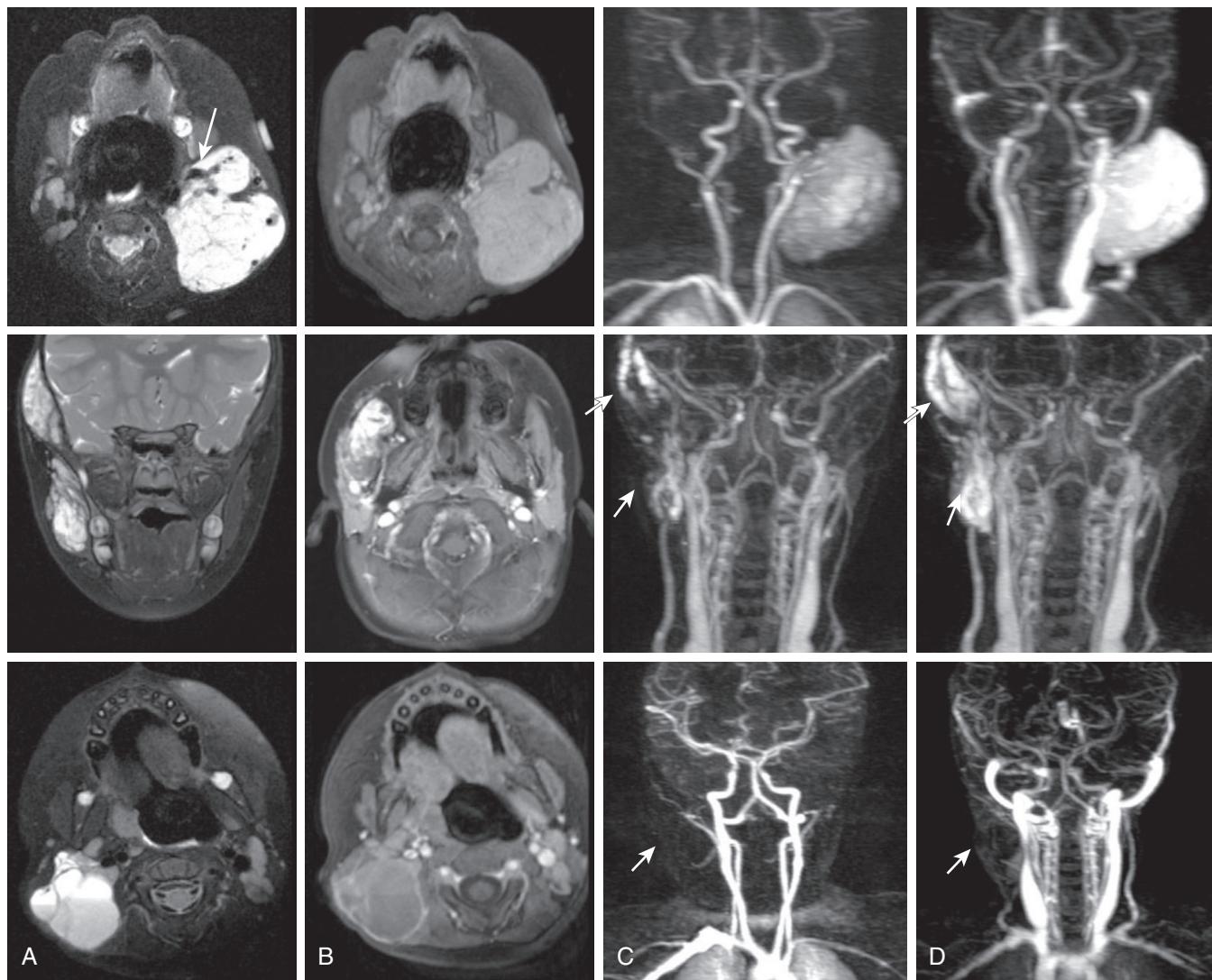


Figure 172.2 *Top row:* Infantile hemangioma (IH). (A) Axial T2-weighted fat-saturated image and (B) axial T1-weighted postcontrast fat-saturated image demonstrating a well-demarcated T2 hyperintense mass with clean borders and homogeneous internal enhancement. Note the serpiginous internal flow void (arrow) (A) from an arterial feeder. Coronal TWIST demonstrates avid enhancement in the arterial phase (C) with a feeder from the external carotid artery and lack of washout during the venous phase (D). Note the venous drainage to the left subclavian vein. *Middle row:* Venous malformation (VM). (A) coronal T2-weighted fat-saturated image demonstrates a predominantly T2 hyperintense mass infiltrating the right masticator and temporalis muscle. Note multiple small round T2 dark foci, representing phleboliths. (B) Axial T1-weighted postcontrast fat-saturated image demonstrates strong but somewhat heterogeneous internal enhancement. (C, D) Coronal TWIST demonstrates progressively increasing enhancement during the venous phase (arrows). There was no enhancement in the arterial phase (not shown). *Bottom row:* Lymphatic malformations (LMs). (A) Axial T2-weighted fat-saturated image demonstrates a lobular multicystic mass with a fluid–fluid level in the soft tissues of the right lower neck. Axial T1-weighted postcontrast fat-saturated image (B) demonstrates enhancement of the cyst wall only without any internal enhancement. Lack of internal enhancement distinguishes LMs from VMs. The layering bright T1 signal is likely due to internal hemorrhage. Coronal TWIST did not demonstrate enhancement in the arterial or in the venous phase (arrows) (C, D). (Reproduced from Higgins LJ, Koshy J, Mitchell SE, et al. Time-resolved contrast-enhanced MRA (TWIST) with gadofosveset trisodium in the classification of soft-tissue vascular anomalies in the head and neck in children following updated 2014 ISSVA classification: first report on systematic evaluation of MRI and TWIST in a cohort of 47 children. *Clin Radiol.* 2016;71(1):32–39, Fig. 1.)

TABLE 172.2

Typical Magnetic Resonance Imaging Features of Vascular Anomalies

	IH	VM	LM	AVM	AVF
Solid mass	Yes	No	No	No	No
Phlebolith	No	Yes	No	No	No
Enhancement	Avid, homogenous	Variable	None (cyst periphery)	Avid, serpiginous	Avid, serpiginous
DCE-MRA	Arterial	Venous	None	Arterial with early venous drainage	Arterial with early venous drainage

AVM, arteriovenous malformation; AVF, arteriovenous fistula; DCE-MRA, dynamic contrast-enhanced magnetic resonance angiography; IH, infantile hemangioma; LM, lymphatic malformation; VM, venous malformation.

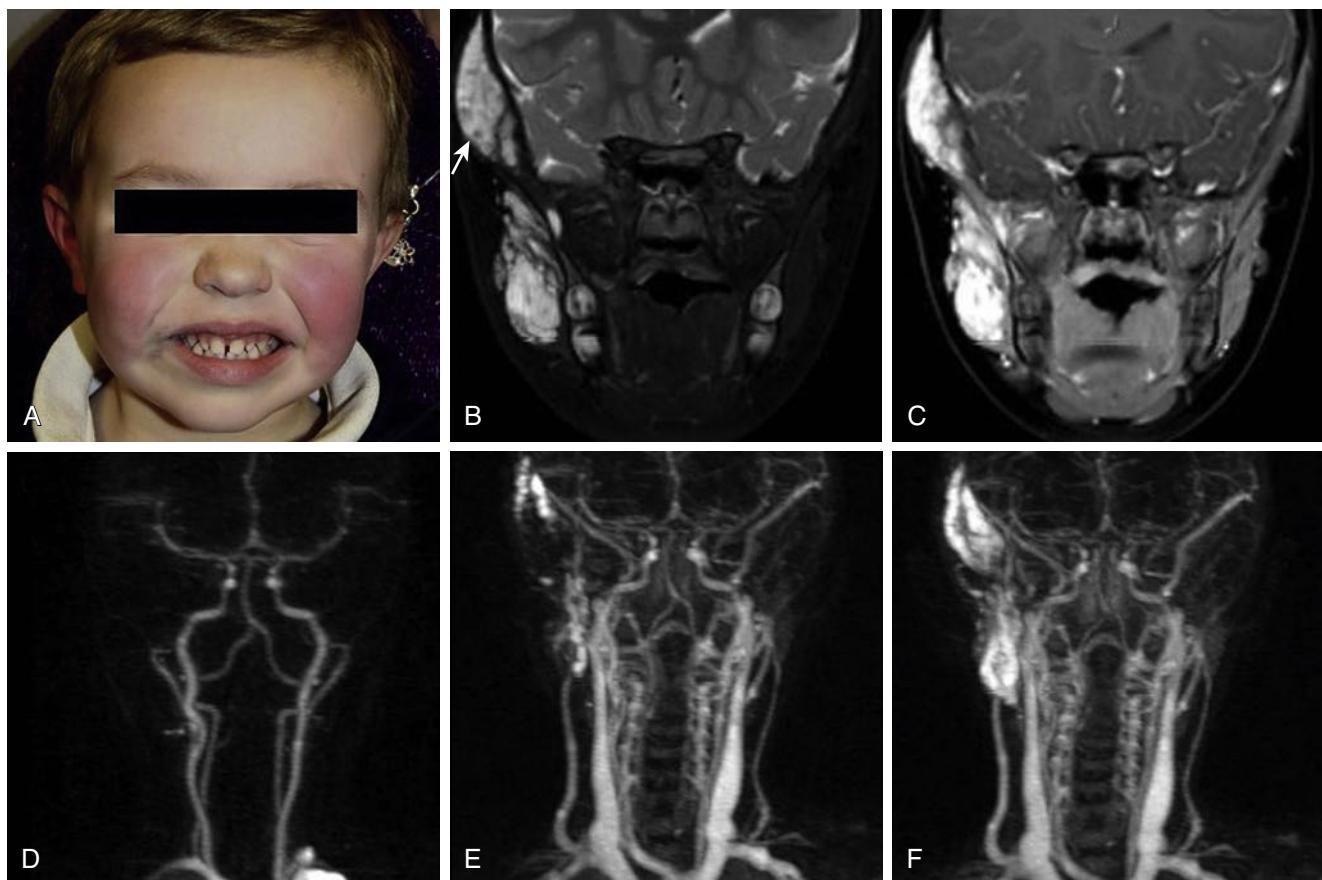


Figure 172.3 Venous Malformation (VM). (A) A 4-year-old male with blue discoloration of his right cheek and the corner of right lip; it was noted to have been present since birth and was stable. Note that the right cheek is fuller than the left. The lesions are soft and compressible. (B–C) Coronal images show infiltration of the right temporalis muscle and right masticator space by a T2 bright (B) and enhancing mass (C). Note the T2 dark round foci in (B), representing phleboliths (arrow). (D–F) Dynamic contrast-enhanced magnetic resonance angiography (DCE-MRA) demonstrates no enhancement in the arterial phase (D). Enhancement starts in the venous phase (E) and progressively increases in the delayed venous phase (F), which is typical for VMs. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol.* 2014;69(5):443–457, Fig. 6.)

and fat-saturated precontrast and postcontrast T1-weighted sequences (Fig. 172.2). MRA is an integral component of the postcontrast portion of the examination and is typically performed with contrast-enhanced time-resolved angiography

with interleaved stochastic trajectories (TWIST) sequence.⁸ The typical MRI appearance of common vascular anomalies is reviewed in Table 172.2 and discussed in detail in the following sections.

TREATMENT OF LOW-FLOW VASCULAR MALFORMATIONS

Introduction

The two most common low-flow vascular malformations encountered in clinical practice are venous malformations (VMs) and LMs.

VMs are uni- or multilocular lesions composed of postcapillary, endothelium-lined venous channels with abnormal mural smooth muscle. Most VMs occur sporadically; however, 1% to 2% may be inherited as an autosomal dominant trait.⁹ Glomuvenous malformation (GVM), cutaneomucosal venous malformation (CMVM), cerebral cavernous VM, and blue rubber bleb nevus syndrome (BRBNS) are examples of hereditary diseases that can result in multiple lesions.^{10,11} VMs range from small solitary lesions localized to the skin and subcutaneous tissues to diffuse masses that extend across multiple tissue planes and encase vascular, nervous, and visceral structures.

VMs most commonly arise in the head and neck but can also affect the trunk and extremities. On physical examination, superficial VMs appear as compressible, bluish, nonpulsatile masses (Figs. 172.3 and 172.4). Lesions can expand with increased local venous pressure, and may result from dependency or with a Valsalva maneuver. Calcified phleboliths are characteristic and may be found via palpation or imaging. Common complications of VMs include pain and swelling related to phlebothromboses, infection, and psychosocial issues related to disfigurement. Additional morbidities are related to the specific location of the VM. For example, lesions in the head and neck may compromise respiration, speech, deglutition, and vision. VMs in the extremities can cause gait instability and limit mobility. Lesions within the gastrointestinal and genitourinary tracts can cause intraluminal hemorrhage resulting in acute and chronic anemia.

LMS are benign unilocular or multilocular cystic lesions composed of dysplastic endothelium-lined lymphatic channels. Cysts vary in size and may be classified as macrocystic



Figure 172.4 Venous Malformation (VM). (A) A 4-year-old female with extensive blueness in her left leg and buttock region. She had no leg-length discrepancy on measurement. (B–C) Coronal T2-weighted image shows an extensive VM infiltrating the muscle groups in the left lower extremity and buttock. Note infiltration in the skin. (D) Dynamic contrast-enhanced magnetic resonance angiography (DCE-MRA) shows enhancement of the VM in the venous phase. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol*. 2014;69(5):443–457, Fig. 13.)

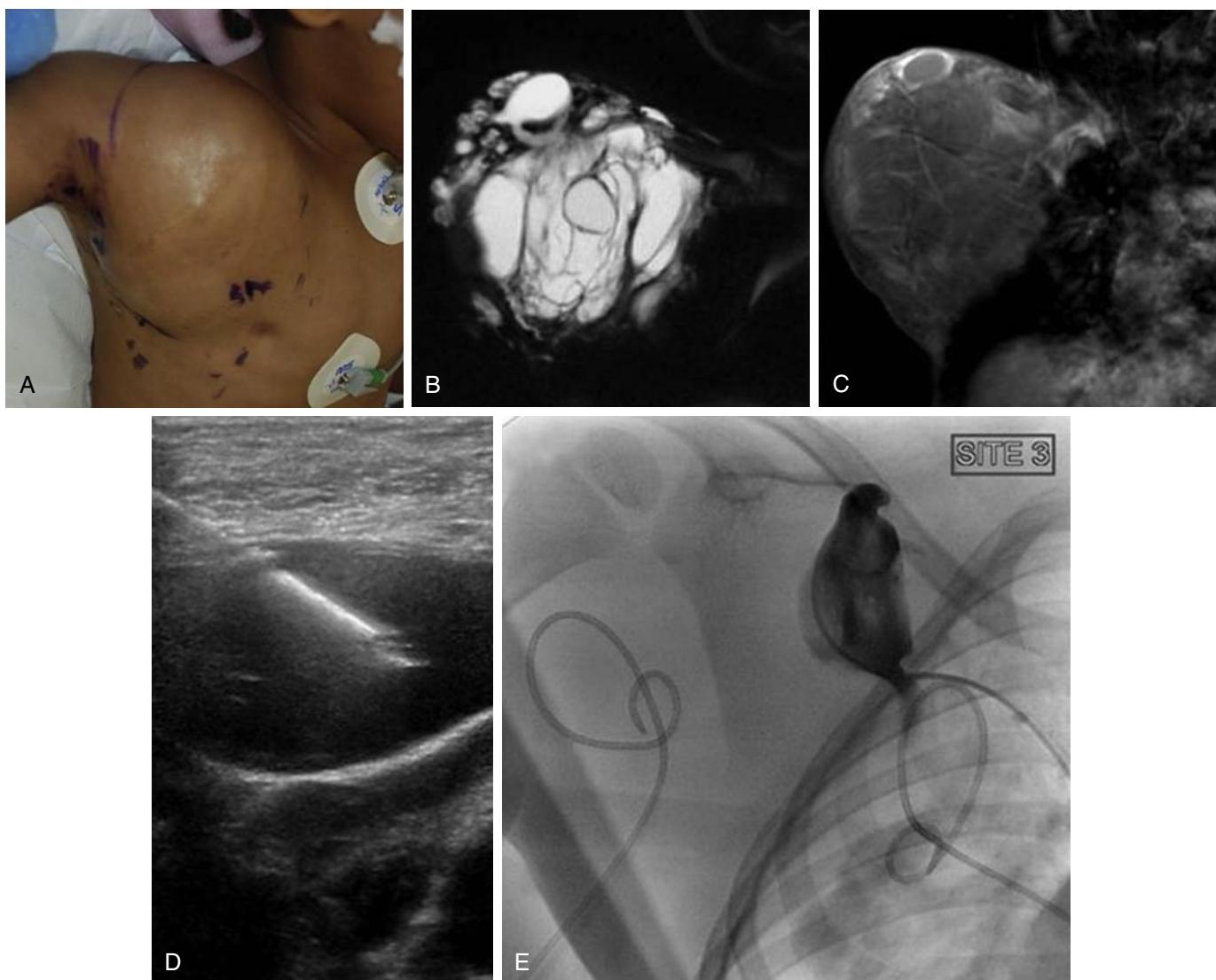


Figure 172.5 Lymphatic Malformation (LM). (A) A 4-year-old male with a large mass on his right shoulder/chest wall. It was first noted soon after birth, and he underwent surgical debulking at that time. (B–C) A known LM that had recently grown larger. (C) Coronal T2-weighted image with fat saturation shows a T2 bright multilocular/septate large mass that shows enhancement of only the cyst walls and septa, typical for LM. The relatively large size of each cyst qualifies for a macrocystic LM. (D) Ultrasound during percutaneous access demonstrates a macrocystic LM. (E) Injection of contrast medium into one of three macrocysts being treated with doxycycline sclerotherapy. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol*. 2014;69(5):443–457, Fig. 7.)

(individual cysts >1–2 cm), microcystic, or mixed. The majority of lesions are sporadic, although some lesions are associated with Turner and Noonan syndromes.^{12,13} Similar to other vascular malformations, LM are usually diagnosed at birth or during the first few years of life, but they may occasionally present later, in childhood, adolescence, or adulthood. The majority of LM occur in the head and neck, but lesions are also found in the chest, axillae, and perineum. On physical examination, macrocystic LM in the superficial soft tissues are palpable as cystic, rubbery, or ballotable masses (Fig. 172.5). Cutaneous LM appear as small vesicles that discharge clear or milky lymphatic fluid when ruptured. A microcystic LM may simply appear as an area of soft tissue overgrowth. Intralesional

hemorrhage is a common complication and typically results in pain and swelling. LM may also enlarge and become painful in the presence of systemic infections. Like other vascular malformations, LM in the head and neck can cause airway compromise.¹⁴ Lesions deep in the chest and abdomen can cause pleural, pericardial, and peritoneal chylous effusions.¹⁵

Imaging

Both VMs and LM appear isointense to skeletal muscle on T1-weighted imaging and hyperintense on T2-weighted imaging, although intralesional hemorrhage will result in variable T1 and T2 signals depending on the age of blood products

(Figs. 172.3–172.5). VMs and macrocystic LMs are cystic in appearance, whereas microcystic LMs appear as solid masses. VMs will characteristically demonstrate foci of signal void, corresponding to phleboliths, and will enhance during the venous phase of dynamic MRA. The cystic channels of LMs do not contain phleboliths or enhance internally during MRA, but the channels may contain fluid levels related to prior hemorrhage, and the peripheries of the cysts can enhance.⁷ Duplex ultrasound is useful to diagnose vascular malformations in the prenatal setting, to differentiate high- and low-flow lesions, and to monitor for complications such as thrombosis and hemorrhage. Sonographically, vascular malformations appear as hypoechoic or anechoic fluid- or debris-filled cystic lesions. Phleboliths in VMs will appear as hyperechoic foci with posterior acoustic shadowing. Low-flow lesions typically exhibit essentially no flow on Doppler analysis.

Therapy Overview

Low-flow vascular malformations typically grow and become more symptomatic over time. Treatment is often indicated to ameliorate pain, functional impairment, or disfigurement. Therapeutic options range from palliative to surgical measures. Compression garments can be used to decrease blood stagnation and swelling associated with vascular malformations in the extremities. Pharmacotherapy with aspirin and low-molecular-weight heparin (LMWH) may decrease the risk of thrombotic complications.¹⁶ However, these measures do not decrease the overall disease burden, and more invasive therapies are usually indicated. Among the various minimally invasive and surgical options, percutaneous sclerotherapy has emerged as the first-line treatment.^{10,11,17}

Sclerotherapy

Sclerotherapy involves percutaneous placement of needles into the cystic spaces of a vascular malformation under US and fluoroscopy. Cystic spaces are then filled with an endothelium-damaging agent, or sclerosant. The goal of this therapy is to cause fibrosis and eventual contraction of the vascular malformation. This technique has been shown to be safe and effective for treating low-flow vascular malformations throughout the body.^{18,19}

Preintervention Assessment

Patients who are being considered for sclerotherapy should ideally first be assessed in the clinic setting. A careful history and physical examination should be performed. A preintervention MRI should be obtained and reviewed with the primary goals of defining the extent of treatable (non-thrombosed) disease and identifying critical nearby structures that could be damaged during sclerotherapy. Details of the treatment approach, risks, benefits, postoperative expectations, and length of treatment should be clearly discussed with the patient.

VMs continuously undergo cycles of spontaneous thrombosis and thrombolysis in a phenomenon called localized intravascular coagulopathy (LIC).¹⁶ Although anticoagulants

and platelet inhibitory medications are not typically withheld prior to the procedure, LIC is common with large VMs, causing elevation of D-dimer, hypofibrinogenemia, and thrombocytopenia.²⁰ Immediately after sclerotherapy, LIC can progress to disseminated intravascular coagulopathy (DIC), and basic coagulation parameters (complete blood count, prothrombin time/international normalized ratio, partial thromboplastin time, fibrinogen, and D-dimer measurements) should therefore be obtained prior to interventions for large VMs. Patients with signs of LIC are prescribed LMWH for 10 days before and 10 days after the procedure. This therapy corrects the coagulopathy by halting the abnormal consumption of fibrinogen.

Patient comfort and immobility are important considerations during sclerotherapy; treatments are therefore generally performed in conjunction with general anesthesia. Patients who have cardiac, pulmonary, or other diseases that increase their risk for perioperative morbidity or mortality due to anesthesia should be identified and thoroughly evaluated by an anesthesiologist prior to undergoing sclerotherapy.

Technical Details

Sclerotherapy is best performed in an angiography suite. The patient should be positioned on the angiography table such that the area of interest can be safely and easily accessed by the operator. A preliminary US can be performed to identify the optimal skin entry sites, which are then prepped in sterile fashion. The procedure is considered “clean,” and antibiotic prophylaxis is recommended.²¹ Typical agents include intravenous cefazolin, and, for the penicillin-allergic patient, clindamycin.

Once preparations are complete and the patient is adequately sedated, US is used to guide a 21- or 22-gauge needle into the vascular malformation (Fig. 172.5). Several needles can be placed during a single procedure to treat multiple noncommunicating components of a lesion concurrently. In the case of a VM, intralesional placement of a needle is confirmed with blood return upon aspiration and digital subtraction angiography (DSA). DSA is used both to estimate the capacity of the lesion and to determine the presence of rapidly draining veins, which, if present, must be closed via manual pressure or coil or glue embolization to allow adequate sclerosant dwell time. A negative-contrast-technique sclerosant is hand-injected into the vascular spaces under fluoroscopic guidance. Commonly used sclerosants for the treatment of VMs include ethanol, sodium tetradecyl sulfate (often foamed), ethanalamine oleate, and more recently bleomycin.^{22–24} Ethanol causes an inflammatory response that results in thrombosis and fibrosis and it typically has the lowest rate of recurrence after treatment. STS also causes an inflammatory response similar to ethanol that results in thrombosis and fibrosis. STS can also be administered as a foam (i.e. 1 cc STS 3%, 0.5 cc lipiodol, 4 cc of air) allowing for greater endothelial surface area coverage at a lower dose. Bleomycin is a chemotherapeutic agent that causes DNA damage leading to endothelial cell death. Since bleomycin does not induce significant thrombosis and inflammation, it is a safer agent to use in regions where compression of critical structures can occur from swelling (e.g., head and neck, orbit).²³ Bleomycin does carry a risk of pulmonary fibrosis over a particular

lifetime dose and can also cause permanent skin rashes in areas of inflammation. Adhesives should be avoided in patients being treated with bleomycin in order to avoid permanent skin hyperpigmentation.²⁵

The sclerosant is allowed to dwell within the lesion for a period of time, typically 15 to 20 minutes. Once the target dwell time is reached, the syringe is disconnected and the lesion assessed for venous return. If venous return is present, DSA is repeated to assess for residual disease and additional sclerosant is injected as needed. Once the treated area is closed and no venous return is noted, the needle is removed and the skin site is cleaned and dressed.

Sclerotherapy is also used for the treatment of macrocystic LMs. Needles are placed into the cystic spaces of the lesion, and lymphatic fluid is then completely aspirated and partially replaced with a sclerosant. In the case of larger macrocysts, placement of a drainage catheter and repeated infusions of sclerosant over several consecutive days may be necessary to close the cyst. Commonly used sclerosants for the treatment of LMs include doxycycline and bleomycin, although there are reports of using other agents such as ethanol, sodium tetradecyl sulfate, and OK-432 (Picibanil).^{22,26} For microcystic LMs, bleomycin has been used with some success.²⁷ Microcystic LMs refractory to sclerotherapy can be considered for surgical resection.

Postintervention Care and Complications

Patients should be monitored in a post-procedure care unit as they recover from anesthesia. Procedure-related inflammatory pain and swelling are expected, and pain management, icing, and elevation of the treated area are routinely implemented during the recovery period. Steroids are often given to control swelling, particularly when the treated lesion is in the head or neck or in an area susceptible to compartment syndrome, such as the forearm or leg. Most patients who undergo sclerotherapy are admitted for overnight observation and pain management.

Patients should be evaluated in the clinic 1 week following the procedure to assess for complications and again in 1 to 2 months after MRI has been performed to assess for reductions in symptoms and lesion size. Decreased T2 signal and enhancement are additional radiographic findings that are expected following sclerotherapy.²⁸ Successful treatment is often incremental, and large multifocal lesions will likely require additional procedures. In many cases clinical results are seen long before imaging results appear significant. As the goal of therapy is to treat the patient's symptoms, treatment can often be stopped despite little change on MRI.

The majority of complications are related to unintentional extravasation of sclerosant outside the lesion.²² Extravasation is of particular concern during the treatment of superficial VMs because it may result in irritation, blistering, and necrosis of the adjacent skin or mucosal surface. It is paramount that the fluoroscopic images and skin site be carefully examined during the injection phase of treatment in order to detect and minimize extravasation. Extravasation appears as a blush of contrast material outside the lumen of the lesion on fluoroscopy. Any instance of extravasation necessitates the immediate cessation of sclerosant injection. Skin necrosis is usually heralded

by blanching, erythema, or other discoloration of the skin at the end of the procedure. Patients with suspected cutaneous complications should be examined frequently in the clinic and standard wound care, including topical antibiotics and clean dressings, should be practiced. Patients with areas of large or deep ulceration should be referred to a wound care specialist.

Hematuria, a consequence of sclerosant-induced hemolysis, is another common complication, particularly when large doses of sclerosant and intravenous contrast material are used. Placement of a urinary catheter is helpful to detect and monitor this complication, which tends to be a minor transient finding that resolves with oral and intravenous hydration.²⁹

Acute compartment syndrome is an uncommon complication that can arise when the treated lesion is located in a fascia-bound compartment, such as a muscular compartment in an extremity. Inflammatory swelling causes high intracompartmental pressures and insufficient blood supply to the muscles and nerves. Recognition of the intracompartmental location of a lesion is important for proper treatment planning, as the inflammatory response can be mitigated by the avoidance of excessive treatment. Post-procedurally, ice packs should be applied and tight circumferential dressings avoided. Steroid therapy (e.g., intravenous dexamethasone) can be considered for patients who do not respond to more conservative measures.

Patient-Reported Outcomes

Patient-reported outcomes (PROs) have become an increasingly important metric when evaluating treatment outcomes after therapy of any type for vascular malformations. Outcomes reported by the patient are broad and can include somatic and psychosocial symptoms, functional limitations, and cosmetic concerns. This is of particular importance with low-flow malformations, which may not show significant changes on follow-up imaging despite clinical changes; thus, the patient's report will often drive treatment decisions. Patient-reported outcome measures are usually obtained through structured questionnaires; however, there is currently no tailored PRO measure for vascular malformations.³⁰ Recent studies of VM outcomes used existing PRO measures to determine that improvement rates reported by patients are lower than physician-reported improvement rates.³¹⁻³³ A preliminary content analysis of existing PROs applied to VM outcomes demonstrated that specific symptoms and functional limitations related to VMs are often not elicited through nonspecific PROs.³⁴ As such, specific PRO measures for vascular malformations need to be developed in order to accurately assess patient outcomes, especially since treatment decisions are heavily influenced by patient reported symptomology.

Additional Endovascular Techniques and Other Therapies

Magnetic Resonance Imaging-Guided Sclerotherapy

The majority of sclerotherapy procedures can be performed with ultrasound and fluoroscopy for image guidance. Both of these modalities are easy to use and widely available. However, some vascular malformations, such as those deep in the

abdomen or beneath scar or bone, are not adequately visualized or targeted with US. If these lesions require treatment, interventional MRI should be considered. The technique commonly relies on steady-state free precession imaging, which is a gradient echo-based MRI technique that provides real-time sequences for needle targeting and the monitoring of sclerosant delivery.^{35–37} Large initial investments in equipment and MR-specific training are necessary prerequisites that currently hinder widespread usage of this useful technique.

Coil and Glue Embolization

Permanent embolic agents, such as coils and glue (e.g., N-butyl cyanoacrylate), can be used for percutaneous closure of draining veins and capacious venous spaces that are not responding to sclerotherapy.^{38,39} Glue can be injected into vascular malformations through a percutaneous needle, whereas coils require

placement of an endovascular catheter. Preoperative coil and glue embolization of VMs can be performed to reduce surgical morbidity and promote complete surgical excision by reducing disease volume and intraoperative blood loss.

Laser Therapy

Laser photocoagulation is an option to treat facial VMs.⁴⁰ Electro-optical synergy, a technique that combines laser light and radiofrequency energy, has also been effective.⁴¹ Laser treatments can be combined with sclerotherapy to treat lesions with superficial and deep components.

Sirolimus

Ideally vascular malformations could be treated noninvasively by medical therapies that target the cellular pathways promoting abnormal vascular growth. In particular, inappropriate

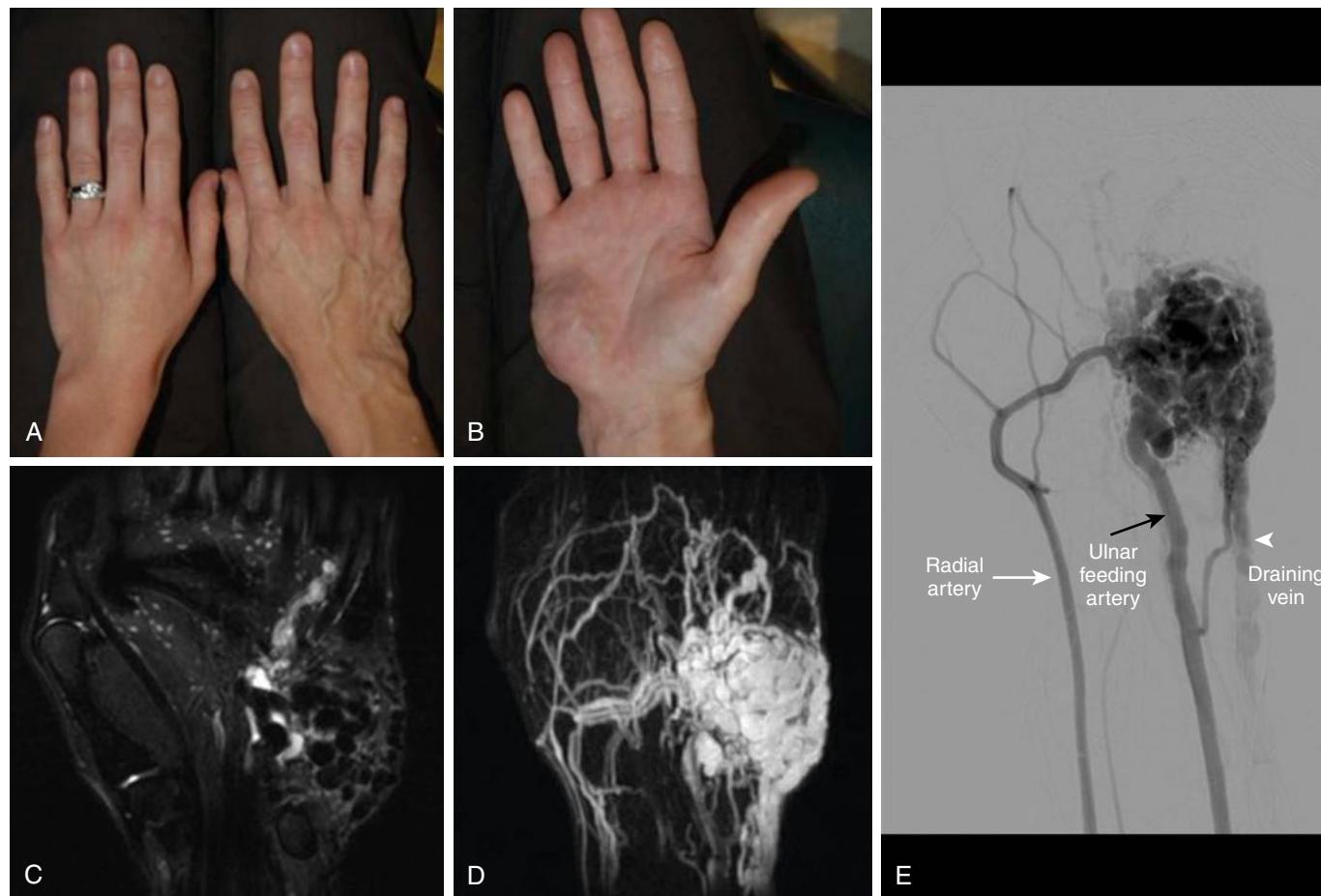


Figure 172.6 Arteriovenous Malformation (AVM). (A) A 30-year-old female with a swollen pulsatile mass on the hypothenar eminence of her right hand. View of the dorsal surface of the patient's right hand compared with the left. Note the enlarged draining veins and relatively larger size of the right hand. (B) Note the mass on the hypothenar eminence of the right hand's palmar surface. (C) Coronal T2-weighted image with fat saturation demonstrates a serpiginous tangle of flow voids indicating high flow and infiltration of the hypothenar eminence and subcutaneous fat. Note the absence of associated soft-tissue mass. (D) Magnetic resonance angiogram demonstrates strong enhancement of the AVM with arterial feeder from the ulnar artery and venous drainage into the basilic vein. (E) Angiogram demonstrating predominant ulnar feeder (black arrow) to the AVM. Note early venous drainage to the basilic vein (arrowhead). Enlargement of the ulnar artery becomes more conspicuous when it is compared with a normal radial artery (white arrow). The draining vein is also patulous (arrowhead). (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol.* 2014;69(5):443–457, Fig. 9.)

activation of the mammalian target of rapamycin (mTOR) intracellular signaling pathway is associated with some vascular anomalies, and the PI3 kinase/AKT/mTOR pathway has been proposed as a target for therapy.^{42,43} Sirolimus, a compound that inhibits the mTOR pathway, has been approved by the US Food and Drug Administration for the treatment of lymphangioleiomyomatosis, which is also associated with abnormal activation of mTOR. More recently, a prospective phase II clinical trial has demonstrated sirolimus to be efficacious and safe in treating complicated vascular anomalies that were refractory to other therapies, including medication, interventional procedures, and surgery.⁴² The use of sirolimus demonstrates the growing importance of molecular pathway and genotype considerations when determining how to treat a vascular malformation.⁴⁴

TREATMENT OF HIGH-FLOW VASCULAR MALFORMATIONS

Introduction

High-flow vascular malformations include *AVM* and *AVF*. AVMs are high-flow vascular anomalies composed of a complex primitive network of arterial and venous channels (a nidus) – a network that bypasses the normal capillary bed.

TABLE 172.3 Schöbinger Staging of Arteriovenous Malformations

Stage	Clinical Findings
I (Quiescence)	Warm areas of pink-blue discoloration, shunting on Doppler ultrasonography
II (Expansion)	Mass associated with thrill and bruit
III (Destruction)	Mass associated with ulceration, bleeding, pain
IV (Decompensation)	Lesion associated with cardiac decompensation

Schöbinger R. Proceedings of International Society for the Study of Vascular Anomalies Congress, Rome I, June 23–26, 1996.

TABLE 172.4 Yakes' Arteriovenous Malformation Classification

Type	Description	Treatment
I	Direct AVF	Mechanical occluding devices (e.g., coils, plugs)
IIa	Typical AVM nidus	Transcatheter and direct puncture ETOH embolization
IIb	AVM nidus with shunt into an aneurysmal vein	Transcatheter and direct puncture ETOH embolization or coiling the aneurysmal outflow vein
IIIa	Aneurysmal vein whereby the vein wall is the nidus with single outflow vein	Coiling of the aneurysmal single outflow vein
IIIb	Same as IIIa but with multiple outflow veins	Coiling of each outflow vein
IV	Infiltrative form of AVM	Transcatheter embolization and direct puncture embolization (50% ethanol and nonionic contrast mixture)

AVF, arteriovenous fistula; AVM, arteriovenous malformation; ETOH, ethanol.

Yakes WF. Yakes' AVM classification system. *J Vasc Intervent Radiol*. 2015;26(2):S224.

Arterial inflow is diverted via these shunts into draining veins, resulting in local and occasionally systemic hemodynamic disturbances such as tissue ischemia and venous hypertension. AVMs occur in the central nervous system, limbs, trunk, and viscera.^{11,17} Like that of other vascular malformations, the diagnosis of AVMs can usually be made based on history and clinical examination alone.⁴⁵ On physical examination, an AVM is commonly detected as a warm palpable mass with overlying skin discoloration and an associated palpable thrill and bruit (Fig. 172.6).^{11,17,45,46} In advanced stages, AVMs can cause ulceration of the surrounding soft tissues, bleeding, and high-output heart failure. The Schöbinger staging system classifies AVMs according to biologic behavior and clinical effects; it is useful for determining the progression of disease (Table 172.3).⁴⁷ The Yakes' classification system sorts AVMs by angiarchitectural features and suggests specific endovascular treatment options for each subtype (Table 172.4).⁴⁸

AVFs are characterized by a direct connection between an artery and a vein without the presence of an intervening nidus.⁴⁹ AVFs can be acquired or congenital, but only congenital lesions are considered vascular malformations. Trauma is the most common cause for AVFs. Congenital AVFs are rare lesions that commonly manifest in infancy as high-output heart failure and are known to occur in certain anatomic locations, such as the vein of Galen malformation of the deep cerebral venous system. AVFs in the extremities may be associated with ischemic complications distal to the arteriovenous shunt, such as claudication, rest pain, and ulceration.⁴⁹ AVFs detected on physical examination typically present as pulsatile masses with an associated bruit.

Imaging

Imaging of an AVM or AVF is usually indicated to evaluate the extent of disease. Gray-scale and Doppler US demonstrate the abnormal network of vascular channels that make up the nidus and connect the feeding arteries to the draining veins. The feeding arteries have high-velocity diastolic (low resistance) blood flow resulting from the lack of a normal capillary bed between the arteries and veins.⁵⁰ The draining veins demonstrate pulsatile high-velocity (arterialized) flow.⁵⁰

Given its wide field of view, MRI is the preferred imaging modality for assessing a large AVM (Fig. 172.6). MRI can determine the extent of the lesion as well as its proximity to critical structures.^{11,17,45} In general AVMs appear as T1 and T2 hypointense serpentine flow voids that demonstrate post-contrast enhancement during the arterial phase of MRA.^{45,46,50} There may be surrounding edema, fibrin deposition, and tissue overgrowth. Conventional angiography has the advantages of high spatial and temporal resolution and is therefore the most accurate modality to identify and differentiate the feeding arteries, nidus, and draining veins.

Ultrasound examination of an AVF demonstrates the abnormal direct connection between an artery and vein without a nidus. The feeding artery has low-resistance flow, and the draining vein has arterialized flow. Aliasing around the AVF can occur, representing perivascular thrill. MRA similarly demonstrates the abnormal arteriovenous connection with early filling of the draining vein.

Treatment of Arteriovenous Malformations

AVMs are recalcitrant lesions with an inherent ability to persist despite therapeutic intervention. The main treatment options for AVMs are surgical resection and endovascular embolization.^{11,17,45,51} Both therapies target the nidus of the lesion with the goal of eliminating the abnormal arteriovenous shunt. When the nidus is completely removed, surgical resection is associated with a reduced recurrence rate. However, the architecture of the nidus is often complex, making complete surgical resection difficult.^{45,52} In these cases, embolization may be performed either as a primary treatment or as neoadjuvant therapy prior to surgical resection.^{11,17,45,49,52}

Endovascular closure can be quite challenging and should be attempted only after careful study of the lesion's vascular anatomy. Treatment should be directed at the nidus, which can be difficult to identify due to the presence of multiple tortuous feeding arteries that overlap and obscure the more distal areas of shunting. Treatment of the nidus results in improved long-term outcomes and fewer complications.⁵³

Embolization can be performed by approaching the AVM from the arterial side or the venous side. In approaching from the arterial side, the main feeding artery of the AVM is selected with a guiding catheter. A microcatheter is then advanced to subselect the distal branches just proximal to the arteriovenous site of shunting. A sclerosant agent like ethanol or a semiliquid embolic agent like N-butyl cyanoacrylate or ethylene vinyl alcohol copolymer (Onyx) is then injected.^{45,53–55} Additional branches are subselected and treated as needed.

A venous approach is possible when there is a single draining vein or venous sac. When there are multiple draining veins, treatment from the venous side is unlikely to be successful. However, when possible, the venous approach is often preferred, as the risk of nontarget embolization of normal nutrient arteries is decreased. Additionally, treatment of the venous side often decreases the number of arterial feeders, which makes complete obliteration of the nidus more feasible.⁵⁶ The technique involves subselection of the draining vein with a catheter.

Prior to the injection of a sclerosant or liquid embolic agent, the venous outflow can be occluded with a balloon catheter to prevent uncontrolled spread of the embolic/sclerosant agent. When a large sac is present, N-butyl cyanoacrylate and coils are typically used to fill the capacious channel.

When transarterial or transvenous access is not possible and the AVM is in an amenable location, direct percutaneous access and treatment of the lesion can be performed.^{11,17,45} Liquid agents, semiliquid agents, and coils can all be delivered through the percutaneously placed needles.

Approximately 57% of AVMs treated with surgical resection and embolic therapy will recur within the first year following treatment, and approximately 98% of AVMs will enlarge or recur within 5 years following treatment.^{45,52} The patient should therefore be followed regularly for at least 5 years. Additional interventions should be performed when lesions recur or cause symptoms.

Complications of arterial side embolization are typically related to treatments performed too proximally in the arterial feeder. Proximal treatment provides ineffective therapy; it also increases the risk of nontarget embolization of normal nutrient arteries and leads to loss of future arterial access to the nidus and recruitment of the collateral vessels that foster growth of the AVM.^{11,17,45}

Treatment of Arteriovenous Fistulas

Acquired AVFs commonly resolve spontaneously within a few months, allowing for a conservative approach consisting of serial imaging and clinical evaluation. Congenital AVFs and AVFs with large fistulous connections that do not close spontaneously require more invasive measures. Treatment options include surgical or endovascular repair.⁴⁹ Endovascular placement of a covered stent over the fistula is the most common approach. When there is a long fistulous tract, coil embolization is another possible approach.⁵⁷

SYNDROMES ASSOCIATED WITH VASCULAR MALFORMATIONS

A number of syndromes are associated with vascular malformations (Box 172.1). These include KTS, BRBNS, unilateral limb VM, mucocutaneous VMs, Sturge–Weber syndrome, Proteus syndrome, congenital lipomatous overgrowth, vascular malformations, epidermal nevi (CLOVE) syndrome, and Maffucci and Gorham–Stout syndromes, all of which are associated with low-flow vascular malformations.⁵⁸ Parkes–Weber syndrome (PWS); hereditary hemorrhagic telangiectasia (HHT); and Cobb, Wyburn–Mason, Bannayan–Riley–Ruvalcaba, and Cowden syndromes are associated with high-flow vascular malformations.⁵⁸ The following discussion delves into some of the more commonly encountered syndromes associated with vascular malformations.

Klippel–Trénaunay Syndrome

KTS is characterized by the clinical triad of capillary malformation of the skin (port wine stain), low-flow

BOX 172.1**Examples of Syndromes Associated with Vascular Malformations****Syndromes Associated with VMs**

Klippel–Trénaunay
Blue rubber bleb nevus
Maffucci

Syndromes Associated with CMs

Klippel–Trénaunay
Sturge–Weber

Syndromes Associated with LMs

Gorham

Syndromes Associated with AVMs

Parkes–Weber
Hereditary hemorrhagic telangiectasia
Bannayan–Riley–Ruvalcaba

AVMs, arteriovenous malformations; CMs, capillary malformations; LMs, lymphatic malformations; VMs, vascular malformations.

(capillary–venous–lymphatic) vascular malformation, and local soft tissue and bony overgrowth.^{59,60} KTS is diagnosed by the presence of at least two out of three of these clinical elements. The syndrome is typically sporadic, although familial cases have been reported.⁶¹ The vascular malformation can occur anywhere in the body but typically manifests as a persistent embryonic vein.^{50,59} The lateral marginal vein (also known as the vein of Serville) is the most common anomalous vein.⁶² Similar to other low-flow vascular malformations, the lymphatic and vascular malformations present in KTS may be treated with percutaneous sclerotherapy. Patients with superficial valveless varices may experience limb swelling and pain and can be treated with compression garments and intravenous laser therapy. The deep venous system can also be anomalous (hypoplasia, aplasia, valvular incompetence), and patency and adequacy of the deep system should be confirmed prior to occlusion of superficial varices to avoid exacerbating venous insufficiency.⁶³

Parkes–Weber Syndrome

PWS is characterized by a congenital AVF with associated varicosities and overgrowth (Fig. 172.7).⁵⁹ A red vascular skin stain (also known as a “pseudocapillary malformation”) may be present, representing part of the high-flow vascular malformation rather than a true capillary malformation.⁶⁰ PWS can affect any limb but most commonly occurs in the lower extremity.⁶⁴ Varicosities form as a result of high-flow shunting from the AVF. Lymphedema and lymphatic vesicles can be seen in the skin. High-output congestive heart failure can result if there are multiple AVFs. Conservative management of PWS is preferred, as invasive therapies can worsen the vascular shunting through an AVF.⁶⁰ In complicated cases, such as those associated with intractable pain or heart failure, superselective arterial embolization of the AVF can be performed.⁶⁰

Hereditary Hemorrhagic Telangiectasia

HHT, also known as Osler–Weber–Rendu disease, is an autosomal dominant disorder characterized by the presence of AVMs in multiple organ systems including the brain, lung, liver, and gastrointestinal tract.^{11,65} The diagnosis of HHT is made clinically on the basis of the Curaçao criteria, which assess for the presence of epistaxis, telangiectasias, visceral lesions, and an associated family history (a first-degree relative with HHT).⁶⁶ The HHT diagnosis is considered definite if three or four criteria are present, possible or suspected if two criteria are present, and unlikely if fewer than two criteria are present. Recurrent and severe epistaxis related to mucocutaneous telangiectasia is the most common presentation. Treatment of HHT is aimed at decreasing the amount of hemorrhage and minimizing complications. In the case of acute hemorrhage, volume resuscitation with intravenous fluid or blood products may be needed. Patients with chronic anemia should receive iron supplementation. Patients with pulmonary AVMs may have symptoms of dyspnea, hemoptysis, hemothorax, and stroke.⁶⁷ Pulmonary AVMs with feeding arteries measuring greater than 2 to 3 mm in diameter should undergo transarterial embolization with retrievable permanent embolics.⁶⁵ Hepatic involvement in HHT ranges from small telangiectasias to large AVMs.⁶⁸ Intrahepatic shunting is the result of solitary or multiple abnormal connections between the hepatic artery and portal vein, hepatic artery and hepatic vein, and portal vein and hepatic vein. Patients who experience complications – such as high-output cardiac failure, portal hypertension, and encephalopathy – should receive medical therapies directed at those conditions (e.g., diuretics, beta-blockers, antiarrhythmics).⁶⁸ Patients who have progressive worsening of their clinical condition despite medical therapy should be considered for invasive treatment, including transarterial embolization and orthotopic liver transplantation. Cerebral AVMs may be treated with transarterial embolization, stereotactic radiation, or surgery or a combination of methods.⁶⁵ Gastrointestinal AVMs are managed with endoscopic photoablation or electrocautery, although episodes of severe acute gastrointestinal hemorrhage may necessitate segmental bowel resection.⁶⁵

FUTURE DIRECTIONS: MOLECULAR AND GENETIC THERAPEUTIC TARGETS

Tailored molecular genetic therapies are becoming commonplace in oncology (i.e. precision medicine). Different malignancies possess specific somatic or germline mutations that confer an alteration in the molecular pathway leading to abnormal vascular proliferation. Similar to malignancies, several overlapping somatic and germline mutations have been implicated in vascular tumors, malformations, and malformation syndromes. As discussed above, the PI3 kinase/AKT/mTOR pathway has an established role in vascular proliferation and



Figure 172.7 (A) Foot and lower leg of a 24-year-old male with Parkes–Weber syndrome. Note thickened skin lesions as outlined by white arrows. Similar changes are also noted in the anterior lower shin. (B) Lateral arteriogram of the foot from a popliteal injection. Note hypervascularity of the arteriovenous malformation (AVM) nidus (white arrows) underneath the thickened skin lesions on photo (A). Note that the dorsalis pedis artery is the feeding artery (black arrow). The posterior tibial artery (arrowhead) is marked for orientation purposes. (C) Selective arterial phase on the dorsum of the foot on a lateral view. Note the catheter in the dorsalis pedis artery (black arrow). The AVM nidus (white arrows) demonstrates early arterial enhancement with an early draining vein (arrowhead). (D) Selective arterial phase on the dorsum of the foot on an anteroposterior view. Note the microcatheter in the distal part of the feeding artery (black arrow) supplying the nidus of the AVM (white arrows). The draining vein is marked with an arrowhead. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol*. 2014;69(5):443–457, Fig. 15.)

organization. Understanding this pathway led to the application of sirolimus for the treatment of low-flow vascular malformations. Though early, the overlap between somatic and germline mutations in oncologic processes and vascular malformations provides exciting new targets for novel drug

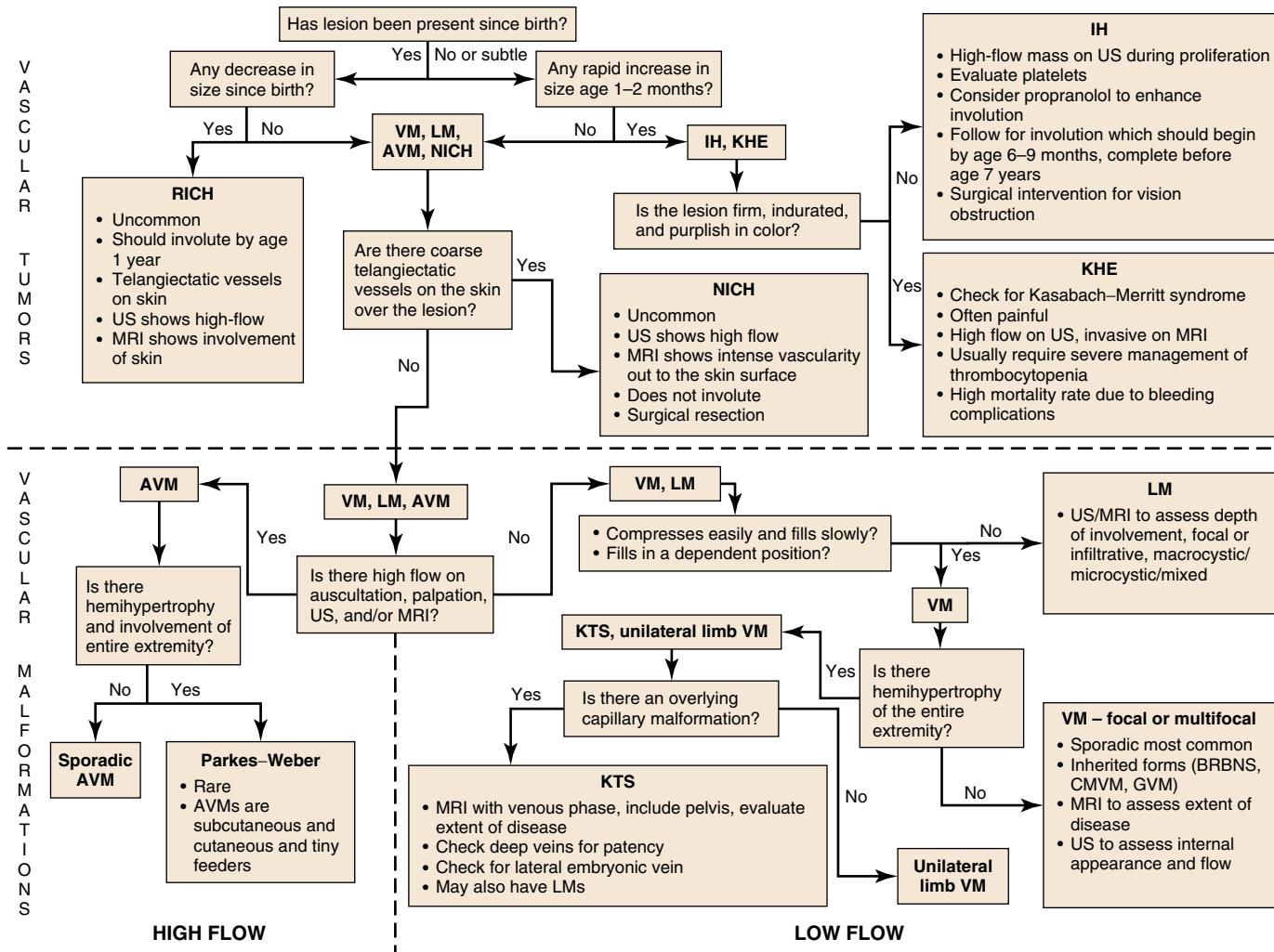
development.⁶⁹ Most recently, PIK3CA mutations in endothelial cells have been implicated in capillary–lymphatic–venous malformations.⁷⁰ Given this finding, PIK3CA inhibitors may be a viable therapeutic option for these malformations. Similarly, gain of function PIK3CA overgrowth syndromes

have been identified, and early treatment investigations using a PIK3CA inhibitor (BYL719) have shown promising results with vascular tumor size reduction and decreased hemihypertrophy.⁷¹ Given the myriad of gene mutations implicated in vascular anomalies and the rapid growth of new targeted agents from the oncologic literature, it is highly likely that tailored molecular genetic testing and treatments will become commonplace in this field.

CONCLUSION

Vascular malformations are non-neoplastic vascular anomalies that are subdivided into low-flow and high-flow lesions. Common low-flow vascular malformations are VMs and LMs, which are most commonly treated with percutaneous sclerotherapy. High-flow malformations include AVMs and AVFs, which are treated with surgery, endovascular intervention, or both.

CHAPTER ALGORITHM



S. E. Mitchell Vascular Anomalies Flow Chart. AVM, arteriovenous malformation; BRBNS, blue rubber bleb nevus syndrome; CMVM, cutaneomucosal venous malformation; GVM, glomuvenous malformation; IH, infantile hemangioma; KHE, Kaposiform hemangioendothelioma; KTS, Klippel-Trénaunay syndrome; LM, lymphatic malformation; MRI, magnetic resonance imaging; NICH, noninvolving congenital hemangioma; RICH, rapidly involuting congenital hemangioma; US, ultrasonography; VM, venous malformation. (Reproduced from Tekes A, Koshy J, Kalayci TO, et al. S.E. Mitchell Vascular Anomalies Flow Chart (SEMVAFC): a visual pathway combining clinical and imaging findings for classification of soft-tissue vascular anomalies. *Clin Radiol*. 2014;69(5):443-457.)

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Additional information regarding the new classification system.

A complete reference list can be found online at www.expertconsult.com

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Acquired Arteriovenous Fistulas

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The earliest description of an acquired arteriovenous fistula (AVF), the abnormal communication between an artery and vein, is attributed to William Hunter, who in 1761 reported two cases of brachial AVFs following attempted phlebotomy. He also described the adaptive dilation of the artery and veins

proximal to the AVF, as well as the associated tremulous motion, (“thrill”) and hissing noise (“bruit”).^{1,2}

AVFs were infrequently identified and diagnosed until the introduction of high-speed projectiles during 19th-century conflicts, which altered the magnitude and complexity of

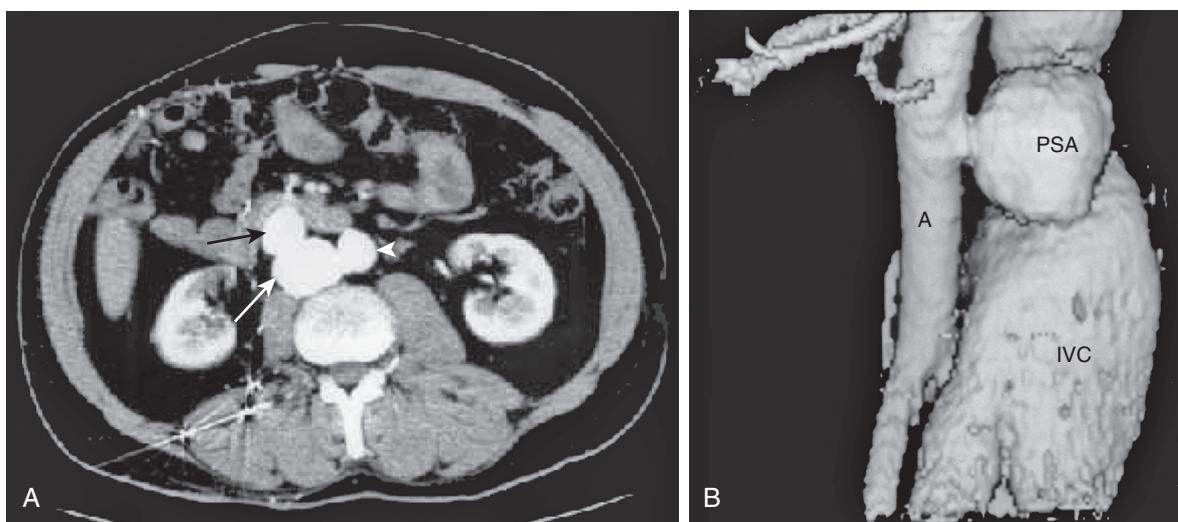


Figure 173.1 (A) Axial CT scan demonstrating the aorta (arrowhead), pseudoaneurysm (white arrow), and inferior vena cava (black arrow). (B) Three-dimensional reconstruction of the CT scan of a traumatic aortocaval fistula demonstrating a pseudoaneurysm (PSA), enlarged inferior vena cava (IVC), and aorta (A).

military injuries. Successive military conflicts and the increase in blunt, penetrating, and iatrogenic trauma among civilians have resulted in a greater number of vascular injuries (VIs), pseudoaneurysms (PSAs) and, as a consequence, acquired AVFs.^{3–9}

Etiology and Incidence

AVFs may either be congenital or acquired. Vascular malformations, including congenital AVFs, are discussed in Chapters 170, Congenital Vascular Malformations: General Considerations; 171, (Congenital Vascular Malformations: Surgical Management) and 172, (Congenital Vascular Malformations: Endovascular Management). The focus of this chapter is acquired AVFs, predominantly due to trauma and the small number which occur spontaneously, usually from erosion or rupture of an atherosclerotic or infected aneurysm or PSA into an adjacent vein.

Traumatic Arteriovenous Fistulas

The anatomic distribution of VIs and AVFs is related to the mechanism of injury and varies between military personnel and civilians. Blast/explosives and mortars account for 70% and gunshot wounds (GSWs) 30% of VIs among military personnel, whereas penetrating trauma due to GSWs or stab wounds (SWs) account for the majority (61.7%) of civilian VIs reported in the Department of Defense Trauma Registry and the National Trauma Data Bank.^{10,11} The incidence of VIs in the conflicts in Iraq and Afghanistan range from 4.4% to 17.6% comprised of extremity trauma (72%) and injury to the torso and cervical regions (17% and 11%, respectively). The lower extremity was the site of VI in 45% of cases. The more frequent occurrence of extremity VI among military personal is secondary to the use of protective body armor.¹² The incidence of VIs among civilians with GSWs was 9.9% and involved the

extremities (40.8%), abdomen/pelvis (33.6%), chest (10.1%), head and neck (6.7%), and extra-cavitory/face (8.7%).¹³

In a series of 210 civilian traumatic AVFs reported by Robbs et al.,¹⁴ SWs accounted for 63%, GSWs accounted for 26% and blunt trauma for 1%. AVFs due to SWs involve the cervico-mediastinal arteries in 54% to 75% of cases and most frequently (21%) the common carotid artery. Acquired AVFs involved the upper and lower extremities in 22% and 20% of cases, respectively, whereas thoracic and abdominal AVFs are encountered in 4% of patients.^{14–16} Rich et al.¹⁶ in a series of 558 PSAs and AVFs from the Vietnam Vascular Registry found that 85.4% of the AVFs were located in the extremities (upper 16.4% and lower 69%, respectively) (Fig. 173.1).^{14,15}

Iatrogenic Arteriovenous Fistulas

Iatrogenic injuries that cause AVFs usually result from percutaneous cardiac and vascular diagnostic and therapeutic interventions, central venous catheterization, orthopedic procedures on the lumbar spine and knee, diagnostic kidney and liver biopsies, and percutaneous insertion of biliary and urinary drainage catheters. The right common femoral artery (CFA) remains the most common site of iatrogenic injury (37%) in the lower extremities.¹⁷ The increase in the number of percutaneous interventions being performed would be expected to result in a greater number of iatrogenic AVFs. However, the use of micropuncture angiographic needles inserted under ultrasound (US) guidance and small diameter sheaths has significantly reduced the number of access site-related complications (1.9% vs. 4.3%) in patients undergoing coronary angiography.¹⁸ In a prospective study of 635 patients undergoing femoral access for noncardiac diagnostic or interventional procedures randomized 1:1 to receive either fluoroscopic or US-guided access, the authors found that although the use of ultrasound guidance allowed for more efficient and expeditious cannulation of the femoral artery, the rates of early or late complications did not differ between the two groups.¹⁹

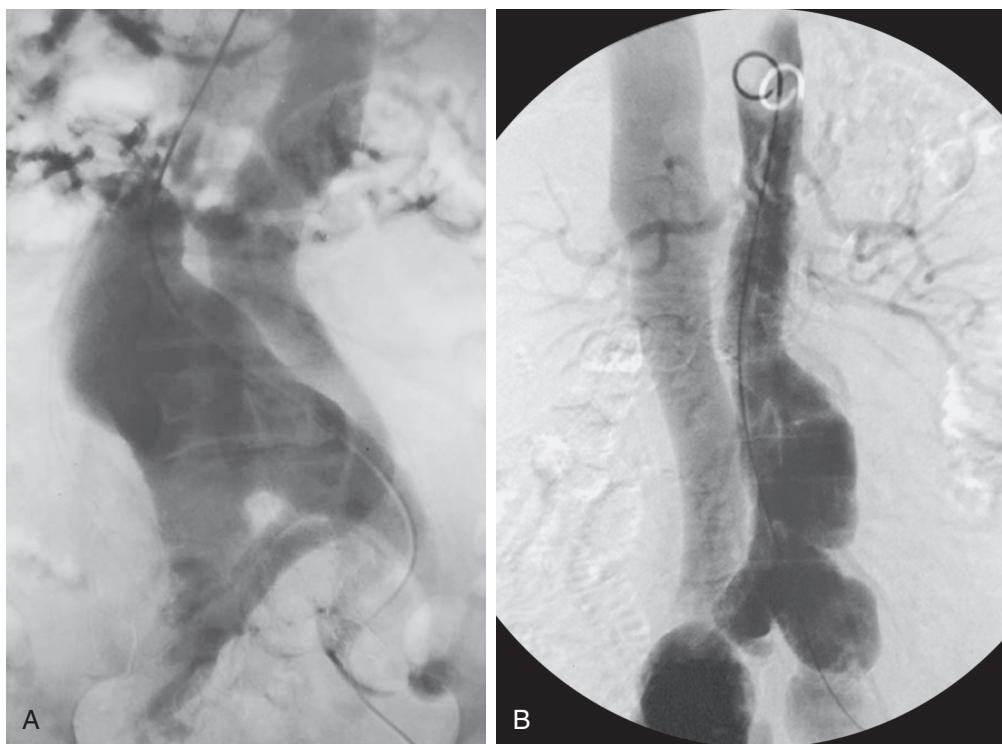


Figure 173.2 (A) Aortogram of a patient with an aortic aneurysm and spontaneous aortocaval fistula treated surgically. (B) Aortogram demonstrating an aortic aneurysm and bilateral iliac aneurysms associated with an arteriovenous fistula between the right common iliac artery and vein treated with an aortic endograft.

Spontaneous Arteriovenous Fistulas

First described by Syme in 1831, rupture or erosion of an atherosclerotic, inflammatory, mycotic aortic or iliac aneurysm into the inferior vena cava (IVC), iliac vein (Fig. 173.2), or retro-aortic left renal vein (Fig. 173.3) can result in spontaneous AVFs.^{20–25} There have been a few isolated case reports of spontaneous AVFs in patients with syphilitic aortitis, HIV arteritis, and Marfan and Ehlers–Danlos syndromes.^{21,26}

Arteriovenous Fistulas in Specific Locations

Innominate Artery Arteriovenous Fistulas

Innominate artery injuries account for 0%–3% of civilian arterial injuries and result from GSWs, SWs or central venous catheterization of the internal jugular and subclavian veins. Fistulas between the innominate artery and the superior vena cava, innominate vein or its tributaries were present in 10% of patients in a series reported by du Toit et al.²⁷ (Fig. 173.4).

Carotid Artery Arteriovenous Fistulas

Carotid artery injury constitutes 5% to 11% of all arterial injuries and usually results from SWs or GSWs, therapeutic or diagnostic catheterization, or blunt trauma to the skull or cervical spine. AVFs between the carotid artery and internal jugular vein or its tributaries occurs following 4% to 27% of such injuries.^{7,14,16,27–30}

Vertebral Artery Arteriovenous Fistulas

Vertebral artery AVFs occur in 0.7% to 7.4% of cases of penetrating trauma. The AVF is usually between the vertebral artery and the epidural venous plexus and/or jugular venous system.

Iatrogenic injury during operative procedures on the cervical spine and catheterization of the internal jugular vein accounts for approximately two-thirds of cases, while cervical spine fractures due to blunt trauma, chiropractic manipulation, or closed head injury, GWs, and SWs for the remaining one-third.^{31–33} Spontaneous AVFs are rare usually due to an underlying collagen vascular disease such as neurofibromatosis type I, Marfan and Ehlers–Danlos syndromes.³⁴

Axillary and Subclavian Arteriovenous Fistulas

Approximately 3% of all neck- and chest-penetrating trauma is associated with injury to the subclavian vein (44%), artery (39%), or both (17%).³⁵ Inadvertent puncture of the carotid or subclavian arteries occurs in up to 8.4% of cases of attempted central venous catheterization,^{27,28} and the incidence of AVFs following subclavian vein catheterization is estimated at 0.58%.³⁶ Penetrating axillary artery injuries and fractures of the clavicle or first rib are rare causes of AVFs.^{35,37–39}

Brachial, Radial, and Ulnar Arteriovenous Fistulas

Upper extremity trauma accounts for 25% to 40% of all VIs.^{7,15} The brachial and forearm arteries are involved in 10% to 22% of cases.⁶ The radial and ulnar arteries are frequently used for cardiac and endovascular interventions; AVFs occur in 0.02% to 0.04% of cases. Peripherally inserted central catheter (PICC) lines may also be complicated by AVFs.^{40–43}

Femoral Arteriovenous Fistulas

Penetrating injuries due to GSWs, SWs, shrapnel injuries from IEDs, or following surgery for intertrochanteric or femoral neck fractures may result in femoral AVFs.^{6,7,44–47} The incidence of AVFs as a result of such injuries varies considerably

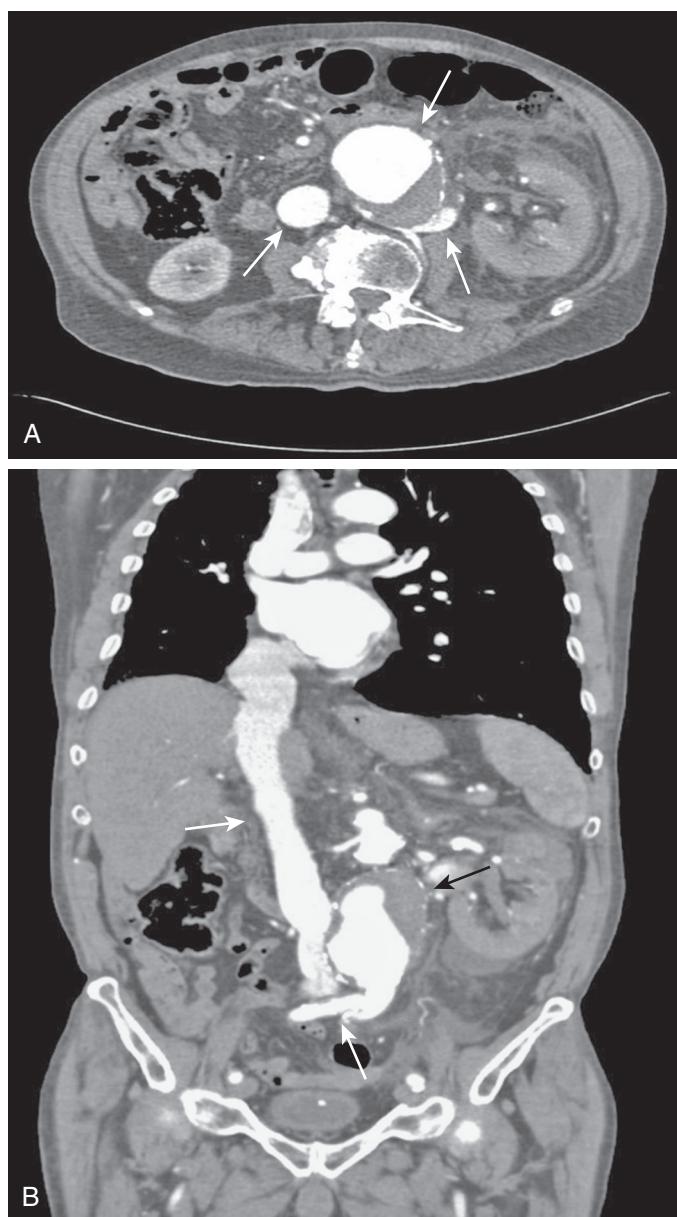


Figure 173.3 (A) Axial CT scan demonstrating an aortorenal arteriovenous fistula. Contrast material is present in the abdominal aortic aneurysm (top arrow), inferior vena cava (left arrow), and retro-aortic left renal and lumbar veins (right arrow). (B) Sagittal reconstruction of the CT scan in (A) showing contrast material in the aneurysm (black arrow), inferior vena cava (top white arrow), and retro-aortic left renal and lumbar veins (bottom white arrow).

between the military and civilian populations. In a review of 558 AVFs due to military injuries, 28% involved the superficial femoral or profunda femoris arteries,¹⁶ whereas in a civilian series of AVFs predominantly due to SWs, the CFA was involved in 12% of cases (Fig. 173.5).¹⁴ Sporadic cases of spontaneous AVFs between the superficial femoral artery and vein have also been described.²⁶ The CFA remains the most common site of iatrogenic AVFs, with an incidence of 0.06% to 0.86% when diagnosed by physical exam but 2.8% using duplex US (DUS).^{44,45} Femoral AVFs are slightly more frequent after interventional than diagnostic procedures. The majority of AVFs close spontaneously: in one study, only 11% became symptomatic and required operative repair (OR).⁴⁸ Femoral and

external iliac artery AVFs are a rare complication of endovenous laser ablation for varicose veins.^{49,50} The risk factors predisposing to iatrogenic femoral AVFs are listed in Box 173.1.

Popliteal Arteriovenous Fistulas

Popliteal AVFs have similar etiologies to femoral AVFs. They account for approximately 16% of AVFs reported in the Vietnam registry and 5% to 14% of civilian AVFs.^{14,16,51} Blunt trauma associated with comminuted femoral and proximal tibial fractures and orthopedic procedures on the knee may also be complicated by AVFs.^{52,53} The number of iatrogenic popliteal AVFs can be expected to increase, due to the more frequent use of popliteal access for interventions to treat deep vein thrombosis and chronic venous insufficiency.

Tibial and Peroneal Arteriovenous Fistulas

AVFs of the tibial and peroneal arteries are a recognized complication of comminuted fractures, blast fragment injuries, balloon catheter thrombectomy, and atherectomy of the tibial vessels (Fig. 173.6).^{54–56} Approximately 24% of the AVFs reported in the Vietnam registry occurred in the tibial and peroneal arteries.¹⁶ The more frequent use of retrograde tibial access to recanalize occluded lower extremity arteries in patients with critical limb ischemia (CLI) may increase the risk of AVFs in these locations.^{57–61}

Aortoiliac Arteriovenous Fistulas

Rupture or erosion of an AAA into the IVC accounts for 80% to 90% of acquired aortocaval fistulas (ACFs). GSWs, shrapnel, SWs, iatrogenic injury, lumbar disk surgery, and nephrectomy account for the remaining 10% to 20% (see Fig. 173.1).^{20–24} Persistent or recurrent ACFs may occur due to the failure to detect or adequately repair the fistula, rupture of a para-anastomotic PSA into the IVC (distal anastomosis of aortic tube grafts), and ongoing pressurization of the aneurysm sac because of persistent endoleaks.^{62–65}

Iliac AVFs account for 0.4% to 1.4% of AVFs and are usually the result of rupture of an iliac aneurysm into an adjacent vein, penetrating trauma or lumbar disc surgery.^{14,16,66–69}

VI occurs in up to 0.05% of lumbar disc procedures. Anatomic anomalies, such as a low aortic bifurcation at L4–L5 (18%) and degenerative changes of the anterior spinal ligament, may contribute to VIs in this location.^{70–72} VIs at the L3–L4 disc space predominantly involve the aorta and IVC; the majority of iliac VIs occur at the L4–L5 and L5–S1 disc space, where the common iliac arteries are most vulnerable to injury (right CIA 43%; left CIA 29%).^{73,74}

Renal Arteriovenous Fistulas

The majority of renal AVFs occur after renal biopsy in approximately 9% to 18% of patients. Factors predisposing to biopsy-related renal AVFs include use of a large-bore needle, lack of US or CT guidance when performing the biopsy, medullary penetration, and the presence of atherosclerotic vessels^{71,75} (Fig. 173.3). Iatrogenic causes resulting from surgical or percutaneous interventions including partial nephrectomy, mass

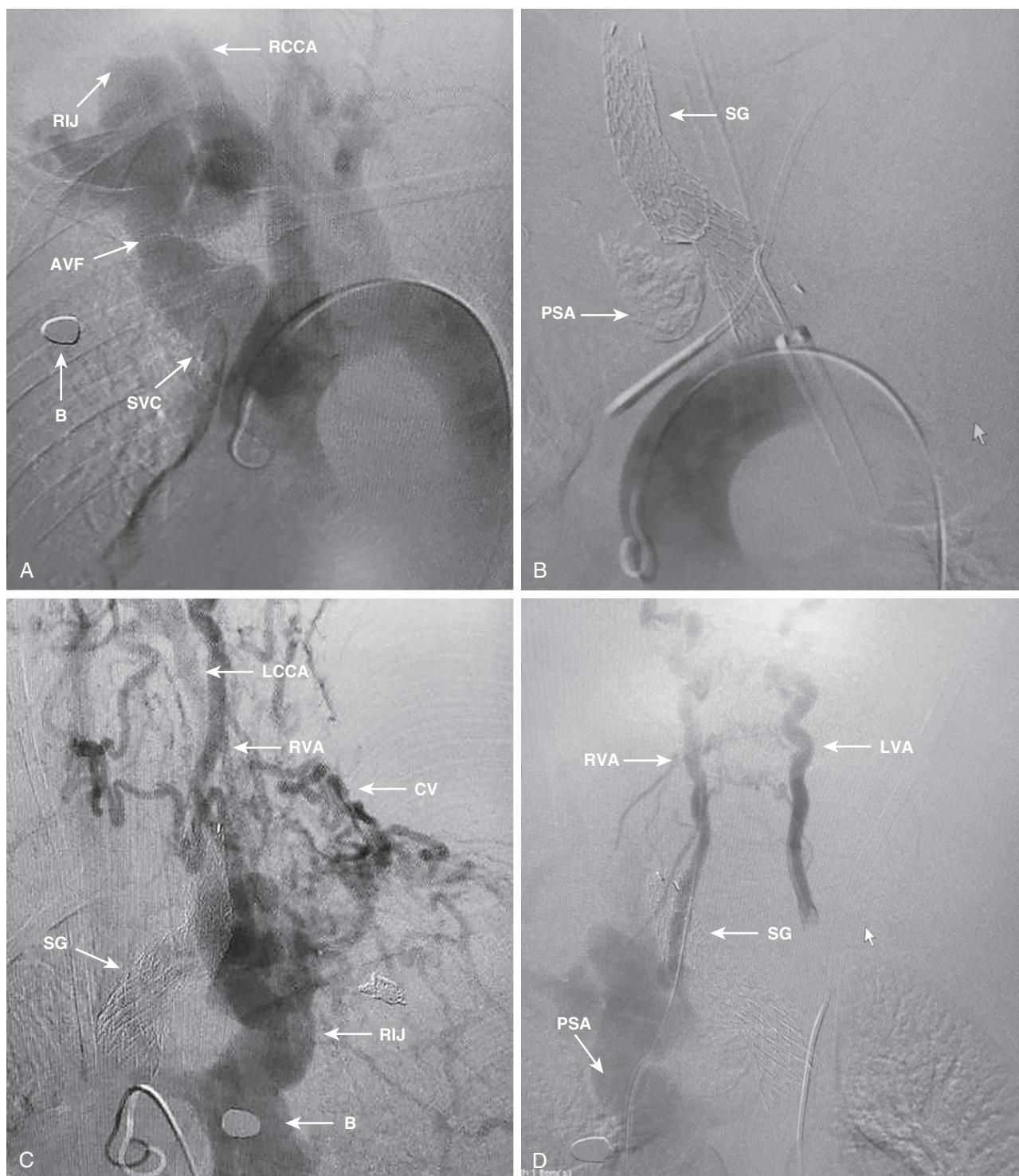


Figure 173.4 Arch aortogram showing (A) an innominate superior vena caval arteriovenous fistula (AVF), (B) stent graft (SG) and calcified pseudoaneurysm (PSA); (C) recurrence of the AVF due to (D) reversal of flow in the right vertebral artery. RIJ, right internal jugular vein; B, bullet fragment; SVC, superior vena cava; RCCA/LCCA, right/left common carotid artery; CV, collateral vessels; LVA, left vertebral artery.

ligation of the renal pedicle, guide wire arterial perforation during angiography or renal stenting, percutaneous nephrolithotomy, laser lithotripsy and percutaneous nephrostomy tube placement comprise most of the remainder. Spontaneous renal AVFs may occur from the erosion of tumors, inflammatory processes, or of an aortic or renal aneurysm directly into a retro-aortic or normally located renal vein or its

tributaries.^{24,25,71,75–77} Isolated renal AVFs due to blunt and penetrating trauma are uncommon.^{78–80}

Splenic, Hepatic, and Mesenteric Arteriovenous Fistulas

Splenic AVFs may result from blunt or penetrating intraabdominal trauma, mass ligation of the splenic pedicle,

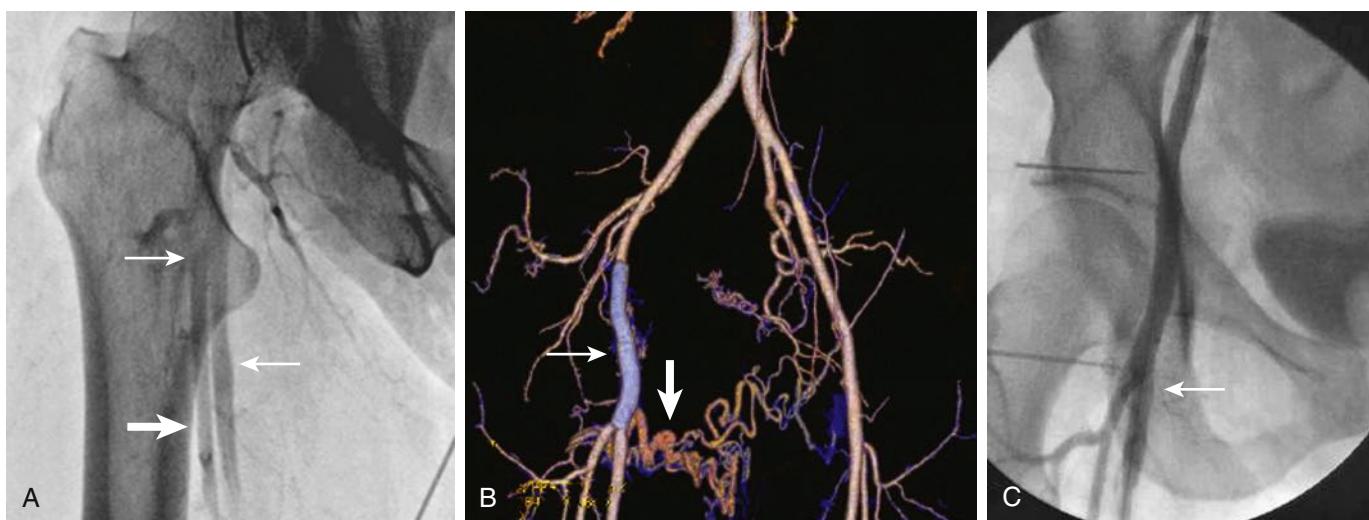


Figure 173.5 (A) Selective femoral angiogram demonstrating an arteriovenous fistula (AVF; upper arrow) at the common femoral bifurcation, outlining the superficial femoral vein (middle arrow) and artery (lower arrow). (B) CT reconstruction showing persistence of the AVF (vertical arrow) below a covered stent graft (horizontal arrow) used to treat common femoral stenosis after attempted operative repair of the fistula. (C) Selective femoral angiogram demonstrating closure of the fistula after placement of an additional covered stent graft (arrow).

BOX 173.1

Factors Predisposing to Iatrogenic Femoral Arteriovenous Fistula

Female gender	Age >65
Emergency procedures	Sheath size >8 F
Intensity of anticoagulation	High body mass index
Low distal puncture	Severe femoral atherosclerosis
Hypertension	Left-sided/multiple punctures
Prosthetic grafts	Hostile groin

iatrogenic injury during splenoportography, and, rarely, erosion of a pancreatic pseudocyst into the splenic artery and vein.^{81–85} Forty-four percent of splenic AVFs are due to rupture of a noncalcified splenic artery aneurysm (SAA) into an adjacent vein; this may be the first indication of the presence of an SAA.^{5,85–91} Hepatic AVFs are most commonly the result of penetrating or vehicular trauma but may occur after percutaneous needle biopsy, transhepatic diagnostic catheterizations, biliary drainage, or TIPS procedures (Fig. 173.8).^{85–91} Hepatic AVFs may be either intrahepatic or extrahepatic and occur in 5.4% of patients after percutaneous needle biopsy.^{85–91} Hepatic artery aneurysms (HAAs) and carcinomas may also erode into an adjacent vein, resulting in an AVF.^{87,92,93} AVFs of the superior and inferior mesenteric arteries are rare and are usually the result of penetrating trauma, iatrogenic injuries, or mass ligation of the vascular pedicle during bowel resection.^{94,95}

Uterine Arteriovenous Fistulas

Acquired uterine AVFs are a rare complication of intrauterine instrumentation procedures, (diagnostic and therapeutic curettage, removal of retained placental products, IUDs, and hysteroscopy) myomectomy, and pathologic processes such as

infection, trophoblastic disease, and malignancies involving the uterus. Uterine AVFs are frequently a single AV communication without involving the surrounding tissue.^{96,97}

Arteriovenous Fistulas Following Deep Venous Thrombosis

Recently, several authors have reported the occurrence of AVFs in patients with thrombosis of the inferior vena cava, iliac and femoropopliteal veins. Patients usually present with progressively worsening symptoms and signs of deep venous insufficiency. The etiology of AVFs associated with DVT is not fully understood but may result from venous hypertension-induced dilatation of pre-existent micro-fistulas, or maybe secondary to perforation of the IVC during placement or removal of IVC filters or recanalization of thrombosed deep veins.^{98–101}

PATHOPHYSIOLOGY

The natural history of an AVF is related to the diameter of the artery and vein, the size and location of the fistula, the adequacy of the collateral circulation, and the competence of the distal venous valves. AVFs may close spontaneously, decrease in size, or progressively enlarge as a result of degenerative changes within the arterial wall.^{102,103}

Fistula Size and Flow

Holman and Taylor established the relationship between arterial flow and the cross-sectional area of a fistula. When the diameter of the fistula was ≤ 1.5 times the diameter of the inflow artery, distal arterial flow was antegrade, but was diminished or reversed when the fistulous opening exceeded the diameter of the inflow artery by $>$ threefold due to the increase in collateral

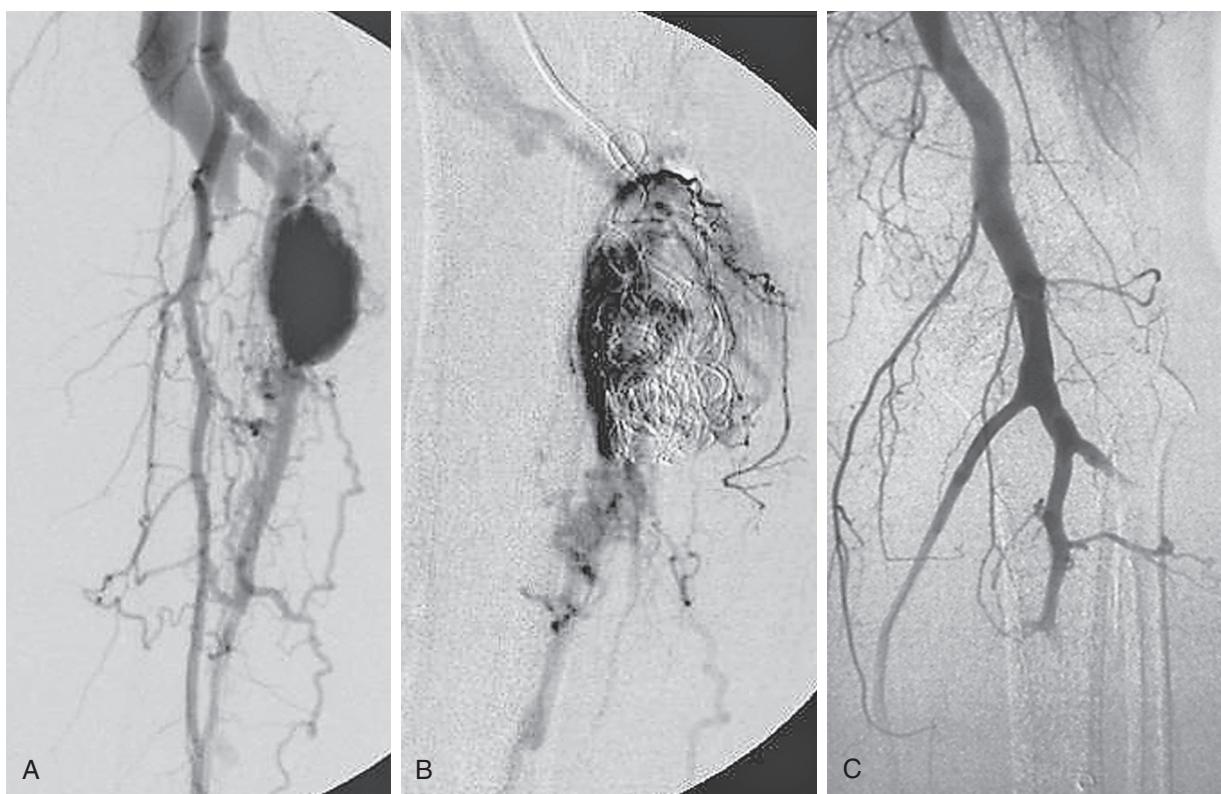


Figure 173.6 (A) Selective femoral angiogram demonstrating an arteriovenous fistula (AVF) between the anterior tibial artery and vein. (B) Coil embolization of the AVF. (C) Occlusion of the tibioperoneal trunk by a dislodged coil, resulting in severe limb ischemia requiring treatment with a popliteal-to-posterior tibial venous bypass graft.

flow distal to the fistula.¹⁰⁴ Flow in the artery proximal to the fistula increased up to fivefold if the fistula was ≥ 1.5 times the arterial diameter and eightfold if the opening was ≥ 3 times the diameter of the inflow artery.¹⁰⁵ Flow rates ≥ 350 mL/min, calcification of the PSA or fistula are associated with failure of the defect to close spontaneously.⁴⁴ Iatrogenic femoral and renal AVFs are usually small with low flow rates and therefore infrequently result in congestive heart failure (CHF). The larger-diameter sheaths used for thoracic and abdominal aortic, cardiac and complex peripheral and venous interventions, TIPS procedures, and orthopedic instrumentation of the lumbar spine and the knee may result in larger defects and AVFs with higher flow rates, and a greater risk of CHF.

Chronic Changes

In chronic AVFs, the increase in hemodynamic shear stress results in attenuation of the arterial wall, accompanied by calcification and lipid deposition at the fistula site and in the inflow artery. These structural changes result in elongation, tortuosity, and ultimately aneurysmal dilatation at the site of the fistula.^{106–108} The adjacent vein also dilates and becomes tortuous and thickened or “arterialized” with pulsatile flow. The high venous pressure at the site of the fistula results in dilatation and valvular incompetence of the distal vein, producing chronic venous insufficiency. The structural changes in the artery and vein become evident at ~ 2 months and established by 15 months but appear to be reversible if the AVF is repaired within 2 years.^{106–108}

Cardiac Effects

In patients with large AVFs, the increase in preload results in cardiomegaly and dilatation of the aorta and vena cava proximal to the fistula. These structural changes may develop within weeks to months or progressively increase over months to years. Young healthy male trauma victims are more likely than older individuals to compensate for the increase in preload, but, ultimately, if left untreated, high-output CHF ensues.¹⁰³

CLINICAL PRESENTATION

History

The majority (75%) of patients with small AVFs are asymptomatic. The most common findings are thrill or bruit (61%–96% of cases) or a pulsatile mass (20%–52% of cases).^{14,16} Symptoms in patients with large AVFs may arise from increased venous return (CHF), diversion of arterial blood flow (ischemia), or venous hypertension (varicosities, edema). An antecedent history of trauma, catheter-based interventions, or AAA should be elicited in all patients. The acute onset of abdominal or back pain (65% to 80%), dyspnea (21.7%) and leg swelling (19.2%) are the presenting complaints in patients with spontaneous aortic and iliac AVFs.¹⁰⁹ Other symptoms and signs may occur as a function of the location of the AVF. Although CHF is most commonly associated with aortic and iliac AVFs, symptoms of cardiac decompensation may occur in patients with large extremity, visceral, or cervical or thoracic AVFs.¹¹⁰

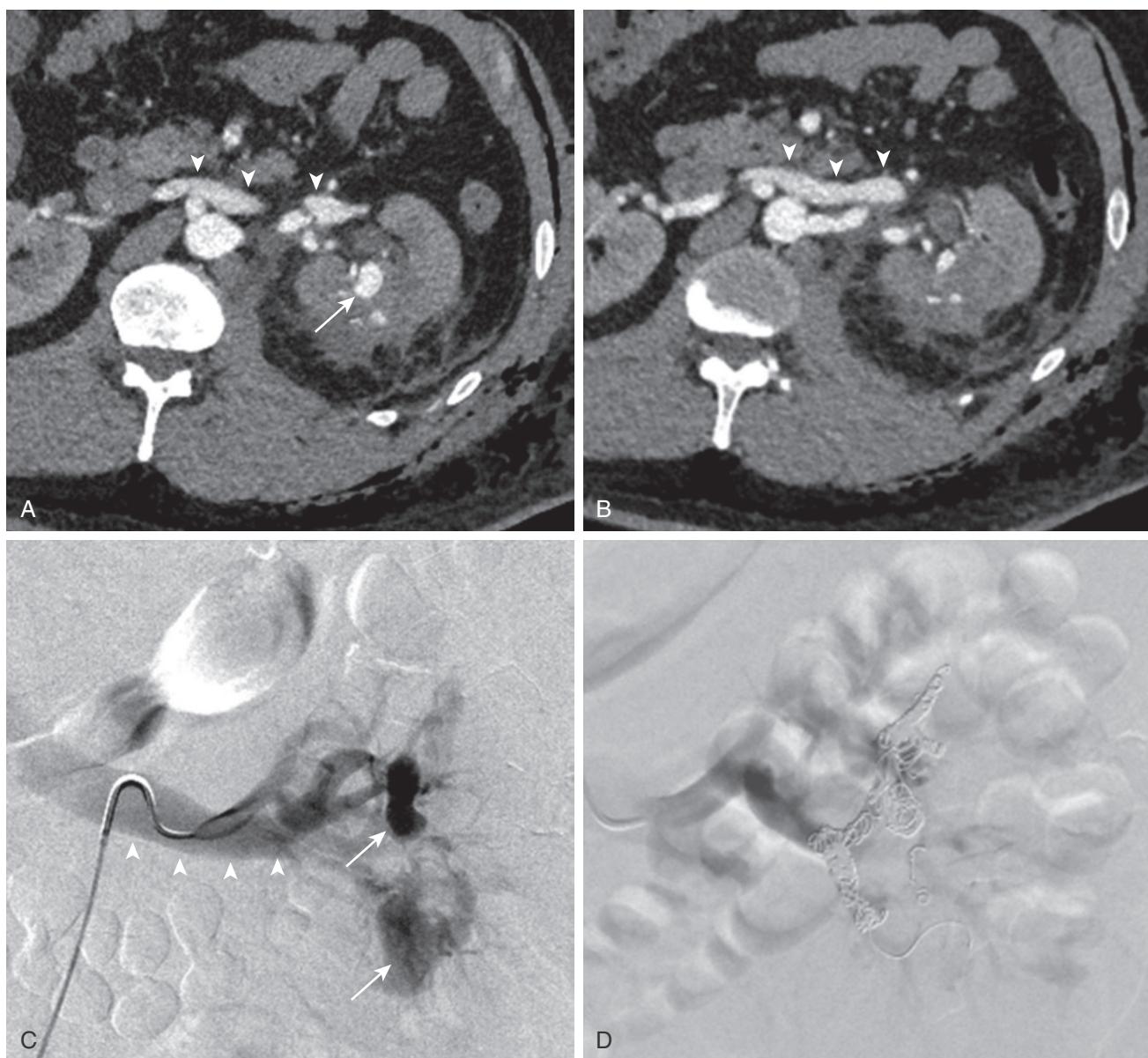


Figure 173.7 CT and angiogram of a patient with iatrogenic left renal pseudoaneurysms (PSAs) with an arteriovenous fistula (AVF) after partial nephrectomy. Axial arterial-phase CT images (A, B) at the level of kidneys show contrast collection in the left renal parenchyma (arrow), which simultaneously enhances with renal artery and the aorta, consistent with a PSA. In addition, there is early filling of the left renal vein (arrowheads), consistent with a renal AVF. Left perinephric stranding is due to early postoperative changes of partial nephrectomy. Left renal DSA image (C) shows PSAs along the middle and inferior segmental arteries (arrows) with an early draining vein in the arterial phase of the study (arrowheads), consistent with a renal AVF. DSA image of the left renal artery shows coil embolization of the middle and lower pole PSAs and segmental arteries with no opacification of the draining vein.

Physical Examination

Neck and Upper Extremities

A rapidly expanding or pulsating hematoma, carotid bruit or thrill, and dilated pulsatile neck veins suggest the diagnosis of a carotid–jugular AVF. Neurologic deficits due to embolization or shunting of blood through the fistula may also be present.^{15,30} The clinical diagnosis of vertebral AVFs is often unsuspected as only 50% of patients present with overt signs or symptoms of injury; pulsatile tinnitus or a pulsatile mass with a thrill and bruit may be present; neurologic symptoms

are rare. Subclavian, axillary, and brachial AVFs may manifest with pulse deficits, blood pressure abnormalities, arm swelling, a pulsatile mass with a thrill and bruit, dilated venous tributaries or hand ischemia. Radial and ulnar AVFs usually manifest as a thrill or bruit over a small pulsatile mass and, rarely, digital embolization.

Lower Extremities

A careful examination of the groin and lower extremity for evidence of an expanding or pulsatile hematoma and/or a

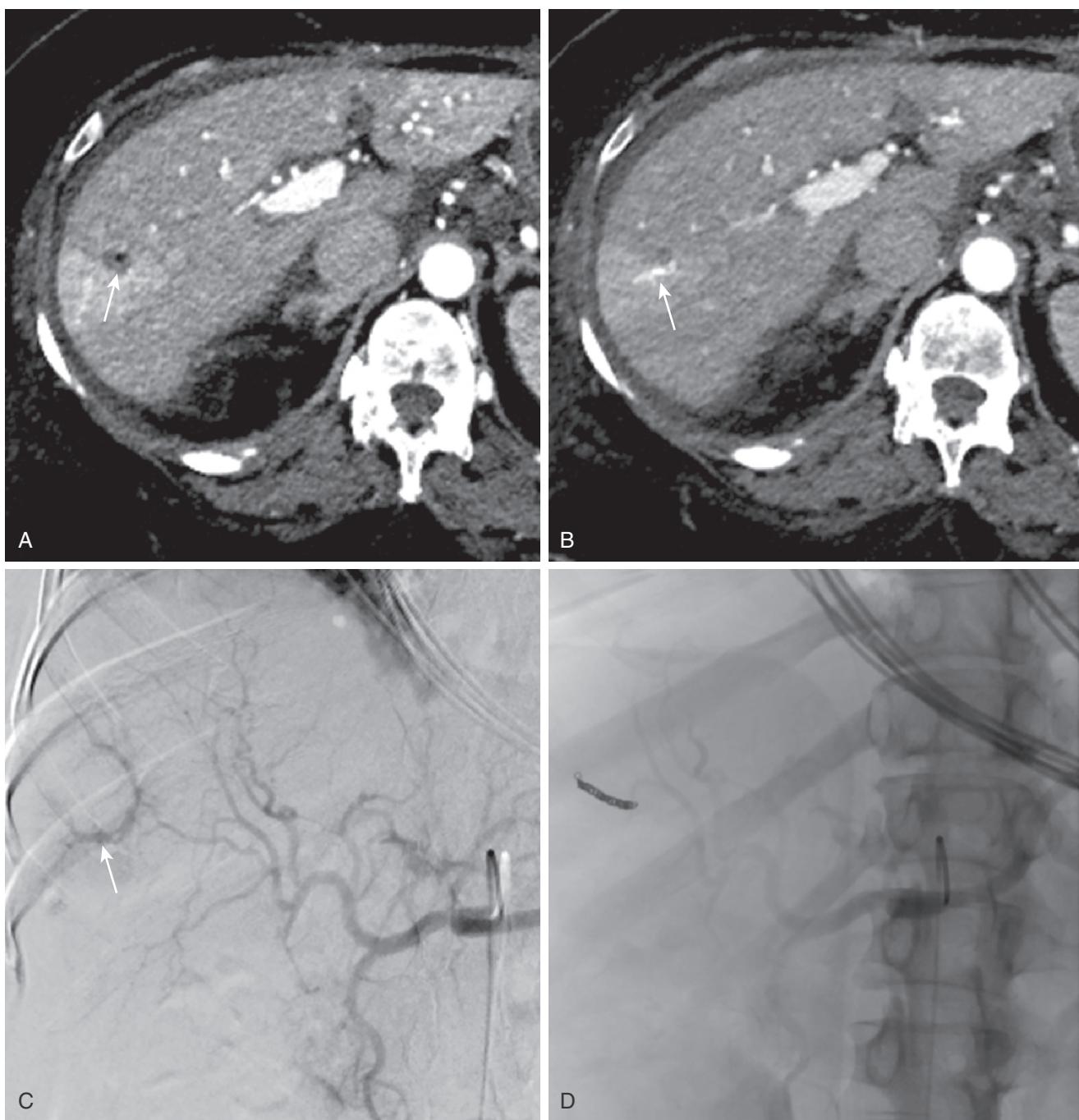


Figure 173.8 Axial CECT images of the abdomen shows changes of biopsy in segment VI (arrow) (A), with a prominent early filling of a small peripheral vein (arrow), suggesting an iatrogenic arteriportal fistula (B). Celiac artery digital subtraction angiogram (DSA) shows early filling of a peripheral portal vein (arrow), consistent with an arteriportal fistula (C). DSA image shows successful coil embolization of the hepatic arteriportal fistula with no early opacification of the portal venous branch (D).

thrill or bruit should be performed. Temporary compression of the artery proximal to the fistula should result in slowing of the heart rate and a reduction in pulse pressure (Nicoladoni-Branham sign). Leg swelling with dilated or varicose veins, pigmentation, and ulceration may be present in more chronic cases. Although signs and symptoms of arterial ischemia are rare, the presence of peripheral pulses and segmental blood pressures should be documented. Pedal access-related fistulae between the crural arteries and their *venae comitantes* usually

present incidentally as a small mass with an overlying thrill and bruit.¹¹¹

Chest and Abdomen

The anterior chest wall should be examined for dilated venous tributaries – a distended pulsatile internal jugular vein accompanied by a thrill and bruit, chest rales or holosystolic murmur may indicate an innominate AVF. A prominent abdominal pulsation or pulsatile mass with a thrill or bruit is suggestive

of an ACF. A holosystolic murmur is present in 75% of ACFs; although it may be absent if there is a large amount of thrombus present within the aneurysm. A thrill is palpable in 25% of patients.^{21–24,82} In patients with AVFs to the aorta or iliac arteries following lumbar disc surgery, symptoms may not manifest until months to years after the event. In these cases, a lower abdominal bruit may be the only finding. Signs of CHF and lower extremity venous hypertension are characteristic findings in patients with larger fistulas.⁶²

Paradoxical embolism from thrombus within a AAA exiting through an ACF into the pulmonary circulation is an uncommon but well-recognized complication. The occurrence of dyspnea, cough, tachypnea, tachycardia, or evidence of hypoxemia and hypocapnia, however, have low specificity and sensitivity, particularly in coexistence of AAA rupture with hemodynamic and cardiac instability.¹¹²

Small renal AVFs are usually discovered incidentally by the presence of a bruit over the kidney. Blood flow through larger renal AVFs may approach 60% to 82% of total ipsilateral flow and result in significant partial renal ischemia, and hypertension.⁷⁵ Patients with spontaneous aortorenal AVFs may present with abdominal pain, hematuria, proteinuria, a varicocele, renal impairment of varying severity, non-contrast-enhancing “silent” kidney, and hemodynamic instability.^{24,71} These patients often present late because they undergo extensive urologic evaluation for hematuria.¹¹³

The clinical findings in patients with hepatic AVFs include jaundice, hepatosplenomegaly, prominent venous collaterals, and epigastric bruits. Hematochezia and hematuria due to rupture of mucosal veins in the rectum and bladder may be present in 11.5% to 35% of cases.¹¹⁴ Patients with uterine AVFs usually present with abdominal pain and vaginal or rectal bleeding. A thrill or bruit at the site of an abdominal AVF or lower extremities in patients with DVT should raise the suspicion of an acquired AVF.

DIAGNOSTIC EVALUATION

Plain radiographs should be obtained in all patients with suspected AVFs for evidence of prior trauma (bullet or metal fragments), abnormal calcifications, healed fractures and signs of CHF. The diagnostic algorithm then proceeds to noninvasive imaging to identify the characteristics of the AVF, with either duplex US, computed tomographic angiography (CTA), or magnetic resonance angiography (MRA). Depending on the outcomes of these, additional testing, such as ankle-brachial indices or venous or carotid duplex imaging, is obtained. A 12-lead electrocardiogram and/or two-dimensional echocardiogram may be obtained if CHF is suspected. Catheter-based angiography and/or cardiac catheterization are reserved for treatment and/or diagnostic uncertainty. Endoscopy may be indicated in patients with active gastrointestinal bleeding or a history of bleeding from esophageal varices or gastric ulceration.

Color-Flow Duplex Ultrasound Imaging

DUS is an appropriate initial choice for the diagnosis of acquired AVFs. Characteristic findings include visualization of

the AVF and/or PSA and a color mosaic in the tissues at the site of the fistula. Loss of triphasic arterial waveforms proximal to the fistula, diminished or reversal of flow in the distal artery, and continuous high-velocity flow in the vein cephalad to the fistula are the usual Doppler findings (Fig. 173.9).^{71,75,115} The diagnostic accuracy of DUS is highly technician dependent and may be difficult to perform in the presence of open wounds, subcutaneous air, hematoma, fractures, obesity, and interference from anatomic structures.¹¹⁶

Computed Tomography Angiography

CTA is an appropriate diagnostic tool for evaluating patients with suspected AVFs. It is operator independent, minimally invasive, accurate, allows for rapid image acquisition, and repeat follow-up exams. Visualization of the fistulous tract is diagnostic of an AVF. Early venous opacification during arterial phase imaging and diminished parenchymal enhancement are the usual findings in patients with visceral AVFs. In prospective studies of arterial injuries, CTA has been shown to be comparable to digital subtraction angiography (DSA) with a sensitivity of 90% to 95% and specificity of 99% to 100%.^{117–121} The major limitations of CTA are: allergic reactions to iodinated contrast, the risk of contrast-induced nephrotoxicity, interference from vessel wall calcification, and the degradation of image quality by metallic, motion, and shoulder streak artifacts. Metal-induced artifacts, affecting ~10% of scans, can be reduced with virtual monochromatic reconstruction of dual energy CT data sets, metal artifact reduction reconstruction algorithms, and post-processing image visualization techniques. The use of 64- and 128-slice scanners have reduced the number of uninterpretable scans from 20% and 40% to 3%.¹²⁰

Magnetic Resonance Imaging and Angiography

MRI and MRA facilitate the diagnosis of AVFs by delineating the underlying defect, measuring flow disturbances, and defining the relationship between the fistula and adjacent soft tissue structures.^{121–123} However, their utility is limited by long image acquisition times, and patient intolerance. Due to heating and object deflection by the magnetic field and radiofrequency gradients, patients with “MRI unsafe” implants or devices (pacemakers and implantable cardioverter defibrillators, implanted neurostimulators, brain aneurysm clips made from ferromagnetic material, hemodynamic monitoring and temporary pacing devices) or bullet or shrapnel fragments located close to the eye or major blood vessels, cannot enter the MRI environment. To mitigate such artifacts in MRI, techniques collectively known as metal artifact reduction sequence (MARS) MRI are used to optimize the framework of the conventional pulse sequences and exploit novel multispectral and multispatial imaging methods such as Slice Encoding for Metal Artifact Correction (SEMAC) and Multi-Acquisition Variable-Resonance Image Combination (MAVRIC). Contrast-induced toxicity and the potential development of nephrogenic systemic fibrosis (NSF) in patients on renal dialysis was until recently a major concern.¹²⁴ The occurrence of NSF with the use of group II and III gadolinium-based

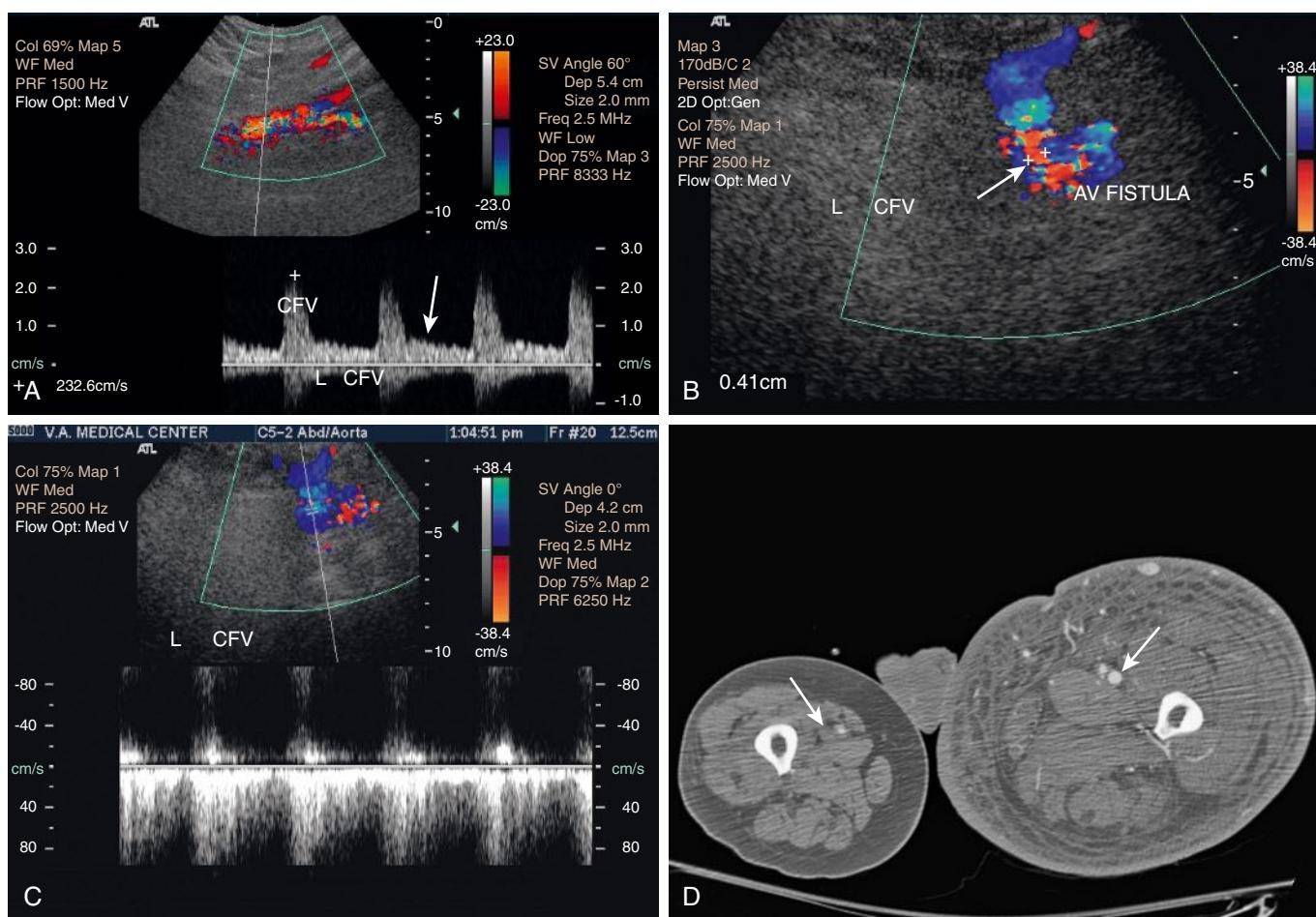


Figure 173.9 Ultrasound image and CT scan of a patient with a large common femoral AVF. Loss of triphasic waveforms with prolonged diastolic flow is observed in the common femoral artery (CFA) proximal to the fistula (A); a large connection is demonstrated by the white arrow between the CFA and common femoral vein (CFV) (B); pulsatile reversed flow is seen in the CFV distal to the fistula (arrow) (C); and early enhancement of superficial femoral vein (arrows) on the side with an AVF (D).

contrast agents (GBCAs) in patients with acute kidney injury (AKI), chronic kidney disease (CKD), or on dialysis occurs with extreme rarity or not at all, eliminating the need for pre-screening for kidney disease in patients who need the exam. Patients on hemodialysis (HD) should, however, be identified prior to GBCA administration to arrange timely HD to optimize gadolinium clearance, although there remains no evidence that HD reduces the risk of NSF.^{125–128}

Digital Subtraction Angiography

DSA provides excellent spatial and temporal image resolution, permits rotational views, and is used for both diagnostic and therapeutic interventions for acquired AVFs. The typical angiographic features of an AVF are early venous filling and failure to opacify distal arteries. A high-quality angiogram to identify the precise location of AVFs is essential for endovascular therapy (EVT). In cases where it may be difficult to locate the fistula by angiography alone, simultaneous catheterization of both the affected artery and vein or balloon catheter occlusion of the inflow artery with contrast injection beyond the balloon can be helpful. DSA with carbon dioxide may be an alternative to

conventional angiography in patients with a history of contrast reaction or chronic renal failure.¹²⁹ DSA is now increasingly being replaced by CTA or MRA for diagnostic purposes.

PRINCIPLES OF MANAGEMENT

The goals of therapy for acquired AVFs consist of closure of the fistula, restoration of normal hemodynamic flow, and re-establishment and maintenance of vascular continuity.¹³⁰ Data from the conflicts in Afghanistan and Iraq suggest that repair of major extremity venous injuries, previously considered unnecessary, is desirable to reduce the sequelae of venous hypertension and improve limb salvage.¹³¹ Patients with ACFs in florid CHF should be admitted to the ICU preoperatively for optimization of cardiac function. Massive leg swelling and ulceration are controlled with diuretics, limb elevation, or compressive bandaging.

Conservative Treatment

The natural history of stable iatrogenic femoral AVFs is relatively benign, with 38% to 81% expected to close spontaneously.

Therefore, patients with small AVFs and normal cardiac function can be monitored with DUS for at least a year.^{44,45,132} Procedure-related renal AVFs are usually small and 33%–90% have been shown angiographically to resolve spontaneously between 6 weeks and 4 years after the initial diagnosis.⁷¹

Compression Therapy

US-guided compression and compressive bandaging have been advocated as treatment for small iatrogenic AVFs. Successful occlusion of an AVF is unlikely if the artery and vein are closely adherent, if the defect is large or located at an arterial bifurcation, or if the communication is deep and not amenable to superficial compression. The low success rate of US compression (0%–30%), the duration of bandage compression required (15 ± 10 days), and the occurrence of local skin ulceration and DVT with the latter, argue against their use.^{133–136}

Endovascular Therapy

Until recently, open surgery was the only option for treating AVFs after conservative therapy had failed. However, the morbidity and mortality of surgery, lesion accessibility and the ongoing advances in endovascular techniques have increased the use of EVT to treat VIs and AVFs. EVT is the treatment of choice for poor-risk surgical candidates, older stable patients with suitable anatomy, and patients with AVFs in surgically inaccessible locations.¹³⁷ EVT can be accomplished by transcatheter embolization, placement of a stent-graft, or a combination of the two modalities. Temporary balloon occlusion is a useful adjunct to control bleeding.

Embolization

Transcatheter embolization can be used to treat many AVFs.^{71,75,138–145} Available embolic agents include autologous clot, gelatin sponges, microfibrillar collagen, polyvinyl alcohol particles, metallic coils, detachable balloons, and liquid embolic agents such as N-butyl cyanoacrylate (n-BCA) and ethylene vinyl alcohol copolymer (Onyx). The choice of embolic agent depends on vessel size, the caliber of the delivery catheter, and whether repeated embolization is anticipated. Gelfoam slurry is the preferred agent for temporary occlusion, and metallic coils and particles are used for permanent occlusion. Successful embolization requires accurate positioning of the catheter at the site of the AVF before delivering the occluding agent.^{140,142} Micro-coils and particulate agents deployed through coaxial microcatheters are ideal for treating small muscular and radicular branch cervical, renal, visceral, or extremity AVFs, with technical success rates of 89% to 92% (Fig. 173.7). Although a limited number of reports have been published on the embolization of visceral AVFs, principles similar to those used for the endovascular treatment of other AVFs can be applied.^{140,143–147}

The major risk associated with transcatheter embolization of AVFs is embolization to arteries related to the fistula and to the lung, resulting in parenchymal or extremity ischemia or

pulmonary embolism (Fig. 173.6). In high-flow fistulae, larger high radial force coils are deployed first to provide a scaffold for smaller-sized packing coils, to avoid inadvertent migration and embolization. Placement of a protective covered stent, Amplatzer plug, or temporary balloon occlusion device can reduce the risk of coil migration or embolization in these situations.¹⁴⁸ With careful technique, the extent of infarction related to catheter embolization of renal AVFs, for example, has been limited to less than 10% in over 75% of patients.⁷⁵

Covered Stent Grafts

Covered stents are used to bridge a fistula and preserve parent vessel flow in large-diameter AVFs. If a PSA is present, it is occluded with embolic material. A wide variety of stent grafts have been used successfully to treat patients with acquired and spontaneous AVFs.^{138,149,150} Because of the limited stent sizes currently available to treat tibial disease, use of a covered stent designed for the coronary arteries can be considered in AVFs involving the crural arteries.^{38,137,151–154} Although, covered stents have been used to treat PSAs, perforations and AVFs in coronary arteries with low thrombosis and restenosis rates, their use to treat patients with tibial PSAs and AVFs has been less successful (8/9 occluded within 7 months).^{56,155,156} Penetrating injuries of the innominate, carotid, and subclavian arteries are anatomically amenable to EVT.^{38,153} In a review of 54 published cases of endovascular treatment of carotid trauma, covered stents were deployed for carotid AVFs in 31% (17 of 54) of cases, with an 88% success rate.¹⁵² AVFs also accounted for 21% of cases of subclavian trauma treated with covered stents over a 10-year period, by du Toit et al.³⁹

The placement of covered stent grafts to treat AVFs in the groin and around the knee joint, although technically feasible, has been avoided because of the perceived risk of kinking or bending in these locations. Because the CFA has been the access site for most angiographic interventions, placement of a covered stent was also believed to preclude/limit its use for repeated procedures.^{157,158} However, the introduction of shorter length (12–28 mm) stent grafts with a wider range of diameters has allowed for accurate bridging of an AVF in the CFA without crossing or impinging on the orifices of the SFA or profunda femoris arteries, while leaving the remaining uncovered CFA accessible for repeated interventions.^{38,137,151–154,157–166}

Abdominal Endografts

Commercially available aortic endografts and their components, initially designed to treat patients with aortoiliac (A-I) and thoracic aneurysmal disease, are currently used to treat aortic, iliac, and aortic arch branch vessel AVFs. AVFs of the descending thoracic aorta are rare but, when present, may be amenable to EVT.^{137,162–165} The major limitations to the use of endografts to repair ACFs are similar to those that preclude their use in conventional aneurysm repair; unfavorable aortic neck or iliac artery morphology and the diameter and tortuosity of the access vessels. Persistent endoleaks occur in 4%–50% of patients potentially leading to continued aneurysm sac enlargement are a concern in patients with ACFs treated with

aortic endografts. Because the natural history of this complication is unclear, early re-intervention with closure of the communication by placement of a stent graft in the IVC or with OR has been recommended. However, van de Luijtgaarden et al.¹⁶⁷ have suggested that conservative monitoring may be appropriate if the patient is asymptomatic, and shrinkage of the aneurysm sac can be demonstrated. The defect in the IVC may not be detected on the completion angiogram and only become evident due to continued enlargement of the aneurysm sac.¹⁶⁸ It is recommended that CTA be done in the follow-up period in cases of uncertainty. ARFs are also amenable to EVT. The depth of the pelvis and the presence of enlarged adherent veins make EVT a practical and safer option than open repair for most I-C and I-I AVFs.^{169,170} The introduction of smaller-diameter grafts and delivery systems has facilitated the management of younger patients with aortic and iliac trauma and AVFs. Careful case selection and limiting graft oversizing has reduced the incidence of endoleaks, sac ruptures, and fistula persistence or recurrence in the short-term follow-up of small numbers of these younger patients.^{137,164} The risk of air embolism, IVC thrombosis and dislodgement of thrombotic material resulting in pulmonary embolism has led some surgeons to advocate prophylactic placement of a removable IVC filter or insertion of a second aortic prosthesis into the IVC to prevent this complication.^{171,172} Placement of a stent graft in the IVC may also be appropriate in treating patients with recurrence of their ACF.

Only case reports of a small number of patients address the treatment of renal, splenic, hepatic, mesenteric and uterine AVFs with covered stent grafts and embolizing feeding vessels when indicated to preserve flow in the parent vessel. Uterine artery embolization is recommended as the first choice for preserving the fertility of young patients with uterine AVFs, with hysterectomy being reserved for older patients with malignancy. Additional embolization of feeding vessels is usually required for larger AVFs to prevent endoleaks, or persistence and recurrence of the fistula.^{88,173,174} Amplatzer plugs have been successfully used to occlude splenic, renal, mesenteric, subclavian, and popliteal AVFs and those occurring after endovascular aneurysm repair in selected patients.¹⁷⁵ In patients with DVT-associated AVFs, treatment should address both the venous obstruction and occlusion of the AVF.^{98–101}

Operative Repair

OR of AVFs is recommended for young good risk patients, individuals with complex anatomy unsuitable for EVT, or when EVT has failed.

Carotid and Vertebral Arteriovenous Fistulas

Although AVFs involving vessels in zone II of the neck are repaired surgically, exposure of AVFs in zones I and III may require median sternotomy or left lateral thoracotomy. Exposure of the distal internal carotid artery (ICA) at the base of the skull, even using the recognized maneuvers to improve the exposure is associated with considerable

morbidity. Therefore, EVT is often the most appropriate treatment for such lesions.

AVFs in zone II are more amenable to OR. Treatment of AVFs involving the carotid arteries may include primary repair of the defect in the artery and vein, patch angioplasty, interposition grafting, and/or proximal and distal venous ligation. The majority of traumatic vertebral AVFs occur deep in the neck between the C2 and C5 vertebrae and are difficult to treat surgically. Lesions involving the V1 segment are the most surgically amenable. Ligation of the VA proximal to the AVF and transposition of the distal segment onto the CCA may be feasible in selected patients. Treatment of more complex lesions usually requires ligation of the VA and vein above and below the fistula, and a subclavian artery–VA saphenous vein bypass at the C1–C2 interspace, if the contralateral VA is atretic or occluded.¹⁷⁶

Axillary and Subclavian Arteriovenous Fistulas

Exposure of subclavian and proximal axillary artery AVFs may require limited median sternotomy, left lateral thoracotomy, a supraclavicular incision, combined supraclavicular and infraclavicular incisions, or division of the clavicle (seldom indicated).¹⁷⁷ The axillary artery is exposed by an incision directly over the artery, beginning below the middle of the clavicle and extending into the deltopectoral groove. The extent of arterial injury determines the repair; damage from blast injuries or GSWs usually requires excision of the damaged artery and placement of an interposition graft, whereas lacerations or transections can be reapproximated and repaired primarily.

Lower Extremity Arteriovenous Fistulas

The OR of lower extremity AVFs is accomplished by isolating the involved artery and vein proximal and distal to the AVF in healthy tissue planes, separating the vessels, and repairing the defect primarily, with an autogenous or prosthetic patch or interposition graft. When the AVF involves the superficial femoral artery, application of a tourniquet can significantly reduce blood loss. The distal runoff should be carefully assessed, especially with GSWs and injuries from IEDs where multiple arteries may be involved. If there is continuity of one or more of the infrageniculate arteries, ligation of the involved artery and vein may be undertaken.

Aortocaval and Iliac Arteriovenous Fistulas

Aortocaval, A-I, and I-I AVFs are repaired using a midline or retroperitoneal incision, which can be extended into the chest if necessary. In patients with spontaneous ACFs secondary to AAA, the AAA and massively dilated IVC are readily recognizable, whereas a thrill with dilation of the aorta and IVC accompany traumatic or iatrogenic ACFs. Repair of the aorta is undertaken in the standard fashion, with ligation of the PSA if present and closure of the communication with the IVC performed from inside the aorta (Fig. 173.10). Attempting to separate the IVC and aorta and repair the IVC externally can lead to massive bleeding and should not be attempted. Back-bleeding from the IVC is controlled

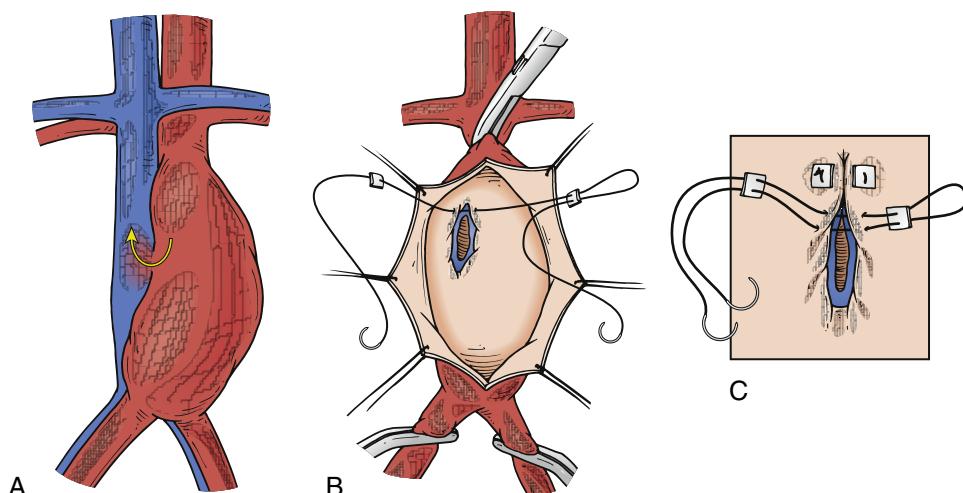


Figure 173.10 Schematic view of operative repair of an aortocaval fistula (A). The defect is closed from within the aneurysm sac (B, C). (From Crawford ES, et al. *Diseases of the Aorta: Including an Atlas of Angiographic Pathology and Surgical Technique*. Baltimore MD: Williams and Wilkins; 1984.)

with digital pressure or sponge sticks. In 10% of patients the defect in the IVC is large enough that a prosthetic patch or placement of a stent graft is required. Care should be taken to avoid air embolism or the dislodgement of thrombus into the IVC during surgical manipulations. Iliocaval or I-I AVFs are much more difficult to repair surgically due to their location deep in the pelvis and the presence of large, dilated veins. To minimize blood loss, temporary balloon occlusion of the iliac and femoral veins above and below the fistula prior to arterial occlusion and exposure of the AVF should be considered. When the AVF is due to rupture of an iliac artery aneurysm, placement of an interposition or bifurcated aortic prosthesis may be required to establish arterial continuity. Arterial lacerations and disruption resulting from iatrogenic or penetrating trauma may be closed primarily or require patch angioplasty. The defect in the IVC or iliac vein can then be repaired to maintain venous patency.

Aortorenal Arteriovenous Fistulas

OR of aortorenal fistulas may require suprarenal aortic clamping to avoid injury to the renal artery and enlarged veins. AVFs associated with renal artery aneurysms or dissection are repaired *in situ* by aneurysmectomy with or without vein patch closure or aortorenal bypass.¹⁷⁸ *Ex vivo* repair may be required in selected cases of branch vessel involvement. Fistulas resulting from mass ligation of the renal pedicle are treated surgically by isolation and ligation of the renal artery and vein at their origins.

Visceral Arteriovenous Fistulas

Visceral AVFs are exposed via a midline or subcostal incision. The splenic artery in patients with AVFs is usually dilated and tortuous and can be controlled at its origin prior to treatment of the AVF. Splenectomy is often performed for AVFs of the hilum or parenchyma.⁸³ The splenic vein

should be ligated close to its junction with the superior mesenteric vein to minimize the risk of thrombus propagation into the portal vein. Exposure of arterioportal and arterio-systemic AVFs may require medial visceral rotation and/or thoracoabdominal extension of the incision to obtain proximal control of the celiac artery.

Definitive OR of hepatic AVFs depends on their location and etiology. Spontaneous AVFs may require placement of an interposition graft, with repair or ligation of the vein. In the case of a fistula resulting from a common HAA, proximal and distal ligation of the aneurysm is an option if collateral flow through the right gastric and gastroduodenal arteries is preserved. Lesions of the proper hepatic artery and its branches require either direct repair or a vein interposition graft to maintain hepatopetal flow. Ligation of the involved artery and segmental or partial hepatectomy may be required with intrahepatic AVFs.

Treatment options for AVFs involving the superior or inferior mesenteric arteries or their tributaries include interposition grafting or ligation and excision of the AVF if a tributary is involved and collateral flow can be preserved. Mesenteric AVFs following mass ligation of the gastric, inferior, or superior mesenteric vascular pedicles are treated by isolation and proximal ligation of the involved artery and vein.

TREATMENT OUTCOMES

In symptomatic patients, repair of A-C, I-C, or I-I AVFs are accompanied by almost immediate improvement in cardiac and pulmonary function. Normalization of renal function may be delayed for 48 to 72 hours. Younger patients with high-output CHF can be expected to recover fully, whereas the recovery of older individuals with spontaneous AVFs is determined by preexisting comorbidities.^{179,180} The comparison of treatment outcomes is listed in Table 173.1.

TABLE 173.1 Comparison of Treatment Outcomes

Year	Author	# Patients (AVFs)	AVF Type	Mechanism of Injury	OR N (%)	EVT N (%)	Technical Success (%)	COMPLICATION RATE (N) %		MORTALITY RATE (N) %	
								OR	EVT	OR	EVT
2020	Choudhary et al.	21	ARF	PT, BT	14 (66.6)	7 (33.3)	100				
2016	Orion et al.	67	ACF, AIF, ARF	SP	41(61)	26 (39)	94	36	46	12	19
2014	Nakad et al.	54	ACF, AIF, ARF,	SP, IAT, PT, IIF,		54 (100)	94		33		10
2011	Davidovic et al.	50	ACF, AIF, ARF	SP	50 (100)		100				12
2019	Wadhwa et al.	12	CJ	IAT	5 (42)	7 (58)					
2013	Briganti et al	31	VV	IAT, PT, SP	1(3)^	31 (97)^	87.5**	(1)3.4	(4)14^		
2011	Herrera et al.	36 (7)	CJ	PT		36 (100)	94.4		2.8		2.8
2009	du Toit et al.	128 (9)	CJ	PT	109	19 (100)	100		5.2		5.2
2007	Schonholz et al.	54 (17*)	CJ, CFF	BT, PT, IAT		54 (100)	72*		28		
2008	Herrera et al.	18 (16)	VV, VJ	PT, IAT		18 (100)	89		5.5*		0
2016	Branco et al.	153	Ax-Subclavian	PT	135 (89)	18 (11)	94.4	25.5	0	27.8	5.6
2015	Naidoo et al.	31 (5)	Ax-Subclavian	PT		31 (100)	83.9				3.2
2012	Dubose et al.	160 (27)	Subclavian	PT, IAT, BT		160 (100)	96.5		3.1		
2010	Sobnach et al.	50 (7)	Subclavian	PT	49 (98)	1 (2)	100				0
2008	du Toit et al.	57 (12)	Subclavian	PT		57 (100)	100		7		1.7
2020	Kim et al.	8	Femoral	IAT	3 (37.5)	4 (50)	100		(1)14		
2019	Rayamajhi et al	158 (9)	Femoral	PT	9 (100)				0		
2018	Şahin et al.	27	Extremity	PT	27 (100)		100	0		0	
2017	Sarac et al.	11	Extremity, CJ	IAT, PT		11 (100)	100		9		0
2013	Yousuf et al.	30	Femoral	IAT, PT	29 (96.6)	1 (3.4)	90		0	0	0
2011	Davidovic et al.	83 (36)	Extremity	PT	83 (100)		100				1.2
2010	Bokhabrine et al	26	Extremity	PT	24 (92)	1 (4)	96	1 (4)			0
2007	Spirito et al	13 (8)	Tibial	PT	3 (25)	6 (75)	100		(1)16.6		
2004	Onal et al.	29 (14)	PFA/SFA/SFV	IAT		10 (100)	90		8.3	3.6	0
1993	Franco et al.	55 (2)	Ilio/Femoral	IAT	55 (100)		100		25.4		
2020	Gao et al.	11	Extremity	DVT	1 (9)	8 (72.7)	100				
2019	Yuan et al.	24	Extremity	DVT	4 (16.6)	13 (54)	100		15.3†		

BT, blunt trauma.

†Had recurrence after EVT.

*Carotid cavernous arteriovenous fistula excluded.

^Initial OR or EVT.

**Initial technical success.

^^Failed initial EVT and required OR.

From references 181–207.

Operative Repair

OR of postcatheterization AVFs is successful in 89% to 96% of cases. However, in cases of unstable patients where emergent surgery is required, EVT may be safer.^{44,45} Intraoperative blood loss, myocardial infarction, pulmonary embolism, stroke, and multisystem organ failure account for a morbidity rate of 36% and a mortality rate of 7.1% to 12% following OR of spontaneous ACFs. Long-term graft patency is 96% in surviving patients.^{9–11,14–25,137,162–165,168,208} There are no large series documenting the treatment outcomes of OR for visceral AVFs. However, treatment outcomes can be inferred from the elective treatment of visceral artery aneurysms (VAAs); the mortality rate for elective procedures is approximately 5% and increases to 10%–25% in patients with ruptured aneurysms. Similarly, limited information is available on the outcome of renal AVFs repaired surgically. The results from repair of renal artery aneurysms suggest that AVF repair can be undertaken with low morbidity and mortality rates in institutions with extensive experience treating these lesions.²⁰⁹

Endovascular Therapy

Stent grafts alone or combined with embolization have been successfully deployed in 83.9% to 100% of selected patients with pseudoaneurysms or AVFs of the carotid, subclavian, and axillary arteries. Early and late stent-graft occlusion (5%–10%), intimal thickening resulting in ≥50% luminal stenosis (4%–20%), re-intervention rates of 6% to 12%, and mortality rates of 0% to 5.9% are the major complications of EVT in these patients. Although these data encompass the treatment outcomes of all types of cervical and upper extremity VIs and not only AVFs, they do provide some insight into the expected results of EVT for patients with these AVFs.^{6,152–154,210–212}

In most cases, EVT is the treatment of choice for iatrogenic femoral, profunda femoris, and popliteal AVFs, with technical success rates ranging from 88% to 100%.^{157,158,213} Whether the routine use of antiplatelet agents will limit intimal thickening and improve graft patency remains undetermined.^{214–216} There are currently no long-term follow-up data addressing the use of complex tibial interventional approaches to treat AVFs in patients with CLI. Abdominal aortic endografts are successfully deployed in 84%–94% of patients with ACFs, with morbidity and mortality rates of 12%–46% and 0%–19%,

respectively.^{168,217} Endoleaks and graft complications due to aortic remodeling, especially in younger patients, require continued monitoring.¹⁶⁸ Only 23%–36% of renal AVFs require treatment. Transcatheter embolization alone or in combination with a stent graft is accompanied by a success rate of 90%. Successful occlusion of VAAs can be achieved with coil embolization in 93.3%–100% of cases, with an overall perioperative morbidity of 10%–12.5% and mortality of 0.0%–8.3%.^{83,218–220} Multiple interventions are usually necessary to achieve this level of success treating VAAs, pseudoaneurysms, and AVFs.^{115,146} The endovascular treatment of SAAs is associated with 0% mortality but a 40% splenic infarction rate; embolization of HAAs has a mortality rate of 11% without significant hepatic ischemia.²²⁰

Operative Repair versus Endovascular Therapy

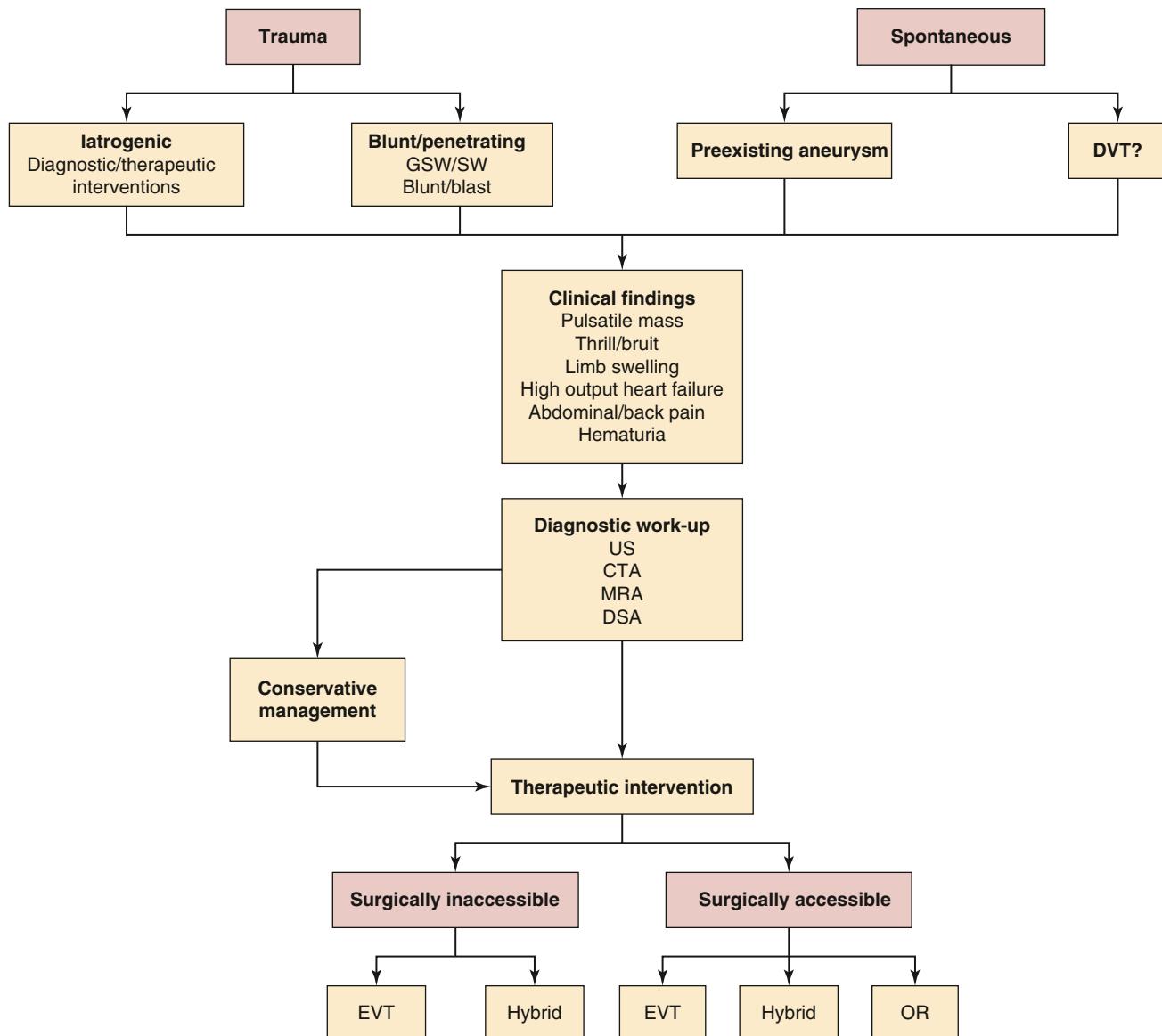
The choice between EVT vs. OR in the management of patients with acquired AVFs should be individualized to reduce morbidity and mortality rates and late complications. There are currently no prospective randomized trials comparing EVT with OR. Only case reports of small numbers of patients and literature reviews are available to guide clinical decision-making.

Embolization is effective and the treatment of choice for the majority of iatrogenic AVFs affecting access sites, solid organs, bleeding side branches, PSAs as well as superficial traumatic AVFs. Covered stent grafts combined with embolization maybe required to treat AVFs with PSAs to preserve organs and tissue perfusion.

EVT is an alternative to OR to treat ACFs in anatomically suitable patients. However, a 10%–32% overall rate of peripheral embolization, thrombosis or stent-graft migration has been reported with EVT. Endoleaks, which affect 4%–50% of patients, remain an ongoing problem predisposing to continued aneurysm sac enlargement, and rarely rupture.¹⁰⁹ OR is currently reserved for young healthy patients, individuals with unsuitable anatomy for EVT, and when EVT has failed, is curative and durable with 90% patency in surviving patients.

The current literature suggests that, despite its recognized advantages, EVT cannot yet be recommended as the standard of care for all patients with aortic or iliac AVFs. Because of the small numbers of patients with acquired ACFs, there is little likelihood of a randomized controlled trial; a prospective registry may provide better comparative long-term outcome data.

CHAPTER ALGORITHM



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Hemodialysis Access: General Considerations and Strategies to Optimize Access Placement

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As the population ages and the incidence of diabetes rises, chronic kidney disease (CKD) and end-stage renal disease (ESRD) are increasingly common diagnoses in the United States. In 2017, data from the United States Renal Data System (USRDS) showed that 124,500 new patients began therapy for ESRD, whereas the prevalent dialysis population reached 746,557. Of note, after a sharp rise in the incidence of ESRD patients in the 1980s and 1990s, followed by a leveling off in 2000 and a peak in 2006, there has been a slight but steady decline through 2017 (Fig. 174.1). Despite this, the number

of ESRD patients continues to rise by about 20,000 patients per year (Fig. 174.2), with a resulting rise in healthcare costs.¹ Medicare fee-for-service spending for ESRD patients increased by 1.3%, from \$35.4 billion in 2016 to \$35.9 billion in 2017, accounting for 7.2% of overall claims (Fig. 174.3). Not surprisingly, most of these costs occur during the transition from CKD to ESRD and are due to the high use of long-term catheters and frequent hospitalizations for permanent arteriovenous (AV) access failures, requiring thrombectomies, revisions, and repeated access placements.²

[†]Deceased.

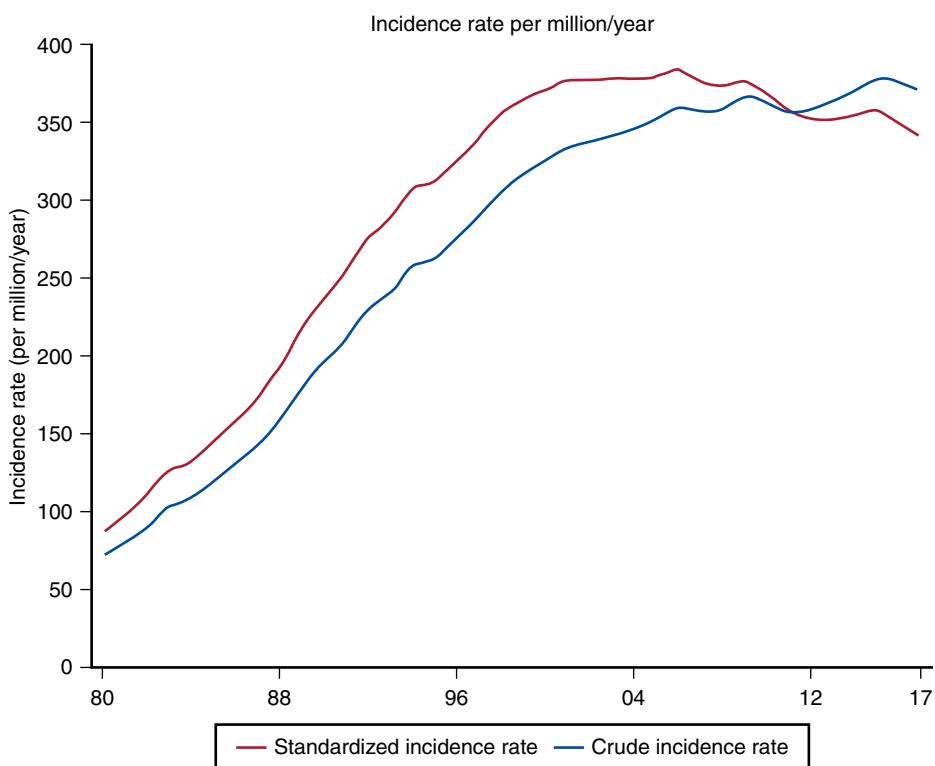


Figure 174.1 Trends in the crude and standardized incidence rates of ESRD in the US population, 1980–2017. (Reproduced from United States Renal Data System [USRDS] 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease, Bethesda, MD: 2019.)

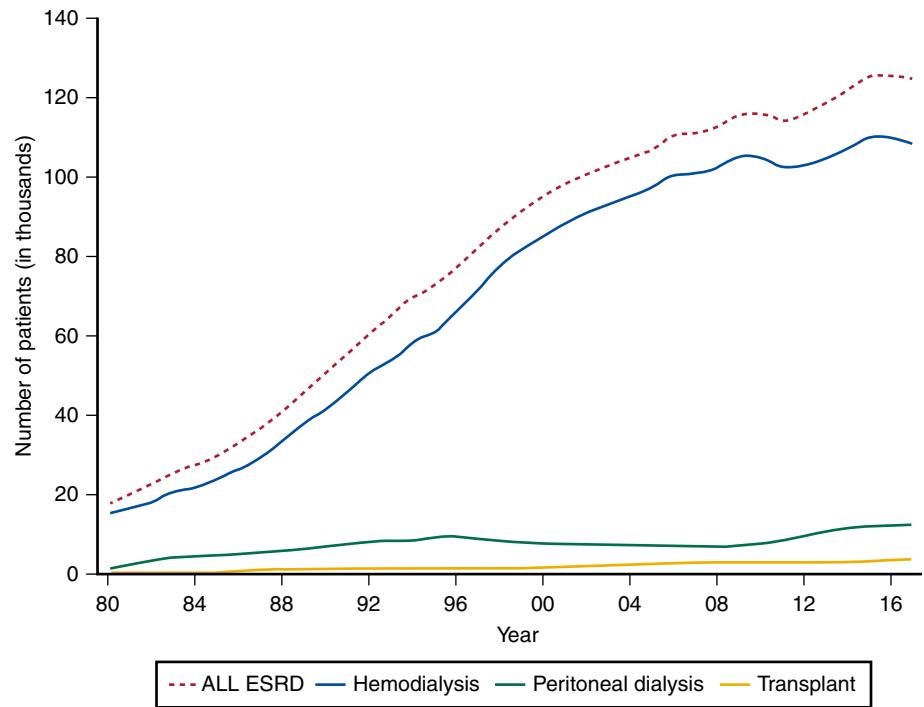


Figure 174.2 Trends in the annual number of ESRD incident cases, by modality, in the US population, 1980–2017. (Reproduced from United States Renal Data System [USRDS] 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease, Bethesda, MD: 2019.)

INITIATIVES AND GUIDELINES

In 1997, the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF KDOQI) Clinical Practice Guidelines for Vascular Access were published in an effort to increase the placement of autogenous AV access and prolong the use of created access by detection of dysfunction prior to thrombosis. These original guidelines recommended that autogenous AV

accesses should be constructed in at least 50% of all new hemodialysis patients and ultimately 40% of prevalent hemodialysis patients. With subsequent NKF KDOQI guidelines, recommended percentages of placement of new and prevalent autogenous AV access continued. These new NKF KDOQI guidelines, while still recognizing the superiority of autogenous AV access in the long term, emphasize an end-stage kidney disease (ESKD) life-plan which is a patient-centered, individualized

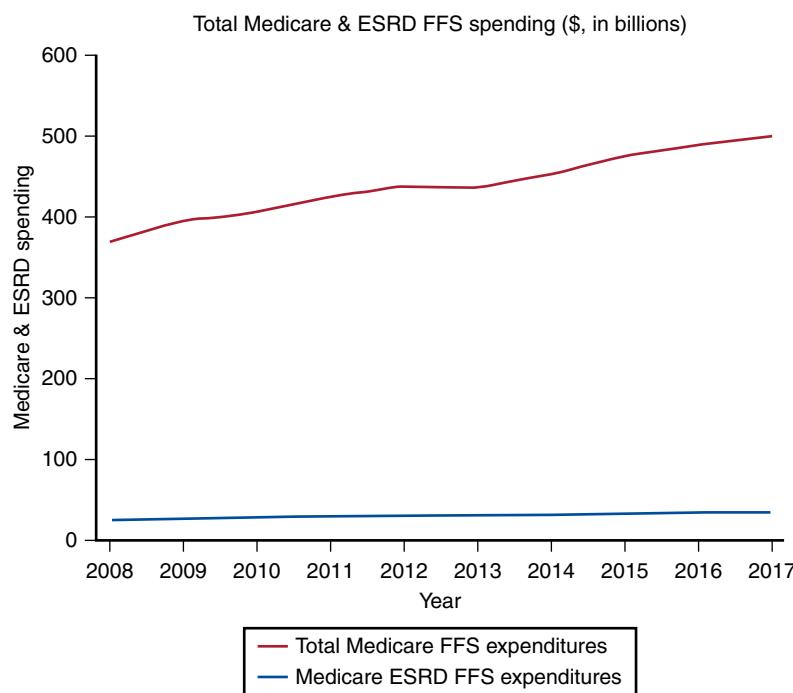


Figure 174.3 Trends in total Medicare & ESRD fee-for-service (FFS) spending (\$, in billions), 2008–2017. (Reproduced from United States Renal Data System [USRDS] 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease, Bethesda, MD: 2019.)

and comprehensive map for dialysis modalities and vascular access for the lifetime of the patient. When planning dialysis access, specific considerations are made to the patient's current medical situation, current and future goals, preferences, social support, functional status, and practical feasibilities – in summary, “the right access for the right patient at the right time”³.

In 2003, in an effort to reach the goals set forth by the NKF KDOQI guidelines, the Centers for Medicare and Medicaid Services (CMS) established the National Vascular Access Improvement Initiative (NVAII), which included vascular access experts and renal stakeholders who were committed to the development and implementation of sustainable system changes to support autogenous AV access placement. In 2005, the NVAII was expanded to the Fistula First Breakthrough Initiative (FFBI) Coalition⁴; a toolkit was developed and branded “Fistula First” to support the renal community in improving vascular access for dialysis patients. As a result of their efforts, the national rate of autogenous access reached NKF KDOQI’s original recommendation of 40% prevalence by August 2005, followed by a steady-state incline until 2011, when a plateau of about 60% was reached. The FFBI recognized this plateau was likely due to patient anatomy and that as an unintended consequence of increased attempts at autogenous AV access in small caliber veins was an increased use of central venous catheters (CVC). Therefore, in 2015, FFBI transitioned to the Fistula First Catheter Last (FFCL) Workgroup Coalition whose current goals are to increase the utilization of autogenous AV access in all appropriate hemodialysis patients to 68%, decrease the use of long-term catheters for greater than 90 days to less than 10%, and to engage patients and all providers to work together to achieve these goals. Similar to the new NKF KDOQI, these new goals emphasize decreasing the use of long-term catheters by changing the focus of dialysis access away from

autogenous access in all patients to autogenous access in all appropriate patients.⁵

The Society for Vascular Surgery (SVS), recognizing the effect of decision making by the individual access surgeon on the successful construction of AV access, has sponsored two further initiatives. First, in 2002, the Committee on Reporting Standards published the recommended standards for reports dealing with AV hemodialysis access. The purpose of this document was to provide standardized definitions related to AV access procedures and to recommend reporting standards for patency and complications in order to permit meaningful comparisons among AV access procedures.⁶ This was followed in 2008 by the clinical practice guidelines for the surgical placement and maintenance of AV hemodialysis access. After a multispecialty panel performed a systematic review of the literature, guideline recommendations were made in seven areas: (1) timing of referral to access surgeons; (2) operative strategies to maximize the placement of autogenous AV accesses; (3) first choice for the autogenous access; (4) choice of AV access when a patient is not a suitable candidate for a forearm autogenous access; (5) the role of monitoring and surveillance in AV access management; (6) conversion of a prosthetic AV access to a secondary autogenous AV access; and (7) management of the nonfunctional or failed AV access.⁷ This chapter focuses on strategies to maximize successful long-term access placement, whether autogenous or prosthetic.

TIMING OF REFERRAL

The NKF KDOQI and the SVS Clinical Practice Guidelines both recommend that patients be referred to a vascular access surgeon for permanent dialysis access when their creatinine clearance is less than 25 mL/min. Once preoperative evaluation

is completed, if the patient is felt to be an adequate candidate for autogenous AV access, the access should be constructed as soon as possible to give it adequate time to mature; ideally this should be greater than 6 months before the anticipated need for dialysis. However, since prosthetic access patency is limited by the duration of access placement, not time of access use, if a patient is felt to require a prosthetic access, the access placement should be delayed until 3 to 6 weeks prior to the initiation of dialysis.^{3,7}

Early access placement, greater than 4 months before the initiation of dialysis, has been shown to decrease the risk of sepsis (relative risk [RR] 0.57) and death (RR 0.76) when compared with late access creation (less than 1 month before the initiation of dialysis or after initiation of dialysis), primarily by reducing the use of central venous hemodialysis catheters.⁸ Despite this, nationwide data suggest that only 25% of hemodialysis patients initiate dialysis with permanent AV access. Lenz et al. reported that 93% of patients in an academic medical center with a well-established dialysis unit and vascular surgery service initiated hemodialysis with the use of a central venous catheter. In a retrospective review, they identified the reason as inadequate predialysis care in 45% of patients, acute illness with failure to recover from an episode of acute renal failure in 31% of patients, and noncompliance with medical and surgical appointments in 17% of patients.⁹ These studies stress the need for early referral and education for predialysis patients to prevent the use of central venous catheters and their subsequent complications.^{8,9}

PREOPERATIVE EVALUATION

Thorough preoperative evaluation of the arterial and venous system is imperative if long-term, permanent AV access is to be placed successfully.

History and Physical Examination

A thorough history should include the dominant extremity, recent history of peripheral intravenous lines, sites of indwelling or previous central lines including pacemakers and defibrillators, all previous access procedures, any history of trauma or previous nonaccess surgery to the extremity, all comorbid conditions, and current medications. On physical examination, the brachial, radial, and ulnar arteries should be evaluated for compressibility and equality bilaterally. An Allen test should be performed to evaluate palmar arch patency. The superficial venous system should be evaluated with and without a venous pressure tourniquet in place, examining for distensibility and interruptions. The arm should be examined for prominent venous collaterals and edema, which may be signs of central venous stenosis.^{3,7}

Medical Assessment

Multiple patient factors may play a role in AV access patency; these include age, sex, diabetes mellitus (DM), peripheral vascular disease (PWD), smoking, obesity, hyperparathyroidism (hPTH), anemia, and medications. As stated earlier, the new

TABLE 174.1

Medical Factors Affecting Arteriovenous Access Patency

Factor	Level of Best Evidence	Best Evidence Suggests Effect of Patency
Age	Meta-analysis	Yes
Gender	Meta-analysis	No
Diabetes mellitus	Prospective series	Yes
Atherosclerosis	Prospective series	Yes
Smoking	Prospective series	Yes
Obesity	Prospective series	No
Parathyroid hormone	Prospective series	Yes
Anemia	Prospective series	Yes
Medications	Systematic review	Yes

NKF KDOQI place a new emphasis on considering these types of comorbid conditions when planning a patient's ESKD life-plan. The literature is split on many of these factors; however, best evidence to date suggests that all except sex and obesity have a negative impact on access patency rates (Table 174.1).¹⁰ In the following paragraphs we review further some of the more studied factors that appear to negatively impact patency further.

Age

Published reports regarding age and its effect on AV access patency are mostly retrospective observational studies with conflicting results. However, these reports, along with a known shorter life expectancy for patients with ESRD, have raised the following question: Should proximal or prosthetic AV access be the first-line approaches in the elderly? To answer this, Lazarides et al. performed a meta-analysis, 13 studies in all, of dialysis outcomes in elderly patients (age range: 50 to 70 years), including studies that compared subgroups of elderly and nonelderly patients as well as forearm and upper arm accesses. They found a statistically significant higher rate of autogenous radial-cephalic direct AV access primary (OR 1.8), 1-year (OR 1.5), and 2-year (OR 1.4) failure in elderly patients compared with the nonelderly. They also found a statistically significant higher rate of autogenous brachial-cephalic direct upper arm access patency (RR 0.1) compared with autogenous radial-cephalic direct forearm access. They noted no statistical differences with the use of prosthetic access.¹¹ Based on these data, it is reasonable to recommend autogenous upper arm brachial-cephalic fistula or prosthetic access over distal radial-cephalic fistula in older patients.

Diabetes Mellitus

Published reports are mostly retrospective observational studies with similar results, stating that DM has a negative impact on AV access patency. These reports, along with a known increase in arterial calcification and atherosclerosis, have raised the following question: Should proximal or prosthetic AV access be

the first-line approach in diabetics? To further evaluate the impact that DM has on the vasculature, Sedlacek et al. compared preoperative noninvasive vascular mapping between diabetic and nondiabetic patients. They noted an increased number of arterial calcifications in diabetics but no difference in arterial diameter or the ability to place autogenous AV access; they did not evaluate long-term outcomes.¹² Looking at long-term outcomes in diabetic patients, Konner et al. noted an increased risk of thrombosis (0.03/patient year [PY] in nondiabetics vs. 0.07/PY in diabetics) and an increased risk of arterial steal (0.6/PY in nondiabetics vs. 7.0/PY in diabetics).¹³ Further studies are needed in this area; however, given the current literature, surgeons should take inflow in diabetics as distal as possible to decrease the risk of arterial steal.

Smoking

Published reports are retrospective observational studies with similar results, stating that cigarette smoking significantly increases early and late failure of AV access.¹⁴ ESRD patients should be referred to a tobacco cessation program before placement of first-time or any new AV access.

Medications

Published reports are mostly observational studies that have yielded conflicting results. One of the largest studies to date, the Dialysis Outcomes and Practice Patterns Study (DOPPS), noted an improvement of autogenous access secondary patency (RR 0.56) with angiotensin-converting enzyme (ACE) inhibitors, an improved prosthetic AV access primary patency (RR 0.86) with calcium channel blockers, an improved prosthetic AV access secondary patency (RR 0.70) with aspirin, and a decreased prosthetic AV access primary patency (RR 1.33) with warfarin.¹⁵ A study sponsored by the USRDS showed a decreased AV access patency with antiplatelet agents including ticlopidine, dipyridamole, and aspirin.¹⁶ Others have shown that angiotensin receptor blockers (ARBs) combined with antiplatelet agents increased autogenous AV access patency by 84%, whereas ARBs alone improved prosthetic AV access patency by 59%.¹⁷ At the present time there is a lack of consensus regarding the role of specific medications in improving AV access patency.

Arterial Assessment

If any abnormality is noted on the clinical arterial examination (absent or reduced peripheral pulses, abnormal Allen test, or asymmetrical arm pressures), the patient should be further evaluated with segmental pressures and duplex ultrasound scanning and/or pulse volume recordings (PVRs). For optimal outcome, no pressure gradient should be noted between the bilateral upper extremities, arterial diameter should be greater than or equal to 2.0 mm throughout the extremity, and a patent palmar arch should be present.¹⁸ Any abnormality noted on noninvasive testing should prompt alternate site selection or be further evaluated with an arteriogram, which gives the surgeon the ability to both identify and possibly treat an arterial inflow stenosis. In patients nearing dialysis, the risk of contrast

arteriography should be weighed against the need for access to mature before beginning dialysis. Renal protective measures are commonly used preceding arteriography including intravenous fluids, *N*-acetylcysteine, and sodium bicarbonate though the data supporting agents other than volume are limited.^{19–22}

Venous Assessment

If superficial veins cannot be visualized with a venous pressure tourniquet in place or any abnormality is noted on the superficial venous examination, the patient should be further evaluated with superficial venous duplex ultrasound vein mapping. Using venous duplex imaging, superficial veins should be examined for diameter, distensibility, and continuity. Minimal diameter for use of the forearm has been reported as low as 2.0 mm by Mendes et al., who noted a successful early maturation rate of 76%.²³ Using a minimal vein diameter of 2.5 mm, Silva et al. were able to perform 63% autogenous access with a 92% early maturation rate and 83% 1-year patency rate.¹⁸ Using a minimal vein diameter of 3.0 mm, Huber et al. were able to perform 90% autogenous access with an 84% early maturation rate.²⁴

Central venous stenosis should be suspected if there are any prominent venous collaterals or edema, a difference in extremity diameter, any history of previous central venous catheter placement, or multiple previous accesses in the planned extremity. If any of these abnormalities are identified, the patient should be examined first with deep venous duplex ultrasound imaging followed by venography if necessary.³ Passman et al. compared duplex ultrasound and venography in 60 upper extremities of preoperative access patients. Five (8%) ultrasounds were nondiagnostic due to artifact from central venous catheters or incomplete visualization of the central venous system. Of the studies that were diagnostic, they noted 81% sensitivity and 97% specificity of duplex ultrasound imaging with no statistical difference as compared with venography. Venography should be performed for further evaluation and possible treatment in patients with either nondiagnostic or abnormal duplex ultrasound imaging.²⁵ As with arteriography, in predialysis patients the risk of contrast venography must be weighed against the need for access to mature in time for dialysis. Before venography, patients should be treated with intravenous fluids, *N*-acetylcysteine, and/or sodium bicarbonate.^{19–22}

SELECTION OF ACCESS TYPE AND LOCATION

As discussed in the introduction to this chapter, with time it has been recognized that permanent autogenous AV access in all patients is not an achievable mission, and instead appropriate dialysis access individualized to the needs of the patients is a far more important goal. This incorporates understanding a patient's wishes, social support, comorbidities, and anatomy. This has been reflected in the new NKF KDOQI guidelines and summarized as "the right access for the right patient at the right time" as well as the transition from the FFBI to the FFCL

workgroups. This has always been recognized by the access surgeon who has been tasked with performing surgery using anesthesia in patients with many medical comorbidities and difficult arterial and venous anatomy. And now has fully been acknowledged as an ESKD life-plan, which is an individualized patient-centered team approach to develop a comprehensive map for dialysis modalities and vascular access for the lifetime of a patient.^{3,5}

The remainder of this chapter focuses on those patients that are felt to be candidates for permanent AV access. The various types of autogenous and prosthetic upper, lower, and body-wall AV access are listed in *Box 174.1*; our focus is on the upper extremity, and further complex access types are discussed in *Chapter 175* (Hemodialysis Access: Complex). In planning permanent AV access, a few general principles apply (*Fig. 174.4*):

1. Due to easier accessibility and lower infection rates, upper extremity access sites are used first, with the non-dominant arm given preference over the dominant arm.

BOX 174.1 Configurations of Arteriovenous Access

Forearm

Autogenous

- Posterior radial branch–cephalic wrist direct access (snuffbox fistula)
- Radial–cephalic wrist direct access (Brescia–Cimino–Appel fistula)
- Radial–cephalic forearm transposition
- Brachial (or proximal radial)–cephalic forearm looped transposition
- Radial–basilic forearm transposition
- Ulnar–basilic forearm transposition
- Brachial (or proximal radial)–basilic forearm looped transposition
- Radial–antecubital forearm indirect femoral vein translocation
- Brachial (or proximal radial)–antecubital forearm indirect looped femoral vein translocation
- Radial–antecubital forearm indirect saphenous vein translocation
- Brachial (or proximal radial)–antecubital forearm indirect looped saphenous vein translocation

Prosthetic

- Radial–antecubital forearm straight access
- Brachial (or proximal radial)–antecubital forearm looped access

Upper Arm

Autogenous

- Brachial (or proximal radial)–cephalic upper arm direct access
- Brachial (or proximal radial)–cephalic upper arm transposition
- Brachial (or proximal radial)–basilic upper arm transposition
- Brachial (or proximal radial)–brachial vein upper arm transposition
- Brachial (or proximal radial)–axillary (or brachial) upper arm indirect femoral vein translocation
- Brachial (or proximal radial)–axillary (or brachial) upper arm indirect saphenous vein translocation

Prosthetic

- Brachial (or proximal radial)–axillary (or brachial) upper arm straight access

Adapted from Sidawy AN, Gray R, Besarab A, et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses. *J Vasc Surg*. 2002;35:603–610.

2. AV accesses are placed as far distally in the extremity as possible to preserve proximal sites for future accesses.
3. As long as the patient is deemed appropriate, given their superior patency rates and lower complication rates, autogenous AV accesses should always be attempted before a prosthetic AV access.
4. These autogenous access configurations should include, in order of preference, direct AV anastomosis, venous transpositions, and venous translocations.

Forearm Access

Cephalic Vein

For autogenous forearm access, use of the cephalic vein is preferred to the basilic vein secondary to its lateral location and the need for only minimal dissection. Possible sites of arterial inflow include the posterior branch of the radial artery in the “snuffbox,” the trunk of the distal or proximal radial artery, the ulnar artery, and the brachial artery. The ulnar artery is usually not the first arterial option due to its distance from the cephalic vein. The access is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to preserve more proximal sites of inflow for future accesses. Therefore in patients with an adequate posterior branch of the radial artery, an autogenous posterior radial branch–cephalic wrist direct access (snuffbox fistula) is performed (*Fig. 174.5*). In patients with an inadequate posterior branch of the radial artery but an adequate radial artery, an autogenous radial–cephalic wrist direct access (Brescia–Cimino–Appel fistula) is recommended. In either of these cases, if the cephalic vein is felt to be too deep, as seen in obese patients, or is not located in close proximity to the radial artery in the wrist, an autogenous radial–cephalic forearm transposition is performed (*Fig. 174.6*). If the radial artery is inadequate, the ulnar artery may provide an alternative distal inflow site; alternatively, the entire trunk of either the radial or the ulnar artery may provide an arterial source. If the radial and ulnar arteries are inadequate but the brachial or proximal radial arteries are adequate, an autogenous brachial (or proximal radial)–cephalic forearm looped transposition is performed.

Basilic Vein

When the cephalic vein is not felt to be adequate for an autogenous AV access, the basilic vein is the preferred alternative. Secondary to its medial location in the forearm, a transposition is always required. Possible sites of arterial inflow include the distal radial artery, the ulnar artery, the proximal radial artery, and the brachial artery. Use of the posterior branch of the radial artery is not possible secondary to the distance from the basilic vein. Similar to the cephalic vein, the AV access is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to preserve more proximal sites of inflow for future accesses. Therefore when the radial artery is adequate, an autogenous radial–basilic forearm transposition is performed. If the radial artery is inadequate but the ulnar artery is adequate, an autogenous ulnar–basilic forearm transposition is performed. If the distal radial and ulnar arteries

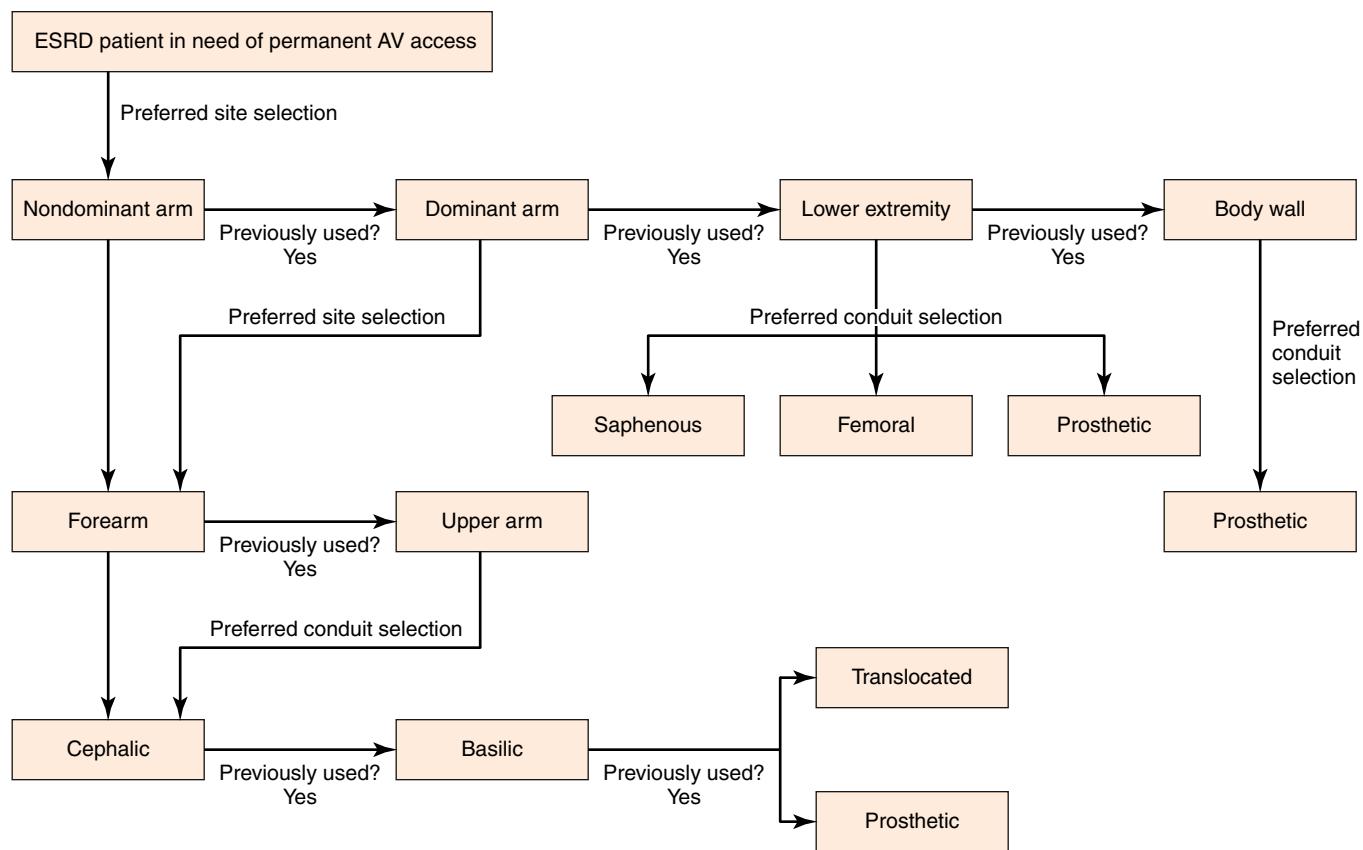


Figure 174.4 Algorithm: Selection of Access Location. AV, arteriovenous; ESRD, end-stage renal disease.

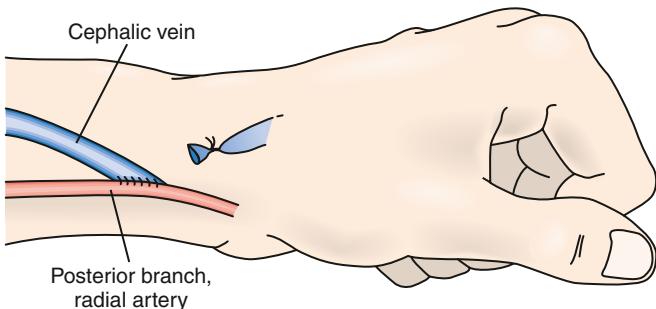


Figure 174.5 Autogenous posterior radial branch–cephalic wrist direct access (snuffbox fistula).

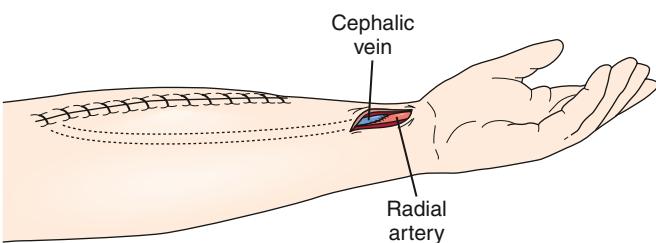


Figure 174.6 Autogenous radial–cephalic forearm transposition. (Reproduced from Silva MB, Hobson RW, Pappas PJ, et al. Vein transposition in the forearm for autogenous hemodialysis access. *J Vasc Surg*. 1997;26:981–988.)

are inadequate, a more proximal segment may be used (autogenous proximal radial–basilic forearm looped transposition). If the radial and ulnar arteries are inadequate throughout but the brachial artery is adequate, an autogenous brachial–basilic forearm looped transposition is performed.

Alternate Vein

When the cephalic and basilic forearm veins are not felt to be adequate for autogenous AV access, translocations of the femoral and saphenous veins are possible alternatives. The 2019 NKF KDOQI guidelines now acknowledge that given the extent of these dissections along with other related morbidities, many patients may not be candidates for such extensive operations. This should be reflected in their ESKD life-plan; these patients may be better served with either prosthetic AV access, long-term dialysis catheters, or an alternative mode of dialysis.³ Further strategies for these complex autogenous accesses are described in Chapter 175 (Hemodialysis Access: Complex).

Prosthetic Graft

If an adequate forearm vein is unavailable, a prosthetic AV forearm access is performed. Sources of arterial inflow include the distal or proximal radial artery or the brachial artery. Similar to autogenous access, the AV graft is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to preserve more proximal arteries for future accesses. Therefore when the distal radial artery is adequate, a prosthetic radial–antecubital forearm straight access is performed (Fig. 174.7). If the radial artery is inadequate but the brachial or proximal radial artery is adequate, a prosthetic brachial (or proximal radial)–antecubital forearm looped access is performed (Fig. 174.8).

One of the interesting debates in this area is whether, after exhausting the forearm autogenous options, the surgeon

should recommend a forearm prosthetic access before placing an upper arm autogenous access. As previously discussed in this chapter, the access surgeon should consider all of the patient and anatomic factors, particularly the adequacy of the upper arm vein. A mutual decision should be made between

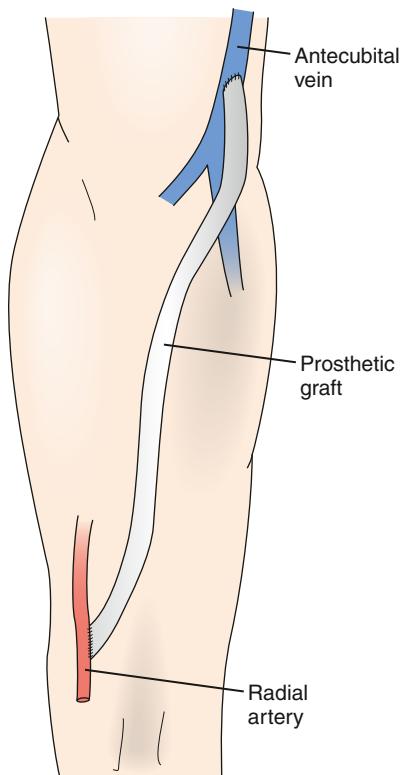


Figure 174.7 Prosthetic radial–antecubital forearm straight access.

the surgeon and patient as part of their ESKD life-plan after a thorough discussion about the risks and benefits of autogenous and prosthetic access. Most importantly, if a prosthetic forearm access is chosen, this should be considered a “bridge” to an autogenous upper arm access. Access surgeons should minimize the number of attempts to salvage the access with endovascular means to avoid damaging the venous outflow. A plan for eventual conversion of the forearm prosthetic access to a secondary autogenous access should be put in place; strategies include conversion of the prosthetic access mature outflow vein to an autogenous upper arm access or the identification of a new, remote site for autogenous access construction.^{3,7}

Upper Arm Access

Cephalic Vein

When use of the forearm has been exhausted, efforts at access are directed to the upper arm. Similar to the forearm, use of the upper arm cephalic vein is preferred to the basilic vein secondary to its lateral location and need for only minimal dissection. For upper arm access, possible sites of arterial inflow include the proximal radial and brachial arteries; the AV access is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to lower the risk of arterial steal. Therefore in patients with an adequate cephalic vein and an adequate proximal radial artery, an autogenous proximal radial–cephalic upper arm direct access is performed. If the proximal radial artery is inadequate and the brachial artery is adequate, an autogenous brachial–cephalic upper arm direct access is performed (Fig. 174.9). If the cephalic vein is felt to be too deep or is located far from the artery, an autogenous brachial (or proximal radial)–cephalic upper arm transposition is performed.

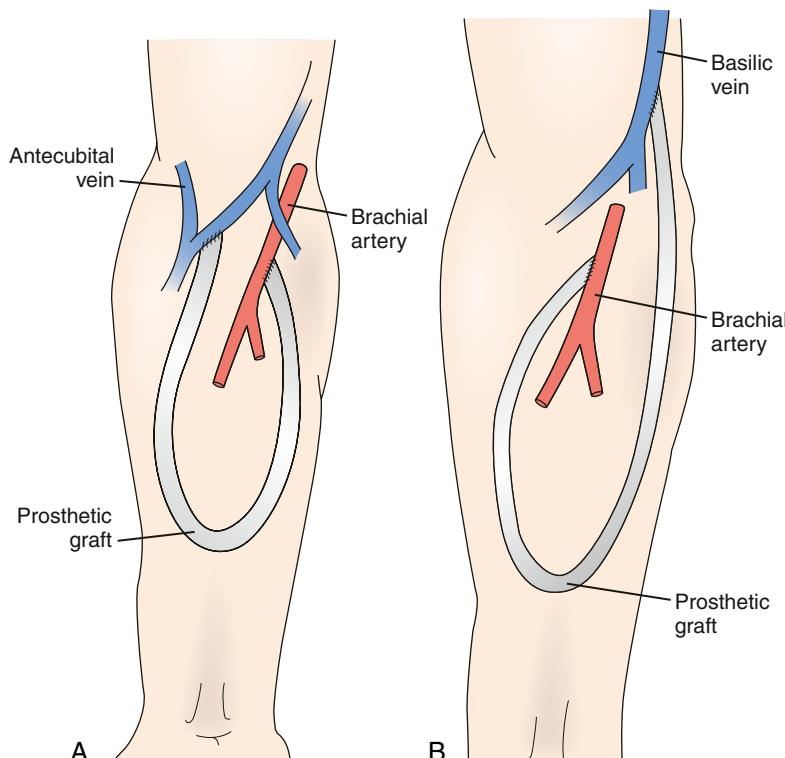


Figure 174.8 (A, B) Prosthetic brachial (or proximal radial)–antecubital forearm looped access.

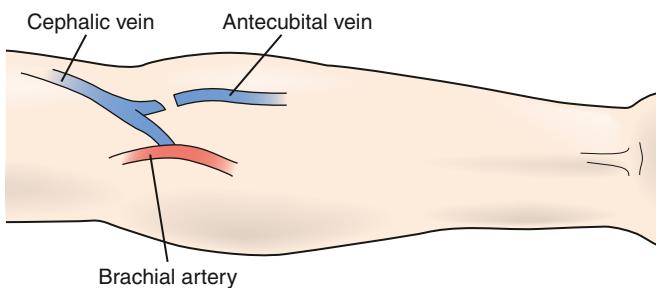


Figure 174.9 Autogenous brachial (or proximal radial)-cephalic upper arm direct access.

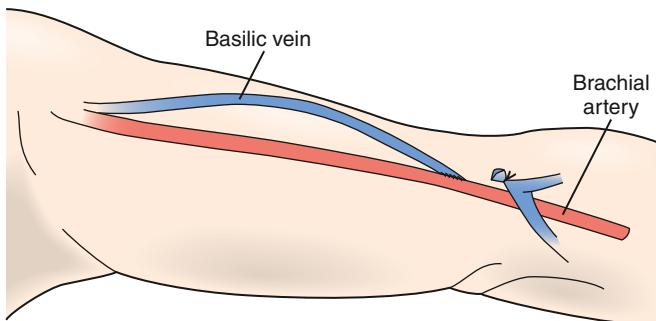


Figure 174.10 Autogenous brachial (or proximal radial)-basilic upper arm transposition.

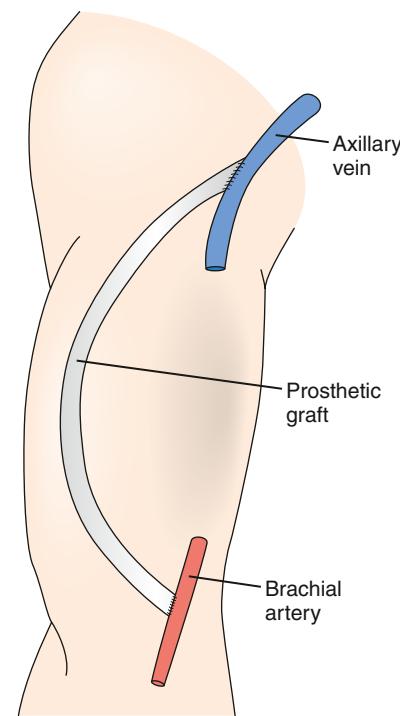


Figure 174.11 Prosthetic brachial (or proximal radial)-axillary (or brachial) upper arm straight access.

Basilic Vein

When the cephalic vein is felt to be inadequate for an autogenous AV access, the upper arm basilic vein is the preferred alternative. Secondary to its medial and deep location, transpositions are required for all accesses using the basilic vein. Similar to upper arm cephalic vein AV accesses, possible sites of arterial inflow include the proximal radial and brachial arteries; the AV access is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to lower the risk of arterial steal. Therefore in patients with an adequate basilic vein and an adequate proximal radial artery, an autogenous proximal radial–basilic upper arm transposition is performed. If the proximal radial artery is inadequate and the brachial artery is adequate, an autogenous brachial–basilic upper arm transposition is performed (Fig. 174.10).

Alternate Vein

When the cephalic or basilic veins are felt to be inadequate for upper arm autogenous access, brachial vein transpositions as well as femoral and saphenous vein translocations are possible alternatives. Similar to use of alternative vein for lower arm access, given the extent of these dissections along with other related morbidities, many patients may not be candidates for such extensive operations. This should be reflected in their ESKD life-plan; these patients may be better served with either prosthetic AV access, long-term dialysis catheters, or an alternative mode of dialysis.³ Further strategies for these complex autogenous accesses are described in Chapter 175 (Hemodialysis Access: Complex).

Prosthetic Graft

If no adequate vein is available, an upper arm prosthetic AV access is performed. Similar to upper arm autogenous AV accesses, possible sites of arterial inflow include the proximal radial and brachial arteries; the AV access is placed as distally in the arm as possible where an adequate artery is identified by preoperative evaluation to lower the risk of arterial steal. Therefore when the proximal radial artery is adequate, a prosthetic proximal radial–axillary vein (or brachial vein) upper arm straight access is performed. If the proximal radial artery is inadequate and the brachial artery is adequate a brachial–axillary vein (or brachial vein) upper arm straight access is performed (Fig. 174.11).

TECHNIQUE FOR PERMANENT ACCESS

Despite the multiple anatomic options for both autogenous and prosthetic AV accesses, the principles of surgical technique remain similar in all AV access procedures.

Autogenous Access

The following techniques are common to all autogenous vein accesses:

1. After identification of the vein, the distal end is transected and flushed with heparinized saline. This allows for evaluation of the caliber and extent of the vein and to identify any side branches.

2. With transposition accesses, the vein is completely dissected and mobilized, ligating all side branches, to its origin.
3. After controlling the artery, an arteriotomy of 4 to 6 mm maximal length is made. The length of the arteriotomy is limited to decrease the incidence of arterial steal.
4. The artery is flushed proximally and distally with heparinized saline to avoid thrombosis during the anastomosis.
5. The AV anastomosis is performed between the side of the artery and the end of the vein; this configuration decreases the subsequent risk of venous hypertension.
6. The AV anastomosis is performed using a 6-0 or 7-0 monofilament nonabsorbable continuous suture to avoid subsequent anastomotic dilation.
7. With nontransposed access, after completion of the anastomosis, large venous branches can be ligated through stab incisions. This encourages flow in the main venous segment, which may promote earlier maturation.

One-Stage Versus Two-Stage Transposed Access

Whether cephalic or basilic, forearm or upper arm, if autogenous AV access requires a transposition, this may be performed with either a one- or two-stage technique. The main benefit of a one-stage technique is obvious: the patient requires only one procedure and one anesthetic. However, if this access fails to mature, the patient has undergone an extensive dissection with no benefit, often leaving him or her reluctant to try again. A two-stage procedure begins with a direct anastomosis between the intended artery and vein, followed by a 4- to 6-week waiting period to evaluate for maturity. If the vein appears to be maturing appropriately, the second stage, transposition of the vein, is performed. This requires transection of the vein just proximal to the anastomosis, followed by its mobilization and tunneling, followed by a new anastomosis in its transposed position. The benefits of the two-stage procedure are assuring that the vein will be mature and usable for hemodialysis access before performing an extensive dissection as well as easier dissection of the maturing vein during the transposition. The drawbacks again are obvious: this requires a second procedure and a second anesthetic, putting patients at increased risk of surgery.²⁶ Therefore we recommend performing this procedure in two stages only with small-caliber (<4 mm) veins.

Prosthetic Access

The following techniques are common to all prosthetic access:

1. The length of the arteriotomy does not have to be limited to 4 to 6 mm. The diameter of the graft will limit the incidence of arterial steal.
2. The artery is flushed proximally and distally with heparinized saline to avoid thrombosis during the anastomosis.
3. A 6-mm polytetrafluoroethylene (PTFE) prosthetic graft is used for conduit (see Considerations, later).
4. The anastomoses are performed using a 6-0 or 7-0 monofilament nonabsorbable suture in a continuous manner.
5. Careful attention to sterile technique is paramount to avoid graft infections.

Choice of Prosthetic Material

A standard-wall 6-mm expanded PTFE (ePTFE) material is our choice for prosthetic access grafts. Variations in the standard ePTFE graft include thin-walled, extended stretch, external rings, various tapered configurations, and heparin coating. These are all meant to ease handling, provide external support, and improve patency rates. To date, there is only minimal evidence that any of these variations improve long-term results; therefore, use of these variations remains a matter of surgeon preference.^{27,28}

Another variation, early cannulation prosthetic grafts, are generally constructed in three layers, with an elastomeric membrane sandwiched in between two layers of ePTFE material. This configuration hinders suture-line and dialysis needle bleeding, allowing for early cannulation reportedly as soon as 24 hours from implantation and the potential for either avoidance or early removal of CVCs. Mean cannulation times have been reported in the literature from 2 to 15 days with minimal hematoma incidence; longer cannulation times were noted to be due to either surgeon or patient preference. Similar to other variations of prosthetic accesses, there is minimal evidence that this variation improves long-term results. Therefore use of this variation remains a matter of surgeon preference.^{29–32}

An alternative option to prosthetic conduit is cryopreserved conduit; this is harvested greater saphenous vein, femoral vein, or femoral artery from multi-organ donors. It is screened for infection, rinsed in antibiotic solution, placed in a manufacturer-specific proprietary cryopreservation solution, and stored in the vapor phase of liquid nitrogen at -110°C to -196°C. The surgeon chooses diameter and length needed, it is matched for ABO/Rh compatibility, and shipped in a solution of dimethylsulfoxide at -96°C. Due to the effects of cryopreservation it has been noted to have poor patency and increased incidence of pseudoaneurysms when used for lower extremity bypass; however, it does appear relatively resistant to infection. Therefore, this conduit may be considered for AV access use when autogenous vein is not available in a patient with either an active or history of infection.³³ Harlander-Locke et al. using a multi-institutional database reviewed 457 patients who underwent placement of cryopreserved vein for hemodialysis access and noted 58% 1-year and 17% 5-year primary patency rates for vein and 49% 1-year and 8% 5-year primary patency rates for artery with a 3% early and 9% late infection rate, concluding cryopreserved allograft to be an acceptable conduit for AV access in patients at high risk for infection.³⁴ However, Bolton et al. caution the use, noting a 25% 5-month primary patency and a 65% major graft-related complication rate in a single-institution 20-patient series.³⁵ Furthermore, Benedetto et al. have cautioned the use of cryopreserved vein in potential kidney transplant recipients warning its use can lead to broad alloimmunization.³⁶

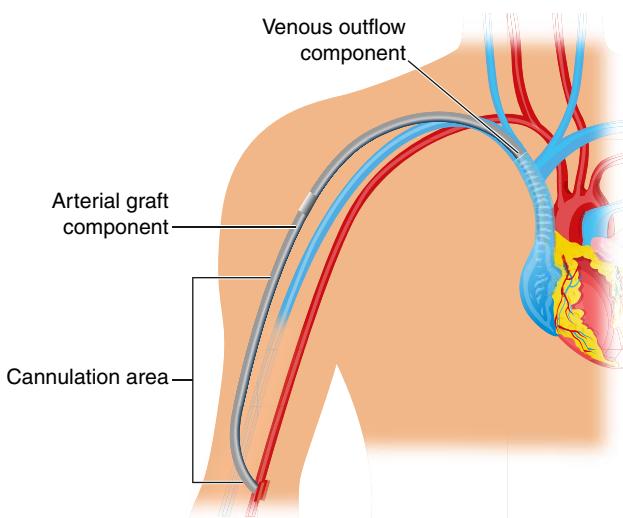


Figure 174.12 Hemodialysis Reliable Outflow (HeRO) Graft.

Hemodialysis Reliable Outflow Graft

The Hemodialysis Reliable Outflow (HeRO) graft (Hemosphere/CryoLife Inc, Eden Prairie, MN) is an innovative approach to obtain permanent AV access in patients with subclavian vein occlusions not amenable to open or endovascular means of recanalization. The HeRO graft has two components: the venous outflow component, which is inserted into the central venous system proximal to any occlusion, similar to a CVC, and the arterial graft component, which is made of 6-mm ePTFE and is tunneled under the skin and sewn into the arterial inflow similar to a permanent AV access (Fig. 174.12). A review on the HeRO graft by Shakarchi and colleagues showed 1-year primary and secondary pooled patency rates of 21.9% (9.6 to 37.2%) and 59.4% (39.4 to 78%), arterial steal rates of 6.3% (1 to 14.7%), and bacteremia rates of 0.13 to 0.7 event per 1000 days. Due to its relatively low patency and high complication rate, HeRO grafts are generally reserved for a last-resort measure on end-stage patients with central venous occlusions and temporary lines or lower extremity AV access as their only alternative options for hemodialysis access.³⁷

POSTOPERATIVE FOLLOW-UP

From the time of its placement, autogenous AV access should be mature and ready for cannulation 12 weeks postoperatively and prosthetic AV access should be mature and ready for cannulation as early as 2 weeks postoperatively. If any access is noted to be failing to mature, it should be further examined with duplex ultrasound followed by venography if further information is necessary. Secondary procedures include open surgical procedures such as vein patches, interposition vein grafts, vein transposition to proximal arteries, branch ligations, vein superficialization, and endovascular procedures such as arterial and venous angioplasties. McLafferty et al. were able to identify treatable problems with 69% of failing autogenous accesses and successfully salvage the access to functional maturation in 83%.³⁸ Similarly, Berman et al. demonstrated an overall 10%

improvement in achieving a successful autogenous AV access using close follow-up and secondary procedures.³⁹

Despite the multitude of secondary procedures available, there are limited options for the treatment of generalized small-caliber veins that fail to dilate after AV access creation. Recent reports have discussed the use of balloon-assisted maturation (BAM); this is a procedure where repeated long-segment angioplasties are performed on the suboptimal outflow vein that is failing to dilate. By disrupting the venous wall, these serial angioplasties essentially transform the outflow vein into a larger-diameter “collagen tube.”⁴⁰ Using this technique, Miller et al. reported successful maturation in 118 of 122 patients requiring an average of 2.6 procedures, with 15% 1-year primary and 77% 1-year secondary patency rates.⁴¹ Similarly, DeMarco Garcia et al. reported an 85% maturation success rate and an 80% 1-year secondary patency rate.⁴² Further reports have discussed the use of BAM at the time of AV access placement for outflow veins measuring less than 2 mm in diameter. Using this technique, Veroux et al. reported a mean fistula maturation time of 32 days, with a 5.2% reintervention rate over 7-month follow-up.⁴³ Challenges to both of these techniques include essentially converting an autogenous access into a prosthetic with subsequent similar long-term patency and reintervention rates of prosthetic access and the economics associated with repeated multiple procedures to achieve AV access success.⁴⁰

LONG-TERM FOLLOW-UP

After initial maturation, the AV access should be monitored routinely while the patient is on dialysis. Previously, the preferred method of monitoring was a monthly determination of access flow by ultrasound dilution, conductance dilution, thermal dilution, or Doppler technique. However, the new NKF KDOQI guidelines felt there was inadequate evidence to recommend surveillance by measuring access blood flow, pressure monitoring, or imaging and now recommend only regular physical examination of the AV access, by a knowledgeable and experienced health practitioner. Furthermore, the guidelines recommended against any pre-emptive interventions to prevent AV access thrombosis without clinical indicators. Only if abnormalities are noted on physical exam do the guidelines recommend further investigation with fistulogram followed by secondary procedures to prevent access failure.^{3,7}

RESULTS

In order to accurately compare AV access procedures, standard definitions regarding patency are necessary and have been defined and published by the Committee on Reporting Standards of the SVS. To review, an AV access is functional only if it can deliver a flow rate of 350 to 400 mL/min without access recirculation to maintain a dialysis treatment time of less than 4 hours. Primary patency is the interval between the time of access placement and any intervention designed to maintain or reestablish patency, access thrombosis, or the time of measurement of patency. Assisted primary patency is the interval

between the time of access placement and access thrombosis or the time of measurement of patency, including any intervening surgical or endovascular manipulation. Secondary patency is the interval between the time of access placement and access thrombosis, access abandonment, or the time of measurement of patency, including any intervening surgical or endovascular manipulations designed to reestablish functionality after access thrombosis.⁶

Using these definitions, autogenous AV access has consistently been shown to have excellent primary and secondary patency rates when compared with prosthetic AV access. One-year primary patency rates of autogenous AV access range from 43% to 85%^{44–51} and 2-year primary patency rates range from 40% to 69%.^{45,48,52,53} In comparison, 1-year primary patency rates of prosthetic AV access range from 40% to 54%^{44,45,50,51} and 2-year primary patency rates range from 18% to 30%.^{45,52,54} Similarly, secondary patency rates are superior in autogenous access, ranging from 46% to 90%^{44,45,48–50} at 1 year and from 62% to 75%^{45,52–54} at 2 years compared with prosthetic access, which ranges from 59% to 65%^{44,45,48} at 1 year and from 40% to 60% at 2 years.^{45,52,54} Also of note, in order to maintain these secondary patency rates, prosthetic AV access requires a higher number of interventions than autogenous AV access. To illustrate further the superior patency rates of autogenous access, Huber et al. performed a meta-analysis of the published literature from 1966 to 2001 and showed that primary patency rates for autogenous accesses were 72% at 6 months and 51% at 18 months, with corresponding primary patency rates for prosthetic AV access of 58% and 33%, respectively. Secondary patency rates for autogenous accesses were 86% at 6 months and 77% at 18 months with a corresponding secondary patency for prosthetic AV access of 75% and 55% (see Fig. 174.13), respectively.⁴⁵ These superior patency rates of autogenous access include basilic vein transpositions, which have demonstrated 1-year primary patency rates from 35% to 76%^{44,47,49,55,56} and secondary patency rates from 47% to 90%, respectively.^{44,49,55} Use of a two-stage technique for smaller-diameter (2.5 to

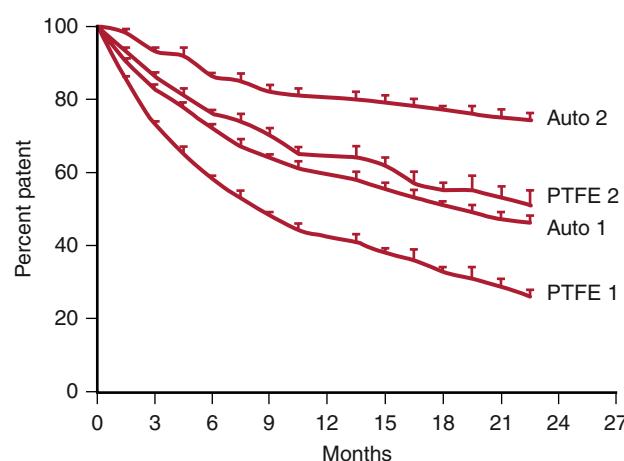
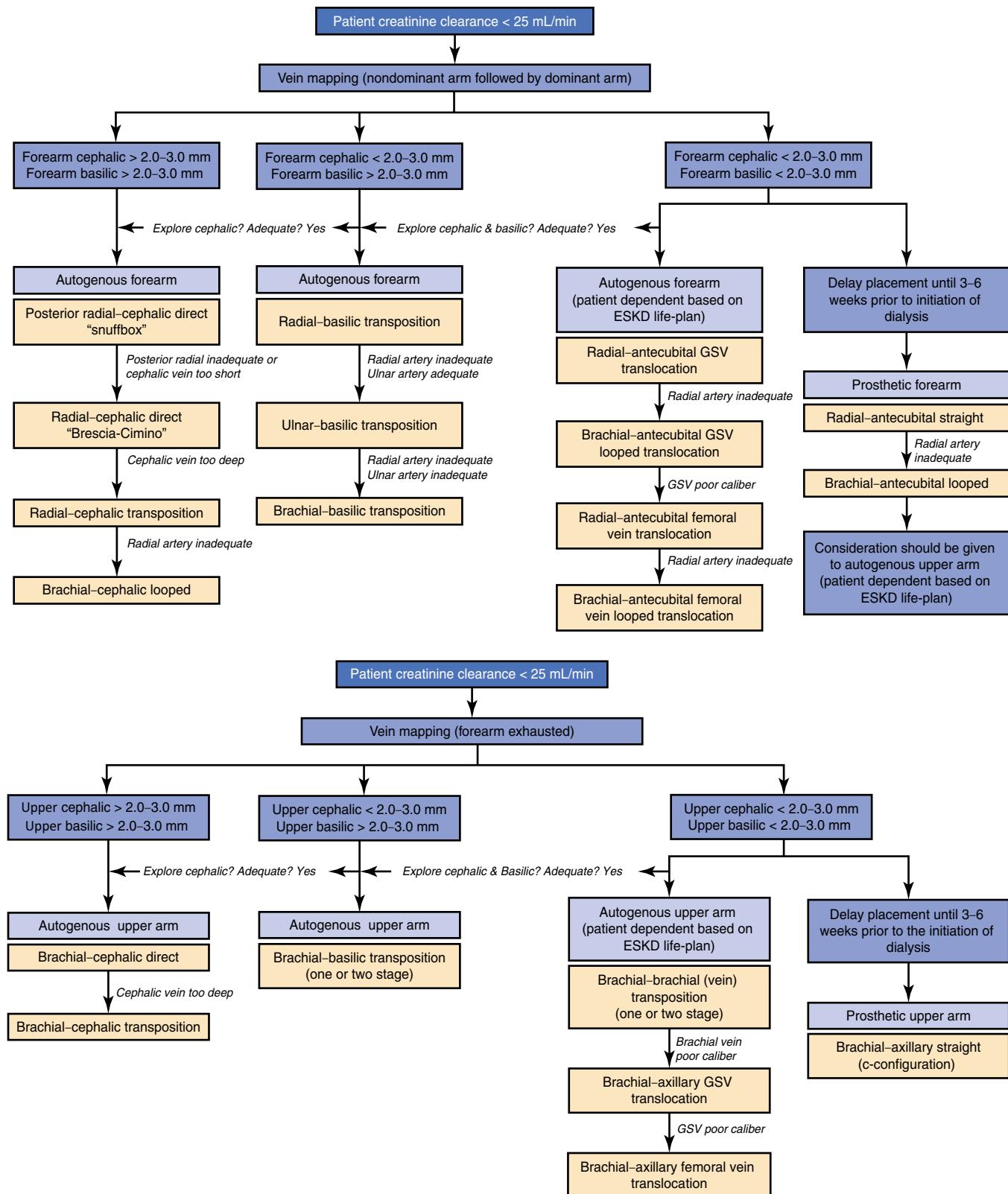


Figure 174.13 Primary and secondary patency rates of autogenous and prosthetic arteriovenous accesses. PTFE, polytetrafluoroethylene. (Reproduced from Huber TS, Carter JW, Carter RL, Seeger JM. Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous hemodialysis accesses: a systematic review. *J Vasc Surg*. 2003;38(5):1005–1011.)

4.0 mm) basilic veins have demonstrated similar 1-year primary and secondary patency rates of 46%⁵⁷ and 84% to 96%, respectively.^{58,59} These studies demonstrate that the use of the basilic vein in either a one- or two-stage procedure is a preferred alternative to prosthetic AV access when direct access is not available.

A common tradeoff for the higher long-term patency rates associated with autogenous AV access is higher primary failure rates due to failure of access maturation or primary thrombosis. Initial success rates leading to a functional AV access range from 55% to 97%.^{46–49,52} These poor maturation rates do appear to correspond to the increasing use of small and suboptimal veins for autogenous access. This was demonstrated by Patel et al., who demonstrated that the use of preoperative duplex vein mapping and venography in the construction of autogenous access increased from 61% to 73%, with a corresponding decline in the functional maturation rate from 73% to 57%.⁵⁹

CHAPTER ALGORITHM



SELECTED KEY REFERENCES

The United States Renal Data System (USRDS) is a national data system that collects, analyzes, and distributes about ESRD in the United States.

U.S. Renal Data System. *USRDS 2017 Annual Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health*. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Disease; 2017. Available at: <http://www.usrds.org>.

NKF-K/DOQI Clinical Practice Guidelines originally published in 1997 and updated in 2019 were published in an effort to increase autogenous arteriovenous access to 50% in all new ESRD patients and 40% overall prevalence of all ESRD patients. Available at: [https://www.ajkd.org/article/S0272-6386\(19\)31137-0/pdf](https://www.ajkd.org/article/S0272-6386(19)31137-0/pdf).

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A complete reference list can be found online at www.expertconsult.com.

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Hemodialysis Access: Complex

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Over the past decade, significant improvements have been made in quality of care and life expectancy for patients on hemodialysis. Consequently, it is not uncommon for the surgeon to be confronted with patients who have “outlived” their arteriovenous (AV) access options in the upper extremities. In one study, nearly 7% of access placements were located at a site other than the upper extremity.¹ For many of these patients, quality of life and long-term survival depend primarily on the

surgeon’s ability to provide a functional and durable AV access. To meet this challenge, the access surgeon must have a number of complex vascular access procedures in his or her surgical armamentarium and must be aware of the advantages and disadvantages of each.

What is apparent from the available literature and our own anecdotal experience is that these complex access procedures are associated with a higher complication rate compared with AV

access procedures of the upper extremity, and the management of these complications is generally more challenging. Although one might be tempted to avoid complex vascular access procedures by simply placing a tunneled dialysis catheter, the significant complications associated with chronic dialysis via a catheter are well established.^{2–4} The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for vascular access recommend the use of a dialysis catheter only as a bridge to AV access placement or in patients with an extremely limited life expectancy.⁵ Despite the challenges of complex AV access placement and the associated complications, their placement is usually justified and preferable to the use of a tunneled dialysis catheter.

GENERAL PRINCIPLES

In facing a complex access situation, the surgeon must obtain a complete access history and delineate the causes of prior failures. A careful investigation of the vascular anatomy is important to identify arterial or venous pathology that may affect access outcome. Although noninvasive vascular testing is useful, it may provide insufficient anatomic information on patients who have had multiple access procedures; therefore, contrast angiography and venography are often necessary. Only after a complete understanding of the history and anatomy can the surgeon consider all access options and create a long-term access strategy for the patient.

Avoiding Complex Access

As noted earlier, the complication rate of AV access procedures of the lower extremity, chest wall, and other “exotic” access sites is high, and these complications are difficult to manage. Therefore one should ensure that alternatives in the upper extremity do not exist before resorting to these locations. Even though a patient has had multiple failed AV accesses in an extremity, a venogram may reveal an alternative vein, such as a paired brachial vein or a patent cephalic vein in the deltopectoral groove that can provide venous outflow for an additional access procedure in the extremity. Such options should be used before moving to sites outside the upper extremity (Fig. 175.1). If a central venous stenosis is present and the vessels in the upper extremity appear adequate for AV access placement, the surgeon should consider angioplasty and/or stenting of the central vein stenosis and then placement of an upper extremity access rather than proceeding with a complex access elsewhere. Although the primary patency of percutaneous central vein angioplasty is only 29% at 12 months, remedial angioplasty procedures either alone or with a stent are generally easy to perform and can extend the 12-month patency to more than 70% (Fig. 175.2).⁶ Now with the availability of hybrid access devices such as the HeRO and innovative techniques such as the “inside-out” (discussed later), central venous occlusion can often be treated successfully and prolong upper extremity access.

Selection of a Complex Access Site

Although algorithms have been developed that define a general order of preference for “routine” access placement in the

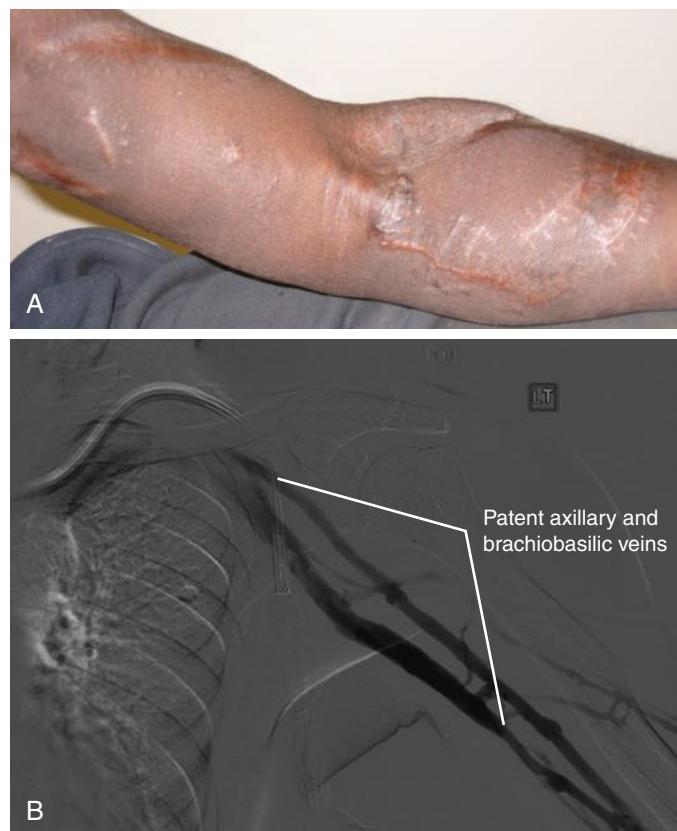


Figure 175.1 (A) Patient with failed prosthetic arteriovenous (AV) accesses in the left forearm and upper arm referred for the establishment of a new access. (B) A venogram was obtained to determine whether any alternative to a “complex” access was available in the left upper extremity. Despite the two previous upper extremity AV access procedures, the brachiocephalic, axillary, and central veins were widely patent. A successful brachiocephalic transposition was performed.

upper extremity, the development of a similar algorithm for “complex” access placement is problematic, given the dearth of evidence-based literature related to these procedures. It is possible, however, to provide broad recommendations regarding the clinical situations in which a particular complex AV access procedure is most helpful and those in which it should be avoided. These recommendations are outlined in Table 175.1. Some have even proposed a classification system to describe options available and report causes of failure to standardize terminology when discussing these difficult patients.⁷

AUTOGENOUS ARTERIOVENOUS ACCESS

Several techniques have been described that use the saphenous and femoral veins to create autogenous AV accesses in the upper and lower extremities. These veins can be completely mobilized and disconnected both proximally and distally to create an access at a site remote from their origin (translocation). Alternatively, the distal portion of the vein can be mobilized and tunneled superficially, leaving the central portion of the vein connected to its normal anatomic position (transposition).

Given the high infection rate associated with AV access procedures of the lower extremity, use of the saphenous vein

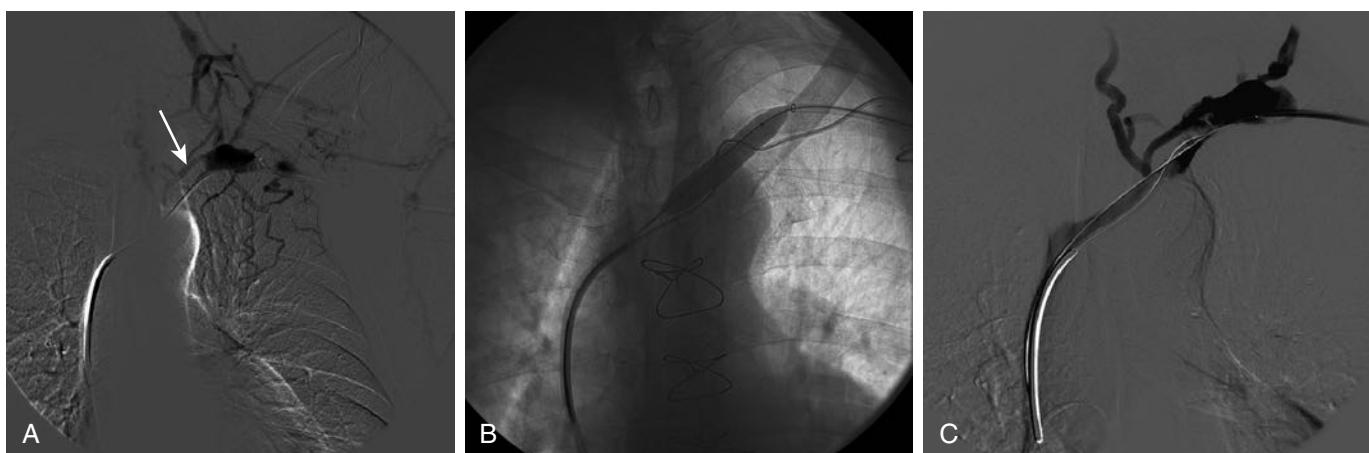


Figure 175.2 (A) Venography of the left upper extremity in a patient with an autogenous brachiocephalic arteriovenous access and symptoms of venous hypertension demonstrates chronic occlusion of the subclavian vein (arrow). (B) The subclavian vein occlusion was crossed with a wire, and angioplasty was successfully performed with a high-pressure balloon. (C) Completion venography demonstrating patency of the central veins.

TABLE 175.1 Major Complex Access Procedures: Indications, Relative Contraindications, and Anatomic Requirements

Access Procedure	Specific Anatomic Requirements	Ideal Clinical Situation	Relative Contraindications
Autogenous femoral vein transposition	Patent femoral vein >3 mm in diameter Patent, noncalcified superficial femoropopliteal artery	Pediatric or young, healthy patients Patients who are hypercoagulable with no other autogenous access options Patients at high risk for infection (poor hygiene, immunosuppressed, multiple previous access infections)	Significant obesity of the thigh Patients who are elderly or "medically fragile" Access sites for temporary catheter placement not readily available Patients with symptomatic PAD
Prosthetic mid-thigh loop femoral-femoral access	Patent femoral or common femoral vein	Patients who are elderly or have significant medical comorbidities	Patients at high risk for infection (poor hygiene, immunosuppressed, multiple previous access infections)
Prosthetic loop femoral–femoral access	Patent, noncalcified superficial femoral artery (mid-thigh access) or common femoral artery		Patients who are morbidly obese Patients with symptomatic PAD
Prosthetic chest wall access	Patent axillosubclavian artery and vein Patent central vein	Patients who are morbidly obese Patients at high risk for access-related limb ischemia	Patients who are reasonable candidates for autogenous or prosthetic thigh access procedures
Tunneled dialysis catheter	Patent central vein	Patients who are "medically fragile" or have limited life expectancy (<6 months) Patients in whom all alternative access procedures have been expended	Patients who are candidates for an alternative complex access procedure (autogenous or prosthetic thigh or chest wall access)
Hemoaccess Reliable Outflow vascular access device	Guide wire access to a patent central vein Brachial artery >3 mm	A central venous stenosis/occlusion that precludes upper extremity autogenous or prosthetic access options Patients otherwise relegated to dialysis via a tunneled dialysis catheter	Active infection Systolic blood pressure <100 mm Hg Ejection fraction <20%

or femoral vein translocation or transposition procedures in the thigh is theoretically appealing. However, these operations have been associated with wound complications related to vein harvest and access-related ischemia or steal syndrome; therefore, their role in AV access procedures remains undefined, and they are not included in the KDOQI clinical practice guidelines.⁵

Translocation Procedures

The autogenous brachial artery–axillary vein fistula with saphenous vein or femoropopliteal vein translocation is an alternative to thigh access for patients with poor superficial upper extremity veins who are not candidates for a traditional upper extremity autogenous access. This access may also be

TABLE 175.2 Results of Complex Thigh and Upper Extremity Accesses

Access Type/Series	Configuration	Number of Accesses	SECONDARY PATENCY (%)			Wound Complications (%)	Access-Related Ischemia (%)
			1-Year	2-Year	Infection (%)		
Prosthetic Thigh							
Cull et al. ¹³	PTL	116	68	54	41	—	11
Taylor et al. ¹⁴	PTL	45	52	47	11	—	16
Bhandari et al. ⁹	PTL	49	85	82	35	—	0
Vogel et al. ¹⁵	PTL	126	62	—	20	—	0
Korzets et al. ¹⁶	PTL	37	73	65	11	—	11
Englesbe et al. ¹⁷	PTL	30	41	26	27	—	3
Khadra et al. ¹⁸	PTL	74	74	63	16	—	3
Tashjian et al. ¹⁹	PTL	73	83	83	22	—	2
Flarup et al. ²⁰	MTL	14	64	18	21	—	0
Scott et al. ²¹	MTL	46	68	43	21	—	13
Autogenous Thigh							
Gradman et al. ²²	FV transposition	25	87	87	0	28	32
Gradman et al. ²³	FV transposition	22	100	94	0	0	0
Autogenous Upper Extremity							
Huber et al. ¹²	BA-Ax FV translocation	30	100	100	0	40	27
Elwakeel et al. ²⁴	BA-BV transposition	21	76	55	5	0	0
Angle et al. ²⁵	BA-BV transposition	20	—	—	—	—	0
Casey et al. ²⁶	BA-BV transposition	17	40	40	—	—	—

Ax, axillary vein; BA, brachial artery; BV, brachial vein; FV, femoral vein; MTL, mid-thigh loop; PTL, proximal thigh loop.

indicated for patients with multiple failed upper extremity prosthetic AV accesses owing to infection or unexplained thrombosis.

Saphenous Vein–Forearm Translocation

Few studies have been published evaluating saphenous vein–forearm translocation for hemodialysis access. Secondary patency rates vary widely between the studies from 50% to 96% at 1 year.^{8–11} The saphenous vein can be translocated as a forearm loop configuration⁸ or placed in a straight configuration from the radial artery to the antecubital vein.⁹

Femoropopliteal Vein–Arm Translocation

Results

Huber et al. reported a series of 30 patients who underwent translocated femoral vein–upper arm brachial axillary access.¹² They reported primary and secondary patency rates of 67% and 100% at 18 months. Although this procedure has the potential advantages of an autogenous access, they must be balanced against a higher incidence of wound hematomas, compartment syndrome, and access-related upper extremity ischemia (Table 175.2).^{9,12–26}

Arm composite autogenous vascular access (ACAVA) using the great saphenous vein and the femoral vein has also been described.²⁷ The rationale for this technique was to decrease

the diameter of the vein at the arterial anastomosis in hopes to minimize the rate of steal syndrome. At 12 months, the secondary patency rate was 81%. Of note, one patient developed steal syndrome.

Technique

Duplex ultrasonography of the lower extremity is necessary to confirm that the femoral vein is patent and has an adequate diameter (>6 mm). To expose the femoral vein, an incision is made in the groin and extended distally along the medial border of the sartorius muscle. The vein is mobilized from the mid-popliteal fossa to the common femoral vein. It is important to preserve the profunda vein to reduce the symptoms related to outflow obstruction. The reversed vein is connected to the brachial artery and axillary vein (Fig. 175.3).

Transposition Procedures

Brachial Vein Transposition

Results

In 2004, Bazan and Schanzer reported two cases of autogenous brachial vein transposition in patients with inadequate superficial upper extremity veins.²⁸ After 1 year, both accesses were functional. Other series report secondary patency rates from 40% to 92% at 1 year. This procedure can be done as a single

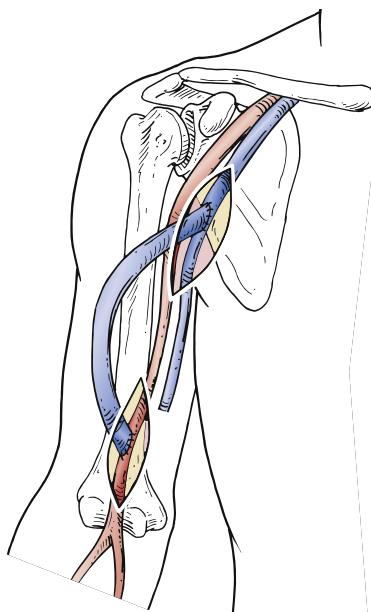


Figure 175.3 Brachioaxillary arteriovenous access using the reversed translocated femoral vein.

stage transposition²⁴ or with a two-stage technique.²⁶ One published series reported a 2-year patency of 55%.²⁹

Technique

We recommend that brachial vein transposition be performed as a two-stage procedure. One-stage procedures are considered only in cases in which the brachial vein exceeds 4 mm in diameter. The brachial artery and vein are exposed in the antecubital fossa. The brachial vein is connected to the proximal radial or brachial artery. The second stage is performed 4 to 6 weeks later to allow the vein wall to arterialize, thereby facilitating its mobilization. Care should be taken to avoid injury to medial antebrachial cutaneous and median nerves while the brachial vein is completely mobilized. Venous tributaries are individually suture-ligated. The vein is divided near the AV anastomosis and passed through a subcutaneous tunnel. An end-to-end anastomosis of the vein is then performed.

Saphenous Vein Transposition

The common femoral artery–saphenous vein loop transposition was first described in a single patient by May et al. in 1969. Based on the limited number of series^{30–32} reporting the outcome of saphenous vein translocation, the following conclusions can be drawn: (1) the use of skip incisions or endoscopic techniques to harvest the saphenous vein may decrease the rate of wound complications associated with this procedure; (2) because the great saphenous vein does not readily dilate after access creation, only veins greater than 3 mm in diameter should be used and the vein must be tunneled just beneath the dermis to allow reliable cannulation of the access; (3) cannulation of the access must be delayed at least 6 weeks postoperatively to prevent puncture-site bleeding and hematoma; (4) the procedure may not be practical

for patients who are morbidly obese or those with a large redundant pannus because access cannulation may require the patient to lie in the supine position and retract the pannus to expose the access.

Alomran et al. described an innovation of the GSV AVF in the form of a semipaneled graft, which aims to overcome the poor dilation of the GSV but requires harvest of its entire length. This technique is labor-intensive because it involves longitudinal venotomy and open valvulotomy of the entire GSV and the creation of panels.³³

Technique

The saphenous vein is exposed and mobilized from the saphenofemoral junction to the knee. The saphenous vein is transected distally at the knee, leaving the saphenofemoral junction intact. The vein is then tunneled to form a subcutaneous loop and anastomosed to the proximal superficial femoral artery.

Femoral Vein Transposition

Results

The largest experience with autogenous femoral artery–femoral vein transpositions was reported by Gradman et al. in two separate series^{22,23} (Table 175.2). Access-related limb ischemia was observed in nearly a third of patients despite the use of adjunctive banding in almost half the patients.²²

In an effort to decrease the incidence of access-related limb ischemia, Gradman modified the technique and patient selection criteria.²³ The size of the arterial anastomosis was limited by inserting a 5-mm mandrel in the beveled vein and closing the excess vein with suture. The tapered vein was then anastomosed end to side to the distal superficial femoral artery. Patients with an ankle–brachial index less than 0.85 or absent pedal pulses were excluded. Prophylactic fasciotomies were performed in patients with weak or absent pedal pulses after access creation. With the modification in technique and patient-selection criteria, the occurrence of limb ischemia necessitating revascularization was reduced from 32% to 0%. Other studies report similar patency rates.³⁴ Complications of this technique include distal limb ischemia, venous hypertension requiring fasciotomies, bleeding, and high-output heart failure.³⁵ Therefore, caution is necessary in creating this access in patients with congestive heart failure.

Technique

A preoperative assessment of the lower extremity arterial and venous anatomy with duplex ultrasonography is necessary. The femoral vein is exposed and mobilized as described previously. It is critical to preserve the profunda vein to prevent venous hypertension and compartment syndrome. The femoral vein is ligated distally and transected. The vein is brought through a subcutaneous tunnel lateral to the vein harvest incision and anastomosed to the superficial femoral artery in the distal thigh. The distal end of the femoral vein should be tapered to 4.5 to 5 mm, as outlined earlier (Fig. 175.4A).

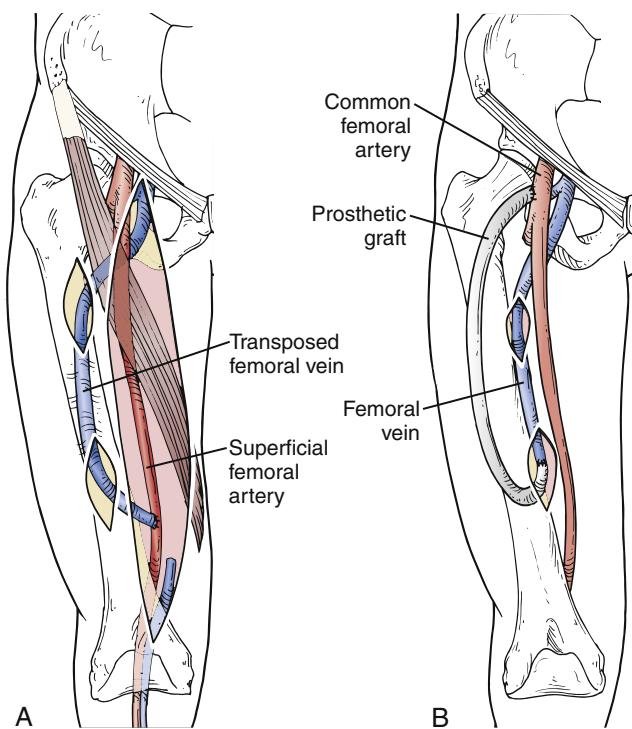


Figure 175.4 (A) Femoral vein transposition procedure. (B) Composite femoral vein transposition and prosthetic access procedure.

In cases where the patient was considered at high risk for access-related limb ischemia or if he or she was significantly obese and superficialization of the vein provided inadequate length for cannulation, Gradman modified the technique by anastomosing a 4- to 7-mm polytetrafluoroethylene (PTFE) graft end-to-end to the femoral vein and tunneling the composite vein-graft laterally in the thigh in a loop configuration. The 4-mm end of the prosthetic graft was anastomosed end-to-side to the common femoral artery (Fig. 175.4B). The smaller portion of prosthetic limb of the access was tunneled deep in the subcutaneous tissue to prevent cannulation of it by dialysis technicians.

A modification of the femoral vein transposition technique has been described in patients with inadequate vein length.³⁶ Rather than passing the vein through a tunnel, the vein is simply elevated by approximating the subcutaneous tissue deep to the vein.

Ankle Fistula

To date, there have only been a few case reports of ankle AV fistula formation either from the posterior tibial artery to saphenous vein or dorsalis pedis artery to saphenous vein. The procedure involves a cutdown at the ankle and end-to-side anastomosis of the greater saphenous vein to the artery. Preoperative assessment with digital pressures as well as angiogram should be performed to guide management. A patient with heavily calcified tibial vessels or absence of a palpable pulse would not be an ideal candidate for this type of fistula. Because of the paucity of literature regarding this procedure, no recommendations can be made regarding its efficacy.^{37–40}

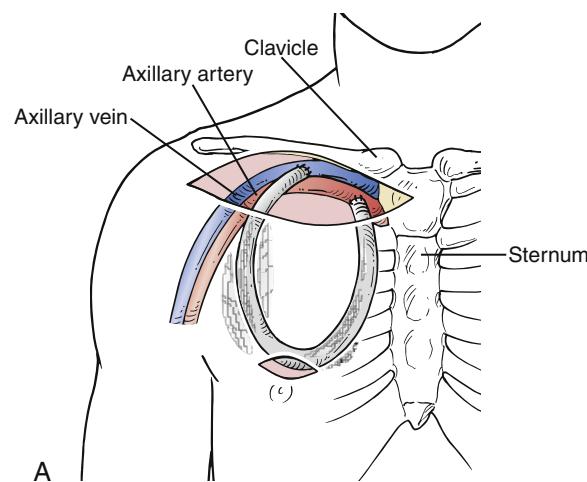


Figure 175.5 (A) Prosthetic axillary artery–axillary vein loop access. (B) Prosthetic chest wall and cervical straight access options.

PROSTHETIC ARTERIOVENOUS ACCESS

Prosthetic Chest Wall and Cervical Arteriovenous Access

Sites for prosthetic AV access placement in the cervical region and on the chest wall are as follows: axillary artery–ipsilateral axillary vein loop access (Fig. 175.5A), axillary artery–contralateral axillary or jugular vein straight access (“necklace access”; Fig. 175.5B),⁴¹ and brachial artery–jugular vein straight access (see Fig. 175.5B). Although the prosthetic chest wall AV access was first described in 1978, the literature reporting the outcomes of this technique is limited primarily to case reports and small case series.^{1,13,16,17}

Results

Necklace access

In 1996, McCann reported outcomes for a series of 26 patients with prosthetic chest wall AV accesses (Table 175.3)^{1,42–47}

TABLE 175.3 Results of Cervical and Chest Wall Access

Series	Configuration	Number of Patients	SECONDARY PATENCY (%)		Infection (%)	Access-Related Ischemia (%)
			1-Year	2-Year		
McCann ⁴²	AA-cAV AA-cIJV	26	75	60	4	0
Gale-Grant et al. ⁴⁴	AA-cAV	35	Not reported	54% (4years)*	6	0
Jean-Baptiste et al. ⁴³	Loop AA-iAV	27	87	80	11	0
Kendall et al. ¹	Loop AA-iAV	34	59	37	15	0
Liechty et al. ⁴⁵	Loop AA-iAV	67	82	58	9	0
Vega et al. ⁴⁶	BA-IJV	51	74	63	2	0
Kim et al. ⁴⁷	BA-IJV	32	93	93	6	3

AA, axillary artery; BA, brachial artery; cAV, contralateral axillary vein; cIJV, contralateral internal jugular vein; iAV, ipsilateral axillary vein; IJV, internal jugular vein.

using a straight graft configuration from the axillary artery to the contralateral axillary or internal jugular vein. In another series, the primary and secondary patencies at 12 months were 72% and 89%, respectively.⁴⁸ All accesses in that series were monitored bimonthly with physical examination and ultrasound in order to detect access dysfunction prior to thrombosis. Recently, the largest study of 35 patients with necklace grafts provided its long-term (9-year) follow-up results. This study reported a secondary patency of 54% at 4 years.⁴⁴ Of note, because the arterial and venous anastomoses are oriented peripherally with the straight graft configuration, thrombectomy may require an incision near one or both anastomoses to effectively clear thrombus from the access and percutaneously treat an anastomotic stenosis.

Brachial to jugular access

Vega et al. reported a series of 51 prosthetic brachial artery-jugular vein accesses.⁴⁶ Patency rates were similar to the rate of axillary–axillary AV access. The prosthetic graft is tunneled over the ventral aspect of the shoulder and over the mid-clavicle. It is important to confirm patency of the jugular vein with a preoperative imaging study (Table 175.3). This option is particularly useful if the subclavian vein is occluded but the remainder of central veins are patent.

Another interesting option for treatment of subclavian vein occlusion, is the “internal jugular turn-down” where the venous limb/outflow of the access is connected to the ipsilateral internal jugular vein via interposition graft. It is also helpful in patients with brachiocephalic fistula who experience a complete occlusion of the proximal portion of the subclavian vein. In this instance, the internal jugular vein is ligated cranially and the caudal portion is “turned-down” to the cephalic arch. Previous case series have described both options with good outcomes and preservation of the access.^{49,50}

Ipsilateral axillary–axillary chest wall loop access

Liechty et al. recently published their series of 67 prosthetic axillary–axillary loop access (Table 175.3). The authors also explain that if there was central venous stenosis or occlusion,

an attempt should be made to recanalize the central veins. If adequate results could not be obtained, they suggest placement of the HeRO graft (discussed later).⁴⁵ The looped graft configuration, which uses the ipsilateral axillary artery and vein, preserves the contralateral axillary vessels for future access placement. Should a subsequent stenosis develop at the venous anastomosis, orientation of the venous limb laterally will facilitate percutaneous intervention.

No case of access-related steal was noted in any of the three largest chest wall access series.^{1,42,43} In each of these series, a number of axillary artery–axillary vein accesses were placed in patients in whom previous accesses in the ipsilateral extremity had caused hand ischemia. Based on this experience, it appears that a history of access-related hand ischemia does not preclude access placement based off the ipsilateral axillary artery.

Chest wall access appears to be associated with a lower infection rate than prosthetic AV access in the lower extremity. Given the technical challenge and higher complication rate associated with prosthetic AV access placement in the thigh position in patients who are morbidly obese, chest wall access may be an attractive alternative. One potential disadvantage of chest wall access, however, is that proximal control of the axillary vessels can be extremely challenging if the graft becomes infected and needs to be excised.

Technique

We recommend that patients undergo venography to confirm central venous patency before surgery. If the proximal axillary, subclavian, or brachiocephalic vein has recently undergone angioplasty or stenting, an alternative site for AV access should be considered, because recurrent stenosis following central venous intervention is common and may influence access patency.

The patient is placed in the supine position with the arm extended 90 degrees on an arm board. An incision is made one fingerbreadth below the clavicle from the sternoclavicular joint to the coracoid process. The pectoralis major muscle fibers are split. The clavipectoral fascia is divided, and the axillary vein is exposed and mobilized. The axillary artery lies deep to the vein. The artery is exposed at its exit from the thoracic outlet

and mobilized to the pectoralis minor muscle. The pectoralis minor muscle is not typically divided. A 6-mm PTFE graft is tunneled in a loop configuration on the chest wall. Before tunneling of the graft, the patient is placed in the reverse Trenelenburg position to reposition the breast in a dependent location. This maneuver is performed to accurately determine graft length and is particularly important for patients with pendulous breasts. The graft is tunneled using a transverse counter-incision made cephalad to the areola. The venous limb of the prosthetic graft is positioned laterally on the chest. The venous end of the graft is oriented nearly parallel to the axillary vein (see Fig. 175.5A). The graft is sewn end-to-side to the axillary artery and vein.

Hemodialysis Reliable Outflow Vascular Access Device

For patients whose options for an upper extremity vascular access are precluded by a central venous stenosis or occlusion, the Hemodialysis Reliable Outflow (HeRO) device (Hemosphere, Inc., Minneapolis, MN) is a reasonable alternative to a lower extremity access or tunneled dialysis catheter. The HeRO device is composed of two components: a graft component, which is a 6-mm PTFE graft with a titanium coupler at one end, and a venous outflow component, which is a 19-F silicone catheter reinforced with a nitinol braid. The graft component is anastomosed to the brachial artery and is tunneled subcutaneously as a standard prosthetic AV access. The venous outflow component does not require a venous anastomosis but rather is percutaneously placed into the right atrium via the internal jugular or subclavian vein. The graft and venous outflow components are tunneled subcutaneously to a counter-incision in the deltopectoral groove, where they are connected with a titanium coupler (Fig. 175.6). The US Food and Drug Administration has approved the HeRO device for use in catheter-dependent patients with central venous stenosis or occlusion.

Results

The initial study reporting results for the HeRO device was an industry-sponsored, multicenter, nonrandomized trial that included 36 patients who were receiving dialysis via a tunneled catheter due to a central venous stenosis or occlusion.⁵¹ The primary and secondary patency rates for the HeRO device at 8 months were 39% and 72%, respectively. A mean of 2.5 interventions were required annually to maintain patency of the HeRO device. The four centers involved in the original industry-sponsored trial subsequently reported their collective experience.⁵² The primary and secondary patency rates at 1 year were 49% and 91%, respectively. A recent meta-analysis included 409 patients with primary and secondary patencies of 22% and 59% at 1 year. The incidence of steal syndrome was 6.3%.⁵³

Occasionally, it is necessary to exchange a functioning tunneled dialysis catheter for the venous component of the HeRO device over the wire, and there are no alternative sites to place a new tunneled catheter for dialysis while awaiting incorporation of the graft. In such cases, the author has used a Super HeRO adapter (Merit Medical, South Jordan, UT) designed

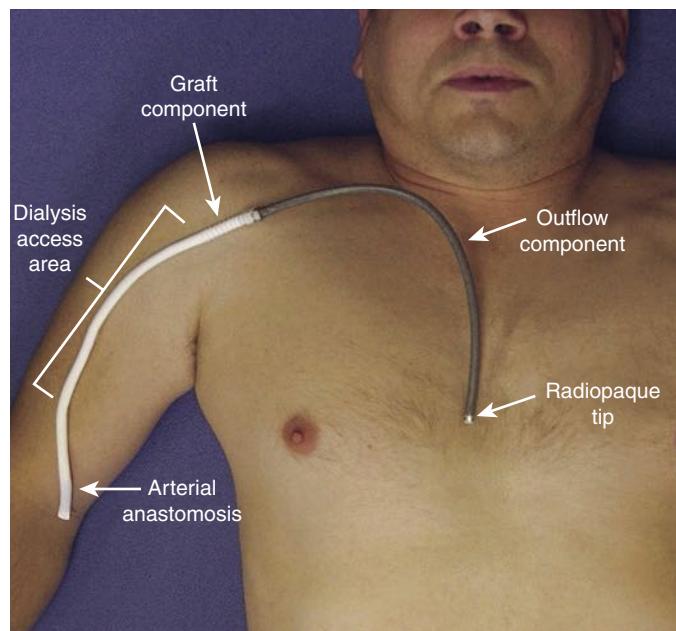


Figure 175.6 Placement of a device for Hemodialysis Reliable Outflow (HeRO) vascular access. (From Katzman HE, McLafferty RB, Ross JR, Glickman MH, Peden EK, Lawson JH. Initial experience and outcome of a new hemodialysis access device for catheter-dependent patients. *J Vasc Surg*. 2009;50:600–607.)

to connect an early cannulation graft, such as an Accuseal (W.L. Gore, Newark, DE) to the venous outflow component of the HeRO device. The graft can be cannulated immediately after HeRO placement, thus eliminating the need for the placement of a tunneled dialysis catheter.

Prosthetic Lower Extremity Arteriovenous Access

The sites and graft configurations most commonly used for prosthetic access placement in the lower extremity are femoral artery–greater saphenous or femoral vein loop AV access and popliteal artery–greater saphenous or femoral vein straight AV access (Fig. 175.7).

For most surgeons, prosthetic lower extremity AV access is the preferred site once options in the upper extremity have been exhausted. Advantages of the procedure include the following: the operation is relatively simple to perform owing to the accessibility and size of the femoral vessels; patency rates for these accesses are comparable, if not superior, to those of upper extremity accesses; the surgical management of complications, such as graft infection and anastomotic stenosis, is easier than for chest wall accesses; and both of the patient's hands are free to self-cannulate the access or to perform activities during dialysis. The major disadvantages of the prosthetic lower extremity access are a higher infection rate compared with AV accesses in the upper extremity as well as an increased risk of lower extremity ischemia.

Results

A number of series reporting the outcome of prosthetic lower extremity AV accesses have been published (Table 175.2). However, different methods of reporting outcomes prohibit

the direct comparison of some results. Antoniou et al. published a meta-analysis discussing 660 upper-thigh AVGs and 60 mid-thigh grafts. The average secondary patency rates at 1 year were 71%, with an average 2-year secondary patency rate of 60%; there was no difference in the patency of upper-thigh grafts compared with mid-thigh grafts.⁵⁴ The infection rates reported in thigh-access series ranged from 8% to 41%.^{9,13,16–19,55} Two reports suggested that prosthetic thigh

AV access may be associated with a high incidence of limb loss; however, neither study objectively documented access-related ischemia as the cause of limb loss.^{13,14} Although other studies reported clinically significant access-related ischemia in up to 11% of cases, limb loss occurred in only 1% to 3% of cases.^{16–19,55}

There are significant disadvantages of prosthetic femoral–femoral AV access for patients who are obese. The abdominal pannus that overlies the groin and the depth of the femoral vessels in obese patients not only make the placement procedure more technically difficult but also increase the risk of complications. The largest series of prosthetic femoral–femoral AV accesses noted significantly higher rates of access reintervention in obese compared with nonobese patients.¹³

Reports have been published describing the technique and outcome in a series of patients who underwent prosthetic looped AV access based off the mid–superficial femoral artery and femoral vein in the mid-thigh rather than the groin (Fig. 175.8).^{20,21} This modification avoids the node-bearing tissue and the panniculus and may, therefore, be associated with a lower infection rate. Furthermore, the prosthetic mid-thigh loop access also preserves the proximal femoral vessels for future access placement.

Crossover femoral artery to femoral vein has also been described as case reports. The potential drawback to this technique is a potential increased wound infection rate because of bilateral groin incisions as well as difficulty in access for dialysis as its course is across the suprapubic area.⁵⁶

Technique

Patients should undergo duplex ultrasonography of the femoral vessels before access placement to verify patency of the

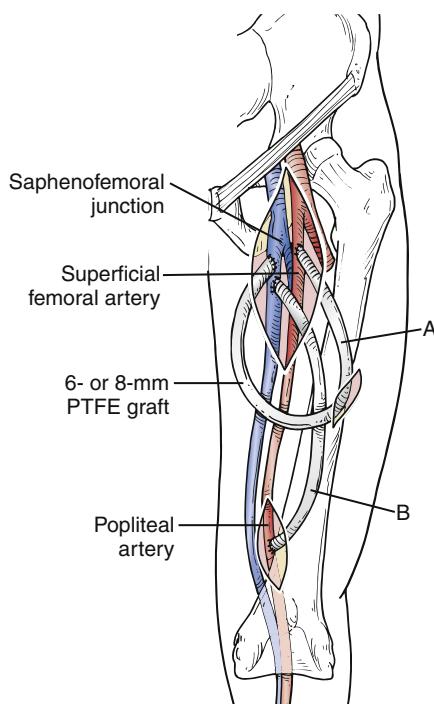


Figure 175.7 Prosthetic thigh access options: femorosaphenous loop access (A) and popliteosaphenous straight access (B). PTFE, polytetrafluoroethylene.

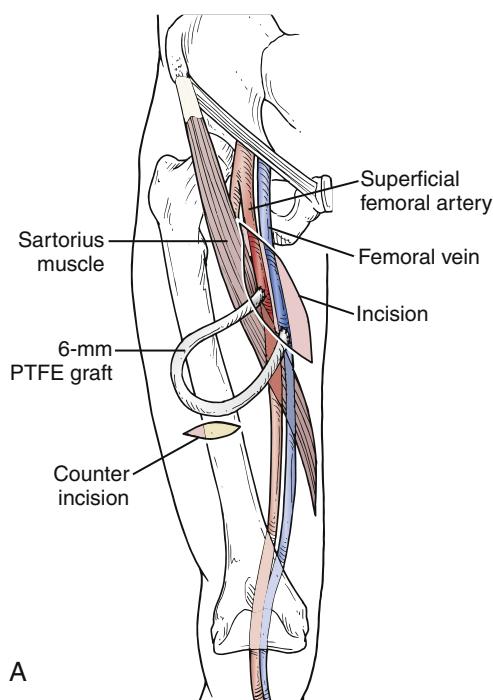


Figure 175.8 (A) Mid-thigh loop access with both graft limbs tunneled medial to the sartorius muscle. Alternatively, if the superficial femoral artery lies closer to the lateral edge of the muscle, the arterial limb can be passed lateral to the sartorius muscle. (B) Photograph demonstrating the location of the incisions for mid-thigh loop access placement and the relation of the mid-thigh loop access to the groin. PTFE, polytetrafluoroethylene.

artery and vein and to determine the degree of calcification of the arterial wall. This is particularly important if a mid-thigh access is planned, because the superficial femoral artery is often diseased or significantly calcified. In selected cases, contrast angiography of the artery or vein may be necessary.

For a proximal loop graft, the femoral artery and great saphenous vein are exposed using a single longitudinal groin incision positioned over the femoral pulse. The proximal superficial femoral artery is the preferred site for arterial inflow, but the common femoral artery can be used. The greater saphenous, femoral, or common femoral vein can be used as the site for the venous anastomosis. Although some use an 8-mm PTFE graft for thigh access, we use a 6-mm graft to minimize the risk of access-related ischemia. The graft is tunneled with the venous limb medial, so that intervention on the venous anastomosis and outflow can be performed.

To expose the superficial femoral artery and femoral vein for the performance of mid-thigh loop access, an incision is made along the medial border of the sartorius muscle in the mid-thigh. The graft is tunneled over the anterolateral thigh. This graft location facilitates graft cannulation without requiring the patient to rotate the extremity externally. Similar to the proximal thigh access, the venous limb of the graft is situated medially and the arterial limb laterally on the thigh. In patients in whom the superficial femoral artery lies beneath the sartorius muscle, the lateral border of the muscle is mobilized and the arterial limb is tunneled lateral to it (see Fig. 175.8A).

CRYOPRESERVED VEIN ALLOGRAFTS

Cryopreserved vein allografts (cadaveric vein) have emerged as an option for AV graft reconstruction; however, indications for their use in hemodialysis access remain to be clearly defined. A recently published study discussed the use of cryopreserved vein allografts in 106 patients over a 10-year period. The investigators categorized the graft placement as central outflow (outflow to the subclavian vein, innominate vein, or right atrium), standard outflow (axillary vein, cephalic or basilic vein), or femoral outflow. The observed primary and secondary patency rates were 22.6% and 66%, respectively, at 1 year. The authors state that the potential benefit of a cryopreserved vein allograft over a prosthetic conduit is realized in patients with multiple repeat accesses and active infections (42% of patients in this series had history of active or recent infection).⁵⁷ The disadvantages of cryopreserved vein allografts are recurrent infection of the allograft and the dreaded complication of rupture, leading to loss of limb or life in our experience. Therefore, this approach should be used only in select cases.

UNCONVENTIONAL VASCULAR ACCESS PROCEDURES

The literature describes a number of “exotic” AV access procedures used to obtain access when options in both the upper

and lower extremities have been exhausted. These procedures are generally described in case reports; therefore, their durability and complication rates have not been established. However, their use may be justified when no other alternative exists.

Unconventional Chest or Abdominal Wall Access Procedures

In several case reports and small case series, direct surgical approaches to the central veins have been described for patients with central venous occlusion who require vascular access or have access-related venous hypertension. These include a bypass to the right atrial appendage through a third intercostal space, or “minipericardiotomy”; a right superficial femoral artery–superior vena cava (SVC) prosthetic access; and a femoral transposition combined with an iliac vein to a suprarenal vena cava bypass.^{58–60}

Karp et al. have published a case report describing a prosthetic chest wall access from the axillary artery to the left renal vein.⁶¹ The left renal vein was exposed through a left flank retroperitoneal incision. The prosthetic graft was tunneled on the chest wall lateral to the nipple and over the 12th rib. A polyurethane graft was used in this case to allow early cannulation of the access. Although several interventions were required to maintain access patency owing to graft kinking over the 12th rib, the access remained patent for 18 months.

The authors have placed a prosthetic external iliac–left renal vein access in a patient with no other access options. The left external iliac artery was exposed just proximal to the inguinal ligament, and the left renal vein was exposed through a retroperitoneal flank incision. To prevent kinking and allow early cannulation of the access, a ringed PTFE graft was used for the intraabdominal graft segment, and a polyurethane graft was used on the abdominal wall. The access functioned without requiring intervention until the patient’s death from a cardiac event 8 months postoperatively.

Another case series of 12 patients, described an abdominal wall graft from the external iliac artery to iliac vein. A curvilinear incision is made 1–2 cm medial to anterior superior iliac spine to the pubic symphysis and preperitoneal dissection performed to isolate the iliac artery and vein. End-to-side anastomoses are performed using ringed PTFE to the external iliac artery and more proximally to the external iliac vein. Each segment of PTFE is tunneled in the abdominal wall and brought out above the fascia through the wound. A counter-incision is made medial, and a second portion of non-ringed graft is tunneled in a loop fashion and anastomosed to the other segments of graft. Mean secondary patency was 33 months and cumulative patency was 83% at 1 year, but with an infection rate of 33%.⁶²

A prosthetic axillary artery–right atrium AV access in a patient with thrombosis of both the superior and inferior venae cavae has been described.^{63,64} The right axillary artery is exposed through an infraclavicular incision, and a median sternotomy is used to expose the atrial appendage. An 8-mm PTFE graft is tunneled beneath the pectoralis muscles into the axilla along the midaxillary line. At the level of the ninth rib,

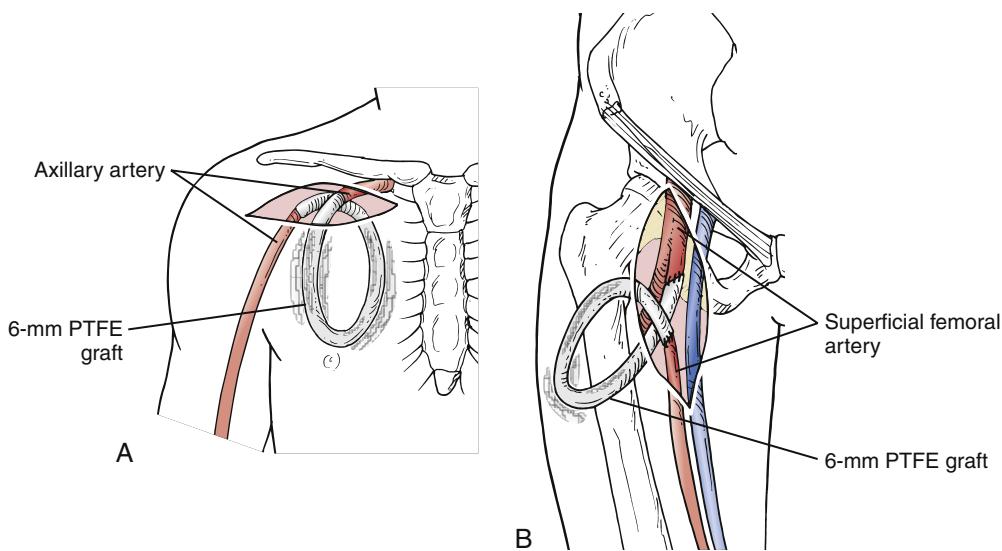


Figure 175.9 (A) Prosthetic axillary artery-axillary artery loop access. (B) Prosthetic femoral artery-femoral artery loop access. PTFE, polytetrafluoroethylene.

the graft is turned medially and cephalad for subcutaneous tunneling to the infraclavicular incision and then medially and caudad to the fifth rib interspace at the sternal border. A space is created in the fifth interspace, and the graft is passed into the mediastinum. This long, tortuous course was chosen to provide a sufficient length in a subcutaneous location that would allow a large number of potential cannulation sites. The graft is anastomosed end to side to the axillary artery and to the right atrial appendage.

A recent study described their experience with axillary-atrial graft as well as axillary-iliac graft. The axillary-iliac graft is created through an infraclavicular incision to expose the axillary artery, a retroperitoneal approach at the level of the umbilicus to expose the iliac vein, and an anterior chest/abdominal wall tunnel. They report a 6-month secondary patency of 100% and 75% for the axillary-atrial graft and axillary-iliac graft, respectively.⁶⁵

Arterial-Arterial Access Procedures

Bunger et al. reported the outcome of a series of 20 patients who underwent axillary artery-axillary artery interposition with PTFE grafts.⁶⁶ The interposition graft was looped on the chest wall and anastomosed end to end to the transected axillary artery (Fig. 175.9A). The diameter of the PTFE graft (range, 6 to 8 mm) was dictated by the size of the axillary artery. Operative or endovascular revision procedures were required in 30% of patients. Limb ischemia occurred in one patient whose access thrombosed, but it resolved after thrombectomy. No symptoms of limb ischemia occurred in the three other patients whose access thrombosed.

Zanow et al. recently reported a series of 36 arterio-arterial prosthetic loop accesses.⁶⁷ Among their patients, 31 of the accesses were based off the axillary artery and five were based off the femoral artery (see Fig. 175.9). In each case, the artery was divided and end-to-end anastomoses were used to interpose the prosthetic graft. The authors noted that thrombosis of the femoral access resulted in severe limb ischemia requiring immediate thrombectomy, whereas occlusion of the

axillary access caused only mild ischemia and was much better tolerated.

Two recent studies reported their experience with brachial arterio-arterial prosthetic loop access.^{68,69} Both series did note certain anatomic and physiologic requirements for placement of this access. The brachial artery should be greater than 4 mm in size and have a flow rate of greater than 50 cc/min based on duplex in a normotensive patient. The access was based off the mid-brachial artery and benefits of this access include a more superficial location, better tolerated ischemic symptoms if graft thrombosis occurred, and the procedure can be done under local anesthesia/block versus an axillary-based access. It is important to note that there was no incidence of limb loss in either series even with permanent graft thrombosis for ligation of the brachial artery and graft removal secondary to infection.

Salgado et al. described the technique of superficial femoral artery transposition for vascular access.⁷⁰ The technique involves the following steps: (1) transection of the sartorius muscle; (2) exposure and mobilization of the superficial femoral artery; (3) elevation of the superficial femoral artery by suturing the ends of the sartorius muscle and closing the subcutaneous tissue beneath the artery; and (4) closure of the skin over the artery. In their series of 14 patients, the authors did not report patency but rather found that these accesses "delivered 3215 hemodialysis treatments."⁷⁰

Lei et al. reported their series of 18 patients with superficial femoral to deep femoral artery loop access. The technique involves exposure of the superficial femoral and deep femoral arteries and subcutaneous placement of a 6-mm PTFE conduit as a loop. End-to-side anastomoses are performed from the graft to the vessels⁷¹ (Table 175.4).

Arterial-arterial access procedures may be considered in patients with previous access-related limb ischemia and high-output cardiac failure. It is important to note that these accesses cannot be used to infuse medications. Also, dialysis unit personnel should be instructed to hold pressure over the needle cannulation site for at least 20 minutes. The arterial-arterial access procedures do not provide flow rates as high as

arterial–venous access. Since dialysis blood flow rates exceeding 400 mL/min can cause recirculation and arm pain, it may be necessary to run patients at slower blood flows for longer periods to deliver adequate dialysis treatment.

Unconventional Sites for Placement of a Tunneled Dialysis Catheter

Transthoracic Superior Vena Cava Catheters

Wellons et al. reported a series of 22 patients with bilateral internal jugular and subclavian vein occlusion who underwent placement of a tunneled dialysis catheter into the SVC via direct transthoracic puncture.⁷² In this procedure, a pigtail catheter is placed in the SVC via access from the femoral vein and a venogram of the SVC is performed. Anteroposterior and lateral fluoroscopic views of the SVC are obtained and used as a reference guide to pass an introducer needle from a point immediately cephalic to the head of the right clavicle to the SVC. Once the SVC is entered, a hydrophilic wire is placed into the inferior vena cava (IVC). A tunneled dialysis catheter is placed in the usual fashion.

Inside-Out Technique

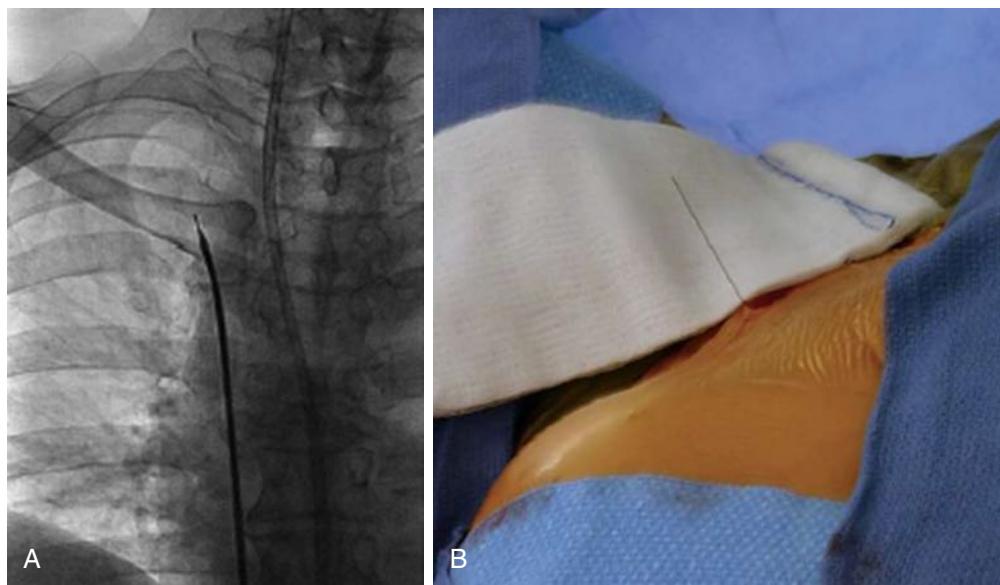
The inside-out technique is most appropriately utilized in patients with internal jugular vein occlusion who need catheter-based access. It was initially described by Davis and Gurley for use in patients needing HeRO access with jugular occlusion⁷³ (Fig. 175.10). The technique is modified slightly to allow for catheter placement. Initially femoral venous access is obtained and a diagnostic catheter is advanced into the superior vena cava. A diagnostic venogram is performed to identify the level of venous occlusion. The diagnostic catheter is then exchanged for an SL-1 transeptal sheath (SL0, Daig Inc., St. Jude Medical, St. Paul, MN). This angled 8-French system is advanced until its tip abuts the venous occlusion in the chest. Care is taken using a variety of oblique imaging views to ensure that the angle of the catheter is oriented anteriorly and slightly laterally. The back end of a stiff solid core 0.014 wire is then advanced through the sheath and dilator and is used to perforate the occluded vein. The wire is advanced under fluoroscopy through the subcutaneous tissue until it tents the skin in the supraclavicular space. Local anesthesia is infiltrated at this site and a small incision is made to allow for wire retrieval from the subcutaneous tissue. Once the wire is retrieved, standard

TABLE 175.4 Results of Arterio-Arterial Prosthetic Loop Access

Series	Access	Number of Patients	Primary Patency	Secondary Patency
Bunger et al. ⁶⁶	Axillary	20	90% at 6 months	93% at 6 months
Zanow et al. ⁶⁷	Axillary SFA	31	73% at 1 year	87% at 3 years
		5		
Khafagy et al. ⁶⁸	Brachial	35	88% at 1 year	68% at 3 years
Ali et al. ⁶⁹	Brachial	89	62% at 2 years	90% at 2 years
Lei et al. ⁷¹	SFA to PFA	18	61% at 3 years	72% at 3 years

SFA, superficial femoral artery; PFA, deep femoral artery

Figure 175.10 Inside-Out Central Venous Access Technique. (A) The sheath and needle are advanced to the point of obstruction in the superior vena cava. The needle and wire are then directed to the posterior aspect of the head of the clavicle. (B) The wire is then exteriorized and pulled through the skin of the supraclavicular fossa.



techniques can be utilized to dilate the tract, exchange for a larger stiff wire and then place a tunneled catheter. Our experience with this technique has been good, with 100% technical success.⁷⁴ Recently, a commercially available device has been developed to assist in this technique (Surfacer® Inside-Out® Access Catheter System, Merit).

Translumbar Inferior Vena Cava Catheters

Rajan et al. have reported a series of 58 translumbar IVC catheters, 37 of which were placed for hemodialysis access.⁷⁵ IVC thrombosis occurred in one case, and stenosis occurred in another. In several cases the catheter migrated into the subcutaneous soft tissues, retroperitoneum, or iliac veins, necessitating catheter repositioning. A case of retroperitoneal hematoma occurred secondary to catheter migration out of the IVC. In another study the cumulative patency rate was 52% at 6 months and 17% at 12 months. Infection of the catheter occurred in six cases.⁷⁶

Transhepatic Inferior Vena Cava Catheters

Percutaneous transhepatic access has been used to place tunneled catheters in the IVC for hemodialysis.^{77,78} Thrombosis or malfunction of the catheter requiring catheter exchange was frequent in both series. In one series of 21 catheter placements, the complication rate was 29%, including one death from massive intraperitoneal hemorrhage. Although the average duration of dialysis via this route in the two series was 24 and 138 days, respectively, one patient was dialyzed for 599 days. Given the catheter maintenance problems associated with the transhepatic approach, this procedure should be used only as a last resort.

PEDIATRIC VASCULAR ACCESS

The preferred renal replacement therapies for the pediatric patient population are renal transplantation and peritoneal dialysis. According to the US Renal Data System (USRDS), approximately 38% of pediatric patients with end-stage renal disease receive a kidney transplant within the first year.⁷⁹ Hemodialysis is considered by many as a bridge to transplantation or as a treatment of last resort. Since the occurrence of end-stage renal disease is less common in children than adults and hemodialysis is not the preferred treatment modality, few surgeons have a sizable experience with pediatric vascular access. As a result, the literature on pediatric vascular access is limited to a few single-institution, retrospective reviews of experiences acquired over many years. Standard methods for reporting outcomes such as patency are not used for the majority of those reports. The chief limitation of the pediatric vascular access literature is the way in which studies define a pediatric patient. Most of the “pediatric” vascular access case series are primarily composed of adolescents whose body sizes approximate those of small adults rather than children. Given the limitations of the pediatric vascular access literature, it is difficult to determine the outcome of

autogenous AV access procedures or to derive algorithms for vascular access for the small child younger than 10 years of age. Therefore only broad concepts related to vascular access for the pediatric patient population can be elicited from the available literature.

Kidney Disease Outcomes Quality Initiative Recommendations and Recent Trends

Given the technical challenges of autogenous or prosthetic AV access placement in very small children, the KDOQI guidelines recommend peritoneal dialysis or hemodialysis via a tunneled dialysis catheter for patients weighing less than 20 kg. Peritoneal dialysis or hemodialysis via a tunneled dialysis catheter is also recommended as a bridge to kidney transplantation if the transplant is expected to occur in less than 1 year. The KDOQI guidelines emphasize the importance of matching the length and diameter of the tunneled dialysis catheter to the size of the patient and provide a table for reference. Catheter placement considerations in pediatric patients are similar to those in adults. The most recent USRDS report shows that the rates of vascular access infection and hospitalization for infection/sepsis among hemodialysis patients younger than 10 years of age are increasing.⁷⁹ This is due in part to catheter infections resulting from patients spending more time on transplant waiting lists.

A commonly used argument against the placement of permanent access is the relative short time for renal transplantation. Catheter placement is used as a bridge to renal transplantation, which is the ideal goal of treatment, but this cannot always be achieved. Furthermore due to the finite life span of an allograft, planning for vascular access poses a unique challenge in this population. As a result, any intervention that could compromise future access must be avoided. Catheters frequently lead to stenosis or thrombosis of central veins, particularly in children who have smaller-diameter veins. These trends support the KDOQI recommendations that an autogenous or prosthetic AV access is preferred for pediatric patients on maintenance hemodialysis.⁵

Autogenous Arteriovenous Access

Autogenous AV access is considered the optimal hemodialysis access in pediatric patients. The outcomes in pediatric patients have been published for the following autogenous AV access procedures: radial–cephalic access, ulnar–basilic access, radial–basilic transposed access, brachial–basilic transposed access, brachial–cephalic access, and femorofemoral transposed access.^{80–87} The secondary patency rates ranged from 70% to 98% at 2 years. However, in most of these series it is unclear whether early access failures and accesses that failed to mature were excluded from patency analysis. Nonmaturation of autogenous AV accesses in children reportedly occurs in as many as 33% of cases. For a pediatric patient with anatomy unsuitable for an autogenous access procedure, a prosthetic AV access can

be placed. One study reported the outcome for prosthetic AV access in children to be equivalent to that in adults.⁸⁴

Technique

The same considerations and diagnostic modalities used to select the appropriate autogenous or prosthetic AV access procedure in adults apply to children. The more distal anatomic sites should be used as a first access, preserving the more proximal sites for access later in life. There are key differences in the techniques used for AV access placement in children compared with adults. AV access placement is facilitated in pediatric patients by the use of microsurgical techniques and microsurgical instruments, adequate magnification, and an interrupted suture technique. The AV anastomosis is performed with 8-0 to 10-0 polypropylene suture. Second, to minimize vessel dissection and vasospasm, vascular control is obtained with a sterile tourniquet.^{80,81}

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The role of the HeRO graft as a tertiary vascular access procedure is not well defined. This article reports the largest experience to date with the device. The article describes insertion techniques and reports the outcomes for the device.

Gradman WS, Laub J, Cohen W. Femoral vein transposition for arteriovenous hemodialysis access: improved patient selection and intraoperative measures reduce postoperative ischemia. *J Vasc Surg.* 2005;41:279–284.

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A complete reference list can be found online at www.expertconsult.com.

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Hemodialysis Access: Dialysis Catheters

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Central venous catheters play an important role in the treatment of patients with end-stage renal disease. Despite initiatives to improve fistula creation, more than 80% of patients initiated hemodialysis with a catheter, a number that has changed little over the past 15 years.¹ Central venous catheters for hemodialysis are categorized by their intended duration as either acute or chronic. Both acute and chronic hemodialysis catheters can be placed percutaneously; however, chronic catheters feature a subcutaneous retention cuff near the skin exit site, whereas acute catheters do not. This cuff serves to provide a point for tissue ingrowth, ensuring that the catheter remains in place, and also acts as a barrier to prevent microbial

migration into deeper tissues. As a result, acute catheters are at higher risk for infectious complications and can easily become dislodged. Thus acute catheters should be placed only in hospitalized patients and used for a short duration, usually less than 2 weeks.² This time frame is in contrast to chronic catheters, which can be used in the outpatient setting indefinitely.

This chapter focuses on tunneled dialysis catheters (TDC) and their management, but the potential complications related to placement of acute nontunneled hemodialysis catheters mirror those of TDC. However, because of the short duration of use of acute catheters, long-term complications are less frequent but infectious complications are more common.

INDICATIONS

The most common indication for placement of a tunneled hemodialysis catheter is for urgent hemodialysis while the patient is waiting for an autogenous arteriovenous fistula (AVF) or arteriovenous graft (AVG) to be created or to mature. Other indications include patients in whom an AVF or AVG is not anatomically feasible or who are not operative candidates because of advanced comorbidities. Temporary TDC placement is also indicated after revision of an AVF or AVG for management of a complication (e.g., access revision for pseudoaneurysm formation or infection), after placement of a peritoneal dialysis catheter, and for a chronic ambulatory peritoneal dialysis patient requiring abdominal or inguinal surgery.

The benefits of TDC over AVF and AVG include immediate use for hemodialysis, uncomplicated and needle-free connection to the dialysis circuit, elimination of cannulation site complications, and simple insertion technique that can be performed by many different interventional specialists. While a mature and well-functioning AVF or AVG is preferred to TDC, recent guidelines recognize that in certain cases, creation of a functional AV access is severely challenged due to anatomic limitations. In these circumstances, a TDC can be considered for long-term or indefinite use.²

TYPES OF CATHETERS

Early cuffed catheters were straight in configuration and stiff. With technological advances, these catheter designs have been largely supplanted by flexible catheters with various tip designs.

Design Characteristics

Catheter designs aim to achieve one main goal: adequate dialysis clearance at a relatively high flow rate of 300 to 350 mL/min.³ In addition, the phenomenon of recirculation must be minimized to ensure adequate clearance. The “arterial lumen” of the catheter is the outflow to the dialysis machine from the patient; the “venous lumen” is defined as the inflow from the machine back to the patient. Access recirculation is the reentry of dialyzed blood from the venous lumen directly into the arterial lumen, thus bypassing the systemic circulation and leading to inefficient dialysis, lack of appropriate solute clearance, and possibly increased morbidity and mortality.⁴

Design Categories

Numerous manufacturer modifications exist in an effort to satisfy the requirements of high flow rates and minimal recirculation. The modifications fall into four general categories.

Split Tip

Split-tip catheters have a double-lumen, single-body configuration in the midbody but separate into two distinct distal tips, each with side holes in all directions (Fig. 176.1A).

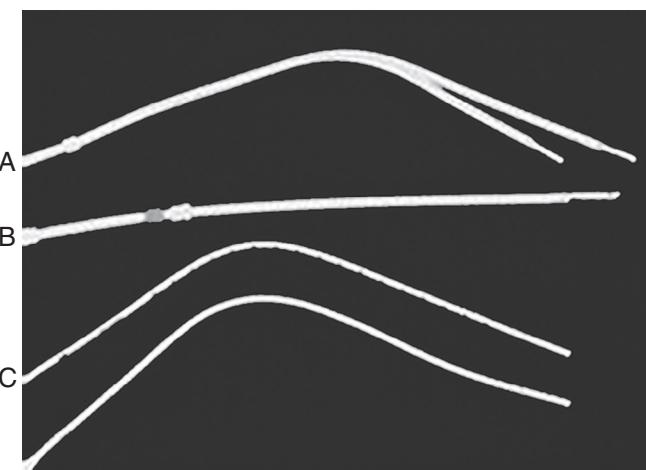


Figure 176.1 Three types of tunneled hemodialysis catheters: split-tip catheter (A), staggered-tip or step-tip catheter (B), and dual catheter (C). (From Richard HM, 3rd, et al. A randomized, prospective evaluation of the Tesio, Ash split, and Opti-flow hemodialysis catheters. *J Vasc Interv Radiol.* 2001;12:431–435.)

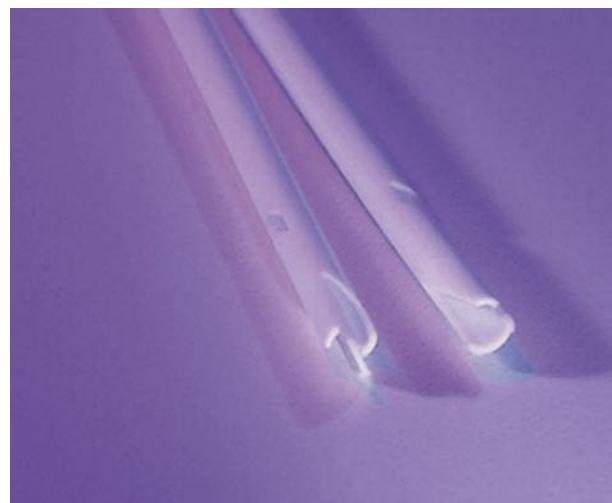


Figure 176.2 Tal Palindrome catheter. (Courtesy Covidien.)

Step Tip

The staggered-tip or step-tip catheter is a double-lumen, single-body catheter with the venous limb extending at least 2.5 cm beyond the inflow tip (see Fig. 176.1B).

Dual Catheter

The dual catheter design consists of two completely separate catheters that can be inserted in two different locations (see Fig. 176.1C).

Symmetric Tip

Symmetric tip catheters have equal length of arterial and venous limbs (Fig. 176.2).⁵

Numerous reviews directly compare performance of individual tunneled hemodialysis catheters with specific outcome variables of flow rate, recirculation time, and patency. Unfortunately, despite isolated beneficial characteristics of a particular catheter design, no particular catheter has been demonstrated

to be superior over others.^{3,4,6,7} A systematic review of catheter tip designs that included seven randomized controlled trials and one retrospective study and encompassed 988 patients demonstrated no advantage of a particular catheter design.⁸

PREOPERATIVE EVALUATION

History and Physical Examination

As with any clinical assessment, the proper preoperative evaluation of a patient begins with a detailed history and physical examination. Specific inquiries should include details such as prior long-term central line placement, prior AVF or AVG placement, prior tunneled hemodialysis catheter infections, history of a coagulation disorder, and history of a pacemaker. Physical examination of the neck and chest is mandatory. Evidence of a previously placed tunneled hemodialysis catheter, previous permanent accesses, upper extremity or facial edema, and ipsilateral venous distention with visible venous collaterals should alert the clinician to the possibility of central veno-occlusive disease.

Numerous specialists have the skill set to properly place a tunneled hemodialysis catheter. However, there is a significant advantage in terms of continuity of care when the same practitioner places the tunneled hemodialysis catheter and the permanent access or when a team approach coordinates these procedures. There are a finite number of access sites available for both tunneled catheter and permanent access placement. Therefore, a comprehensive plan that embraces all forms of hemodialysis access may provide maximum benefit of each crucial access site.

Central Venous Imaging

Color-Flow Venous Duplex Imaging

Noninvasive color-flow duplex imaging is the first-line method of preoperative imaging for the tunneled hemodialysis catheter. Patency of internal jugular veins and axillary veins is easily identified with compression of the vein. However, as imaging moves toward the central chest, the air interface with the lung tissue, as well as obstructing bone structures, makes subclavian vein and central vein imaging virtually impossible.⁹

Magnetic Resonance Venography

Three-dimensional gadolinium-enhanced magnetic resonance venography (MRV) has been shown to be highly sensitive in identifying central vein occlusions and stenoses greater than 50% when directly compared with digital subtraction angiography.¹⁰ Despite the accuracy of MRV, gadolinium must be administered with caution in patients with a glomerular filtration rate of less than 30 mL/min because of the risk of gadolinium-induced nephrogenic systemic fibrosis, which is rare even in this patient population, but has not been described in patients with normal renal function. An alternative to gadolinium is ferumoxytol, an ultrasmall, superparamagnetic iron oxide nanoparticle.¹¹ Ferumoxytol is approved for a variety of magnetic resonance imaging applications, does not carry the

risk of nephrogenic systemic fibrosis and results in accurate and reliable MRV images.¹¹

Computed Tomographic Venography

Computed tomographic venography (CTV) is similar to MRV in being able to image multiple vessels in the chest in one setting. However, CTV does have the advantages of being readily available in most medical centers, fast acquisition times, and fewer deleterious contrast agent concerns. Contrast-enhanced CTV provides excellent imaging of the superior vena cava¹² and a study of 18 patients comparing CTV and digital subtraction venography for the diagnosis of benign thoracic central venous obstruction demonstrated that CTV findings correlated closely with those of digital subtraction venography.¹³

Catheter-Based Contrast Venography

Catheter-based contrast venography remains the “gold standard” for diagnosis of central vein stenosis or occlusion. Contrast venography has the distinct advantage of allowing the clinician to initiate endovascular treatment if a significant stenosis is detected at the time of venography. In addition, it is often possible to perform catheter-based venography with a much smaller volume of contrast material than what is required for CTV, reducing the risk of nephrotoxicity.

CATHETER INSERTION

Site Selection

The right internal jugular vein is the preferred access site for tunneled hemodialysis catheter placement because it has the best patency, presumably owing to shorter length and less kinking due to its straighter path to the right atrium as compared to a left internal jugular vein access. In a prospective evaluation, factors affecting long-term survival of tunneled hemodialysis catheters were analyzed in a cohort of 812 catheters in 492 patients.⁷ A tunneled hemodialysis catheter placed in the right internal jugular vein demonstrated significantly longer survival compared with one placed in the left internal jugular vein. Tunneled hemodialysis catheters placed in the femoral vein had the worst long-term survival. The subclavian vein should be avoided in order to prevent catheter-induced subclavian stenosis, which would negatively affect the future placement of ipsilateral permanent arteriovenous access.^{2,3,7}

A tunneled hemodialysis catheter from the right internal jugular vein should be at least 19 cm in length when measured from the tip to the cuff, though frequently 23-cm long catheters are used; catheters from the left are slightly longer. When femoral access is used, long catheters (greater than 40 cm) should be placed so that the tip is clearly past the iliac veins and reaches easily into the inferior vena cava in order to produce the best flow rates.

Technique

Tunneled hemodialysis catheter insertion should be performed in a procedure room under fluoroscopic guidance for multiple

reasons. First, many of these patients suffer from central venous stenosis or occlusion, which can challenge blind guide-wire placement. Placement in alternative veins like the anterior jugular or external jugular vein can provide an access point to the central veins, but fluoroscopy is essential in order to confirm that the catheter is taking the appropriate path. Second, fluoroscopic guidance is critical during passage of stiff dilators and peel-away sheaths which can potentially kink the guide wire resulting in an iatrogenic injury. Finally, fluoroscopy can verify that the catheter geometry is not kinked and the tip location is appropriate at the end of the procedure. Bedside placement is discouraged because of the need for proper sterility, the possibility of additional endovascular procedures (e.g., venography and venoplasty), and the requirement for fluoroscopy. The procedure is usually performed under local anesthesia with conscious sedation. Preoperative antibiotic prophylaxis directed at Gram-positive bacterial strains is administered before skin incision in each case. The skin is then prepared with isopropyl alcohol and chlorhexidine solutions.

Ultrasound evaluation with a sterile covered transducer confirms access vein patency. The site of vein cannulation should be 2 to 3 cm cephalad to the clavicle. Real-time ultrasound guidance is used to access the vein with a micropuncture 21-gauge needle, 0.018-inch guide wire, and 5F coaxial catheter (Fig. 176.3). After successful cannulation, the introducer and 0.018-inch wire are removed and exchanged for a 0.035-inch wire. Using a micropuncture needle minimizes the injury if an artery is inadvertently punctured. However, a single wall puncture needle can also be used, with immediate placement of an 0.035-inch wire. A 1-cm skin incision is made surrounding the wire entry site (Fig. 176.4, short arrow). Fluoroscopic imaging should be used during all wire maneuvers to confirm wire position.

Because of the large size and stiff nature of most tunneled hemodialysis catheters, a moderate amount of forward pressure may need to be applied during insertion, especially if scarring is present. It is highly advisable to have the guide wire course in the superior vena cava to inferior vena cava channel and not enter the right heart chambers. This is especially true for left-sided placement of a tunneled hemodialysis catheter. Because



Figure 176.3 Ultrasound-guided puncture of the internal jugular vein with a micropuncture needle.



Figure 176.4 Placement of the tunneled hemodialysis catheter alongside the anticipated catheter course to determine where to position the exit site. Internal jugular vein puncture site (short arrow); upper chest catheter exit site (long arrow).



Figure 176.5 Tunneling of the catheter subcutaneously from the chest incision to the neck incision anterior to the clavicle.

of the tortuous path from the left internal jugular vein to the heart, it is possible for the dilator to push the midportion of the guide wire, creating a loop that could perforate the side wall of the central vein.¹⁴ The incidence of this can be reduced by use of a stiffer wire than the one typically provided in the insertion kit and direct fluoroscopic visualization during passage of all dilators and sheaths over the wire.

Antegrade Placement

A small incision is made on the anterior chest where the tunneled hemodialysis catheter is to exit the subcutaneous tunnel (see Fig. 176.4, long arrow). The exit site of the tunneled hemodialysis catheter should be inferior and lateral to the vein entry site. Placement of the tunneled hemodialysis catheter alongside the anticipated catheter course is useful in determining where the exit site should be positioned. The tunneled hemodialysis catheter is then attached to the tunneling device and passed subcutaneously from the chest incision up through the vein entry site incision in the neck, traversing anterior to the clavicle *en route* (Fig. 176.5). The cuff of the catheter should lay 1.5–2 cm from the exit site and care should be taken to tunnel deep enough so that the catheter does not erode through the skin.¹⁵ The venipuncture is sequentially dilated, and the final introducer and peel-away sheath unit is inserted until the sheath is



Figure 176.6 Dilatation of the wire tract.



Figure 176.7 Insertion of the tunneled hemodialysis catheter through the peel-away sheath.

“hubbed” at the skin (Fig. 176.6). The introducer and wire are removed, and the tunneled hemodialysis catheter is inserted through the peel-away sheath (Fig. 176.7). Once the tunneled hemodialysis catheter is fully inserted, the peel-away sheath is withdrawn. When coming from the left, the sheath may not be long enough to provide adequate support for the catheter as it is placed into the SVC, leading to inadequate placement in the innominate vein. In these cases, advancing the TDC over a stiff guide wire through the peel-away sheath can be helpful. When this is done, the wire will typically exit the venous port of the tunneled catheter if it was placed antegrade.

Each lumen of the catheter is aspirated and flushed with dilute heparin (10 units of heparin sulfate per milliliter of normal saline). Both of these actions should be easily accomplished without resistance. If resistance is encountered, the catheter should be examined under fluoroscopy to rule out a kink in the path of the catheter or malpositioning of the tip. Ideally, the tip of the catheter should be in the right atrium.

The vein entry site incisions are closed with absorbable sutures, and the tunneled hemodialysis catheter is secured to the chest wall with nonabsorbable sutures. Each lumen of the tunneled hemodialysis catheter is filled with the manufacturer-indicated volume of concentrated heparinized saline (1000 units/mL) to protect against intracatheter thrombosis. In a meta-analysis comparing low doses (<5000 units/mL) heparin lock versus high-dose heparin (≥ 5000 units/mL), low-dose heparin was

shown to be associated with a significantly lower risk of bleeding-related complications with no difference in the incidence of catheter thrombosis.¹⁶ Sodium citrate 4% solution can be used in patients with heparin allergies. Finally, some practitioners will use normal saline as opposed to an anticoagulant for the locking solution. Data to support one locking solution over another is fragmentary, and consensus has yet to be achieved regarding the superiority of a particular approach.

Retrograde Placement

Tunneled hemodialysis catheters have been developed that can be placed in a “reverse-tunneled” or “retrograde” fashion; these catheters do not have ports attached initially. The catheter is inserted into the vein before tunneling in the same fashion as the standard tunneled hemodialysis catheter. The catheter is then tunneled from the neck incision to the chest incision, and the ports are attached after tunneling. The advantage of this type of insertion is that it allows precise positioning of the catheter tip.

Unconventional Catheter Sites

Patients who have exhausted conventional sites for vascular access may require placement of tunneled hemodialysis catheters in unconventional sites, such as the transhepatic and translumbar routes.

Translumbar catheters are generally placed with the patient in the prone position by percutaneous puncture of the inferior vena cava above the right iliac crest. The catheter is tunneled through a right lateral abdominal exit site. For transhepatic catheters, percutaneous access to the right or middle hepatic vein is obtained through the eighth intercostal space in the midaxillary line under fluoroscopic guidance. The catheter is then tunneled to a lateral anterior chest wall exit site. The tip of the catheter is positioned in the right atrium in both approaches.

The reported mean total catheter service lifespan of transhepatic and translumbar catheters in the literature ranges from 70 days to 1948 days.^{17–19} In addition, unique to this type of access is the high rate of subsequent interventions for maintenance of adequate hemodialysis access. Two of the largest published series reported that more than 60% of their patients required at least one catheter exchange. Catheter migration, thrombosis, and infection are the most commonly reported reasons for catheter exchange.^{17–20} Translumbar catheter exchanges may be more difficult than exchanges through the transhepatic approach because of retroperitoneal fibrosis that develops along the track.¹⁷

PERIOPERATIVE CARE AND COMPLICATIONS

The perioperative management of patients after placement of a tunneled hemodialysis catheter centers on the evaluation for and treatment of potential acute complications. In a compilation of data from 1794 central venous cannulations in critically ill patients, the overall complication rate was 7.1%.²¹ Failure

to place the central line and arterial puncture were the most common mechanical complications, followed by pneumothorax. The keys to successful management of these complications are awareness, prompt recognition, and expeditious treatment.

Pneumothorax

An end-expiratory upright chest radiograph should be performed after placement of a tunneled hemodialysis catheter to confirm tip placement and to exclude a pneumothorax.²² If acute, severe symptoms and signs of pneumothorax develop, a tube thoracostomy should be performed immediately and the patient should be given oxygen by mask. In the setting of tension pneumothorax, decompression of the pleural space with an intravenous catheter placed in the second intercostal space in the midclavicular line can be lifesaving. More frequently, the air leak is relatively small, and the pneumothorax develops during a period of several hours.

When a small pneumothorax is encountered and there are no symptoms or signs of respiratory compromise, decrease in peripheral oxygen saturation, or hemodynamic impairment, a “watchful waiting” approach with repeated chest radiographs is appropriate.²³ If symptoms develop or there is an increase in the size of the pneumothorax on subsequent chest radiographs, tube thoracostomy can be performed, but a small bore pigtail catheter with a flutter valve can also be placed and is usually better tolerated by the patient.

Hemothorax

A hemothorax can develop when the back wall of either a vein or artery and the parietal pleura are perforated by an advancing needle tip, dilator, or sheath.²⁴ The subclavian vein or artery, the innominate vein, or even the superior vena cava may be involved. The lack of effective tamponade combined with negative respiratory pressure may result in a large blood loss through a small puncture. Clinically, patients may develop respiratory compromise accompanied by dullness to percussion and decreased breath sounds on the affected side. A decreased hematocrit and evidence of fluid in the pleural cavity on the chest radiograph strongly support the diagnosis. Drainage of the pleural space with a tube thoracostomy is generally adequate therapy and should be performed for significant hemothorax to prevent entrapment of the lung. Rarely, bleeding must be controlled surgically or percutaneously with the use of covered stents, if possible.

Wire Embolism

Wire embolism occurs when control of the wire is lost during the procedure or the guide wire is sheared off by the access needle as it is withdrawn. In particular, the floppy tip of the 0.018 micropuncture guide wire is vulnerable to shearing if withdrawn vigorously through a metal needle. If resistance to wire removal is encountered, fluoroscopic imaging should be used, and removal of the wire and needle together as a unit may be required. Fortunately, guide wires can usually be removed fluoroscopically with use of a wire snare retrieval system.²⁵

Cardiac Arrhythmia

Cardiac complications related to central venous catheterization are rare. Arrhythmia during placement of a tunneled hemodialysis catheter is associated with the guide wire irritating the myocardium. The problem can be minimized by use of guide wires that have distance markings and fluoroscopy to visualize the location of the tip of guide wires and catheters. If cardiac arrhythmias develop after the placement of a tunneled hemodialysis catheter, the catheter position should be checked fluoroscopically or with a chest radiograph and the catheter tip should be withdrawn if the tip is near or traversing the tricuspid valve. Rarely, in less than 1% of cases, patients will have arrhythmias that require chemical or electrical cardioversion.²⁶

Cardiac Perforation

The soft, flexible hemodialysis catheters that are currently used are unlikely to perforate the heart. More common causes of cardiac perforation are guide wires, dilators, and rigid introducers. Cardiac perforation may result in acute pericardial tamponade from bleeding or fluid infusion into the pericardial space. Signs and symptoms of pericardial tamponade can develop rapidly and include shock and cyanosis with marked cervical venous distention. Tachycardia and muffled heart sounds are generally present, and a large globular cardiac silhouette may be present on a chest radiograph. Any intraluminal catheter devices should be removed and pericardiocentesis or a pericardial window created. If the tamponade recurs after pericardiocentesis or creation of a window, median sternotomy with formal cardiac repair may be necessary.

Nerve Injuries

The brachial plexus is the nerve structure that is most vulnerable during percutaneous catheterization by virtue of its large size and proximity to the subclavian vein and artery.^{27,28} Acute upper extremity pain referred along a neural anatomic pathway suggests impingement on the brachial plexus and necessitates immediate withdrawal of needles or catheters. Permanent injury is rare. The vagus, recurrent laryngeal, and phrenic nerves are also in proximity to the internal jugular vein but are small nerves and infrequently injured. The development of hoarseness after catheter placement suggests injury to the vagus or recurrent laryngeal nerve. Phrenic nerve injuries are generally asymptomatic and are incidentally identified on radiographic examination when an elevated hemidiaphragm is seen.²⁹ The development of Horner syndrome has also been reported by inadvertent trauma to the stellate ganglion during percutaneous cannulation of the internal jugular vein.

Catheter Misplacement

In a prospective study of 1619 patients, the incidence of catheter tip malposition, defined as extrathoracic or ventricular positioning, was 3.3%.³⁰ The use of fluoroscopy during catheter placement should eliminate the occurrence of catheter

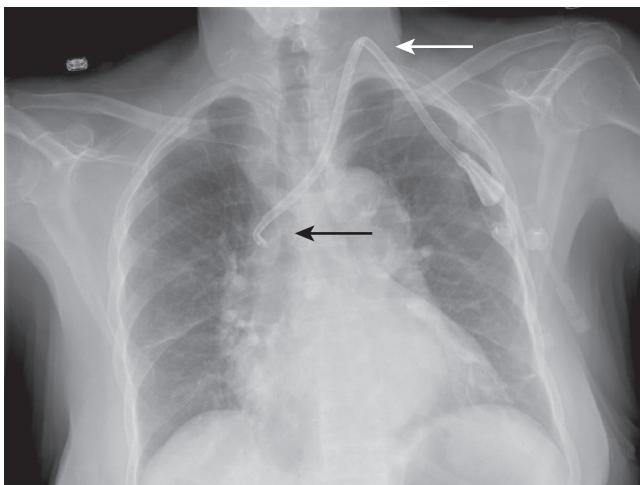


Figure 176.8 Inappropriate TDC placement. In addition to being kinked at the apex (white arrow), the catheter tip is high and kinked at the confluence of the innominate veins (black arrow).

tip malposition. If there is a question as to the location of the tip of the catheter during placement, contrast material can be injected through the catheter under fluoroscopic guidance to help define the anatomy.

Venous

If the catheter tip is left in the subclavian, axillary, jugular, or hepatic vein, the catheter tip or turbulence generated during hemodialysis may cause intimal injury, which leads to thrombosis of the vein.³¹ Stiff catheters or introducers left abutting the wall of the superior vena cava or more peripheral veins can also erode through the vessel wall and produce a hemomediastinum or hemomediastinum.

Use of fluoroscopy at the time of TDC placement can ensure proper length and catheter tip placement. It can also identify catheter kinking, which can lead to inadequate flow through the lumens (Fig. 176.8). The kinking is often related to unintended twisting of the catheter as it was inserted and can easily be addressed by untwisting the catheter under fluoroscopy.

Arterial

Catheters may be inadvertently placed into the subclavian or carotid artery and go unrecognized. This is more common in a hypotensive or poorly oxygenated patient who may not have return of bright red, pressurized blood when an artery is punctured. Because tunneled hemodialysis catheters are generally placed on an elective basis, arterial placement is rare. If there is a question of arterial placement, the pressure can be transduced through the catheter to see if the waveform is arterial or venous. A sample from the catheter can also be sent for a blood gas analysis to determine if the values are consistent with an arterial or venous blood gas. If the injury is recognized immediately, it may be possible to remove the catheter and apply pressure for a prolonged time, though immediate surgical repair is likely required due to the large sheath size.³² If the injury is recognized later, the catheter should be removed in the operating room with open repair of the artery because the incidence

of tract formation and accumulation of thrombus on the catheter is increased.³² Injuries to the subclavian artery are difficult to compress because of the lack of surrounding bony structures and should be monitored closely for evidence of hemothorax. Open or endovascular repair of the artery may be required.³³

LONG-TERM CARE AND COMPLICATIONS

The long-term management of tunneled hemodialysis catheters is primarily performed by the staff at the dialysis center where the patient receives dialysis. Patients with tunneled hemodialysis catheters usually do not come to the attention of the vascular surgeon unless a late complication of the catheter develops.

Air Embolism

Air embolism is a rare but potentially lethal complication of central venous catheterization that can be either an acute or a late complication.²⁴ In its late form, air embolism generally occurs when air enters the catheter either before attachment of the tubing or when the tubing becomes disconnected.^{34,35} Air embolization can also occur through cracks in the catheter or its hub, as well as through the catheter tract after the removal of a central venous catheter.³⁶ Patients should be instructed that in the event the catheter becomes disconnected or uncapped, a life-threatening complication could result. Patients should be instructed to cap the open catheter with a thumb or finger and to call for help immediately. An occlusive dressing should be placed over the skin puncture site when the catheter is removed to allow adequate sealing of the tract.

If sudden cardiorespiratory collapse develops in a patient with a tunneled hemodialysis catheter, air embolism must be strongly considered. Further embolization must be prevented by capping or clamping of the catheter while the patient is simultaneously placed in the Trendelenburg and left lateral decubitus position (Durant maneuver).³⁷ This position displaces air away from the pulmonic valve, which relieves the right ventricular outflow obstruction. The catheter can be advanced into the heart to aspirate the air.³⁸

Catheter Occlusion

Catheter occlusion occurs in 30% to 40% of patients with tunneled hemodialysis catheters.³⁹ Occlusion of the catheter generally is a consequence of the development of a fibrin sleeve or plug at the catheter tip. The ability to infuse fluid into the catheter but the inability to withdraw blood often indicates impending occlusion.

Prevention

Use of antithrombotic agents is not recommended to prevent catheter thrombosis. Low-dose warfarin is ineffective in reducing catheter thrombosis. Both therapeutic warfarin, titrated to an INR of 2 to 3, or aspirin 325 mg/day decrease the risk of catheter thrombosis but are associated with an unacceptable

risk of gastrointestinal bleeding, particularly in the elderly.^{40,41} A meta-analysis of 13 studies of heparin lock solutions versus all other types of catheter lock solutions, including citrate, recombinant tissue plasminogen activator, antibiotic with heparin, ethanol, and taurolidine (a novel antimicrobial agent used in Europe) with a total of 1883 subjects, demonstrated no difference in patency between heparin versus other lock solutions.⁴²

Treatment

Local infusion of fibrinolytic agents has been used in the salvage of occluded central venous catheters.^{43,44} Currently, alteplase is the only fibrinolytic agent that is approved for treatment of occluded central venous catheters. Most commonly, 2 mg of fibrinolytic agent in 2 mL of solution is injected and allowed to dwell in the catheter for 2 to 3 hours. The catheter is then irrigated and flushed, with removal of any residual clot. This process can be repeated until patency is restored. In a study of 815 catheter occlusion episodes, success was achieved in 77% of cases with the first infusion of alteplase and in an additional 10% of cases after the second infusion.⁴⁵ However, use of this technique may result in only a limited number of additional dialysis sessions before the treatment must be repeated. A study of 570 catheters during a 2.5-year period demonstrated a median of five to seven additional dialysis sessions after each treatment.⁴⁶

Because of the frequency of recurrent occlusion and the difficulty in delivery of a highly concentrated fibrinolytic agent to the fibrin sheath around the tip of the catheter, techniques have been developed to mechanically eliminate the fibrin sheath. These techniques generally involve the insertion of a wire snare device through another venous access site, such as the femoral vein, to strip the fibrin sheath from the catheter and remove it. In a study of 131 sheath-stripping procedures on 100 catheters, the technical success of the procedure was 95.6% and the mean primary patency after the first stripping was 89 days.⁴⁷ An alternative technique is to remove the catheter over a wire, then use an angioplasty balloon to rupture the fibrin sheath, and replace a new catheter over the wire. A retrospective review of these two techniques compared with simple catheter exchange demonstrated no difference in patency.⁴⁸

Frequently, the management is simply replacement of the TDC. While one solution is to remove the catheter completely and then place a TDC *de novo*, this strategy obligates the patient to all the risks of a new access, many times at another site due to thrombosis of the original access site. If the catheter is not infected, an alternative is cutting down on the catheter central to the cuff, dividing the catheter, threading a wire through the catheter lumen, removing the catheter over the wire, and using the resulting wire access for replacement of a new catheter. A new subcutaneous tunnel is created. A simpler alternative, again for noninfected catheters, involves utilizing the existing subcutaneous tunnel. After sterile prep and drape, the catheter is clamped, the hubs are cut away, the cuff is dissected free, and stiff wires are threaded through the lumens. The old TDC is removed, and a new TDC is advanced over the wires through the existing subcutaneous tunnel into the right atrium. Infectious complications are rare and comparable to *de novo* TDC placement.⁴⁹

Central Venous Thrombosis

Catheter-related thrombus is present in approximately 30% of all patients with central venous catheters.⁵⁰ However, less than half of these thrombi are clinically significant.⁵⁰ The incidence of pulmonary embolus from catheter-related thrombus ranges from 0% to 17%, although catheter-related thrombus has rarely been reported to be the cause of death.⁵⁰ The more clinically significant implication of catheter-related thrombosis is its association with infection. In a study of patients with catheter-related *Staphylococcus aureus* bacteremia, 71% were found also to have central venous thrombus.⁵¹ Nevertheless, the routine use of low-dose warfarin prophylaxis is not recommended.⁵²

Venous thrombosis should be suspected in patients with tunneled hemodialysis catheters who present with arm, neck, or facial swelling; prominent collateral venous patterns; signs or symptoms of embolic complications; or unexplained fever. Duplex scanning generally is diagnostic, although venography is required on occasion for definitive diagnosis and determination of the extent of thrombosis. Conventional therapy consists of anticoagulation and elevation of the symptomatic arm. If possible, the catheter should be removed. Because patients with tunneled hemodialysis catheters often do not have other sites available for access placement, anticoagulation therapy with the catheter left in place can be considered.⁵³

Central Venous Stenosis

Catheter-associated central vein stenosis develops as a result of injury to the intima of the vein by the catheter.⁵⁴ The association between subclavian vein cannulation for hemodialysis access and subsequent subclavian vein stenosis is well described.^{55,56} The incidence of subclavian vein stenosis after placement of a tunneled hemodialysis catheter is significantly higher than that of internal jugular vein stenosis. In a study comparing venography in 50 patients dialyzed through a subclavian vein catheter and 50 patients dialyzed through an internal jugular vein catheter, 42% of patients in the subclavian group had a stenosis versus 10% in the jugular group.⁵⁷ As such, cannulation of the subclavian vein for hemodialysis access should be avoided if at all possible.

Presentation

Central vein stenosis can be completely asymptomatic. Often, an ipsilateral upper extremity access is created without knowledge of a central vein stenosis, which results in the rapid development of symptoms, the most common of which is arm edema. Patients with brachiocephalic vein stenosis can also present with facial edema. Other manifestations of central vein stenosis are aneurysmal dilatation of the extremity veins and the ipsilateral AVF, thrombosis of the access, inadequate dialysis, prolonged bleeding after use of the access, and superior vena cava syndrome.⁵⁴

Treatment

Elevation and compression of the upper extremity can occasionally be enough to relieve the edema associated with central

venous stenosis but is unlikely to be effective if there is an AV access on the ipsilateral extremity. NKF KDOQI guidelines recommend percutaneous transluminal angioplasty with or without stent placement as the preferred treatment for central venous stenosis.² In a small randomized study of percutaneous transluminal angioplasty and stent placement, 1-year primary patency in both groups was dismal at 12% and 11%, respectively.⁵⁸ However, the secondary patency at 1 year was 100% for percutaneous transluminal angioplasty and 78% for stenting. This marked difference in primary and secondary patency underscores the fact that multiple procedures are usually needed to maintain patency after endovascular management of central venous stenoses.

Catheter-Related Infection

There are three categories of catheter-related infection: exit site infection, tunnel infection, and bacteremia.² The 2019 NKF KDOQI guidelines² define an exit site infection as “Hyperemia, induration, and/or tenderness ≤2 cm from [the] catheter exit site. [It] may be associated with drainage from the exit site. It may or may not be associated with bacteremia.” A tunnel infection is defined as “Tenderness, hyperemia, and/or induration that extends along the subcutaneous tunnel. It may or may not be associated with bacteremia.” Finally, catheter-related bacteraemia is defined as “Clinical manifestations and at least 1 positive blood culture from a peripheral source (dialysis circuit or vein) and no other apparent source, with either positive semiquantitative (>15 colony-forming unit [CFU]/catheter segment) or quantitative (>100 CFU/catheter segment) culture.” The incidence of catheter-related bacteraemia ranges from 0.6 to 6.5 episodes per 1000 catheter days.⁵⁹ Consequences of bacteraemia include infective endocarditis and metastatic abscesses, the incidence of which increases when catheter salvage is attempted.⁵⁹

Treatment

An individualized approach to infected TDCs should be undertaken. As articulated in the 2019 KDOQI guidelines, “Options include CVC exchange via guidewire, CVC removal and reinsertion, CVC salvage, and concurrent antibiotic lock (particularly if the CVC is deemed to be the patient’s final access).” The predominant organism isolated from infected lines is Gram-positive bacteria (52%–84%), with *S. aureus* making up 21% to 43%.⁵⁹ Initial empirical antibiotic therapy should include broad-spectrum coverage of potentially resistant strains of Gram-positive organisms as well as Gram-negative organisms.⁶⁰ This coverage should be adjusted to a focused regimen when culture results become available. Amphotericin B or caspofungin, which has a more favorable toxicity profile, should be used if there is evidence of disseminated fungal infection or if patients demonstrate persistent fungemia after catheter removal.⁵²

Uncomplicated *S. aureus* catheter-related bacteraemia is generally treated with 4 to 6 weeks of antibiotic therapy; Gram-negative bacilli or enterococcus bacteraemia is usually treated with 7 to 14 days of therapy. Bacteraemia with *Candida* is usually treated with a minimum of 14 days of antibiotic therapy.

Complicated bacteraemia with septic thrombophlebitis or endocarditis is usually treated for 4 to 6 weeks and osteomyelitis for 6 to 8 weeks.⁶⁰

Catheter exit site infections alone can usually be salvaged with topical and systemic antibiotics without the need for catheter replacement.⁶⁰ However, there are several indications for immediate TDC removal with delayed TDC replacement: unstable patients, persistent fever or bacteraemia 48 to 72 hours after initiation of systemic antibiotics, metastatic infections, infection with particular microorganisms (e.g., *S. aureus*, *Pseudomonas aeruginosa*, fungi, or mycobacteria), or presence of a tunnel-site infection. A meta-analysis of 28 studies encompassing 1596 patients found that antibiotic lock solution and guide-wire exchange had similar cure proportions that were both superior to systemic antibiotics alone.⁶¹ Cure proportions were highest for coagulase-negative staphylococci, followed by Gram-negative rods and *S. aureus*.

Catheter Removal, Embolism, and Tethering

Removal of a TDC is typically straightforward and can be performed at the bedside or in an office setting. Local anesthetic with epinephrine is infiltrated into the skin around the course of the catheter, and the retention cuff is bluntly dissected away from the surrounding tissues. Once free, the catheter will frequently simply slide out. However, fractures can develop in the material of chronically indwelling catheters, which can become brittle. While rare, this can occur at sites of stress, such as the thoracic inlet especially with catheters based in the subclavian vein.^{62,63} Fractures can result in embolization of the most central portion of the catheter. This can be removed in the angiography suite with use of a wire snare retrieval system.⁶⁴

Occasionally, if a TDC has been in place for multiple years, a fibrin sheath can develop that can become adherent to the catheter, tethering it to the surrounding venous tissue and preventing removal, even after the retention cuff has been successfully dissected.⁶⁵ Multiple techniques have been described to free the TDC. These include sliding a larger vascular sheath over the catheter, using a laser sheath, or serially inflating a balloon within the catheter, which releases the tethering tissues and also dilates the vein simultaneously.⁶⁶

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A complete reference list can be found online at www.expertconsult.com.

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Hemodialysis Access: Failing and Thrombosed

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Based on a previous edition chapter by George H. Meier

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TREATMENT OUTCOME 2356

The maintenance of arteriovenous (AV) hemodialysis accesses in patients with end-stage kidney disease (ESKD) requires as much thought and consideration as their initial creation in order to individualize patient care and preserve future access options. The ESKD Life-Plan, a key concept detailed in the 2019 KDOQI Guidelines for Vascular Access, recommends the development of a written short- and long-term access plan with the patient and interdisciplinary team that is individualized to meet the patient's overall goals of care.

The long-term management of all dialysis patients should focus on preserving the adequacy of their dialysis treatments for as long as possible with limited interruption and minimal intervention while having a plan for succession in the future.

The flow disturbances, hemodynamic changes and cannulation injury associated with an AV access can initiate the development of progressive intimal hyperplasia (IH) resulting in luminal stenosis

and a reduction of blood flow within the AV access circuit.^{1–4} Clinically significant IH occurs primarily at the venous anastomosis of a prosthetic AV access (Fig. 177.1) and at “swing segments” of an autogenous AV access⁵ (Fig. 177.2). The swing segment is the part of the native vein that is circumferentially dissected and mobilized for anastomosis with the inflow artery. Intimal hyperplasia and resulting stenosis can also involve the ipsilateral central veins (e.g., subclavian), even in the absence of previous indwelling catheters.^{6–8} Interestingly, some patients develop intractable IH with the early onset of a critical stenosis, whereas others have a more limited response without any significant hemodynamic impact. The underlying mechanisms responsible for AV access IH are thought to be initiated by surgical trauma and shear stress with resulting biologic response in the vessel.⁹ The exact mediation of this process is still being elucidated but it occurs in the majority of patients with autogenous or prosthetic dialysis access.

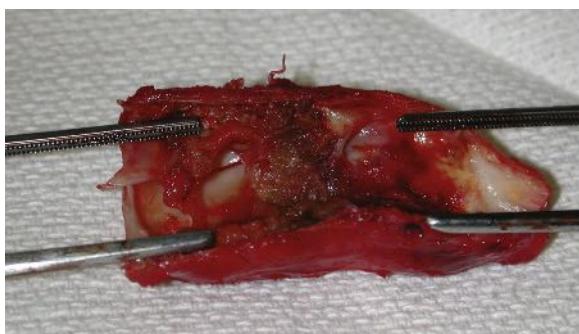


Figure 177.1 Surgical specimen demonstrating typical intimal hyperplasia at the venous anastomosis of prosthetic arteriovenous access.



Figure 177.2 Fistulogram demonstrating intimal hyperplasia throughout an upper arm arteriovenous access.

MEASURING ACCESS FUNCTION

The optimal management of progressive AV access IH is contingent upon detection of access flow dysfunction. A trending decline in dialysis adequacy measurements such as a urea reduction ratio of <65% and Kt/V, or abnormal recirculation, can indicate dialysis access flow dysfunction when combined with an abnormal physical examination. Kt/V can be quite useful to determine the adequacy of dialysis, where K is the rate of clearance of urea, calculated from the pre- and postdialysis measurements; t is the duration of dialysis; and V is the patient's volume of water. In this fashion, the "dose" of dialysis in a given session can be calculated.^{10–12} A Kt/V of 1.2 or greater is the standard for dialysis adequacy.

A dysfunctional AV access affects the prescribed dialysis dose in several ways. Adequate access blood flow is needed to meet a typical U.S. dialysis prescription which generally includes a dialysis machine pump speed of 350 mL/min or greater. A high pump speed allows the dose of dialysis to be delivered over a

shorter time. Recirculation, the retreatment of blood already filtered by the dialysis machine, can be insidious, often showing up as poorer solute clearances with each subsequent dialysis treatment.^{13,14} Ultimately, an unexplained decrease in the delivered dialysis dose without a change in dialysis prescription should prompt a referral for evaluation of the AV access.

Mechanisms of Access Failure

Flow Limitation

A functional AV access requires flow rates that exceed the pump speed of the dialysis machine. With standard U.S. dialysis machine pump speeds between 400 and 450 mL/min, AV access flows of 650–1000 mL/min are needed to avoid recirculation. In addition, adequate cardiac output is essential to maintain these flow rates. If cardiac output is marginal, decreased access flow may occur over the course of the dialysis session because of decreased preload associated with fluid removal during dialysis. Limitation of the access flow, by whatever mechanism, results in the recirculation of already dialyzed blood to the dialysis machine, greatly limiting the effectiveness of dialysis.^{11,15,16} Recirculation can result when the arterial needle pulls blood that has just been returned to the patient via the venous needle. This partially dialyzed blood is then dialyzed a second time, with decreased removal of substrate caused by lower concentrations in the partially dialyzed blood. This results in a decreased effective dialysis dose, with a longer duration of dialysis required to achieve the same clearance.

Venous outflow stenosis

A venous outflow stenosis is often indicated by an abnormally elevated venous pressure measurement during dialysis. The dialysis machine venous pressure transducer measures the resistance of the blood returning to the access. The maximum pressure tolerated is generally around 300 mm Hg and a venous alarm is triggered when this is reached. Dialysis personnel will troubleshoot the venous line or needle and/or reduce the pump speed to maintain flow through the extra-corporeal circuit in the event of high venous pressure readings. If an AV access stenosis is present, the patient may experience recirculation and a decrease in Kt/V. Clinically, venous outflow stenosis may be associated with prolonged bleeding from cannulation sites. Examination of the access may demonstrate excess pulsatility and decreased thrill.

Arterial inflow stenosis

Arterial inflow stenosis can similarly limit flow through the AV access, but in this case, both needles are on the "venous side" of the stenosis. A clinically significant arterial inflow stenosis can be identified on physical exam by a weak pulse in the access and decreased thrill, poor access augmentation with outflow compression and elevated arterial pressure during dialysis. The arterial pressure transducer, measuring the pressure of blood coming out of the arterial line, will be an abnormally high negative number as the pump tries to "pull" blood across the stenosis, indicating inadequate inflow into the AV access.



Figure 177.3 Repeated cannulation at the same site resulted in a pseudoaneurysm associated with infiltration and ulceration.

Cannulation Location

Another important cause of recirculation is inadequate separation of the cannulation needle tips. Access needles are typically one inch in length and 16 gauge (or 17 gauge in new autogenous arteriovenous fistulas) and placed in opposite directions to assure that the tips are separated by at least three inches. Recirculation can result from inadequate cannulation zone length from limited transposition or inability of adequate needle rotation due to limitations from excessive AV access depth.¹⁷

Aneurysms or pseudoaneurysms may adversely impact the efficiency of dialysis. Rotation of needle stick sites can reduce the incidence of pseudoaneurysm formation. If aneurysms/pseudoaneurysms are excessively large, recirculation can occur because of the stagnant flow within the pseudoaneurysm. In addition, pseudoaneurysms can be problematic because they are often the sites of infiltration and bleeding (Fig. 177.3).

Causes of Cannulation Failure

If the vein is too deep or too small in diameter for reliable cannulation (exact numbers subjective as expertise of personnel differ, but generally deeper than 6 mm and smaller than 5 mm), dialysis may be problematic, even with adequate flow. In a morbidly obese patient with ESRD, a vein of any size may be inadequate because of the excessive depth from the overlying skin and soft tissue through which the vein must traverse.^{18–20} In these patients, superficial transposition or “elevation” of the vein conduit may be necessary to allow maturation and reliable cannulation.^{21–24}

CAUSES OF ACCESS FAILURE

For both autogenous and prosthetic AV accesses, the most common cause of access failure is the development of venous outflow stenosis or stenosis of the autogenous access itself resulting from IH.^{25–29} Additional factors that can contribute to access failure and thrombosis include systemic hypotension, underlying thrombophilia, limited cardiac output, or trauma

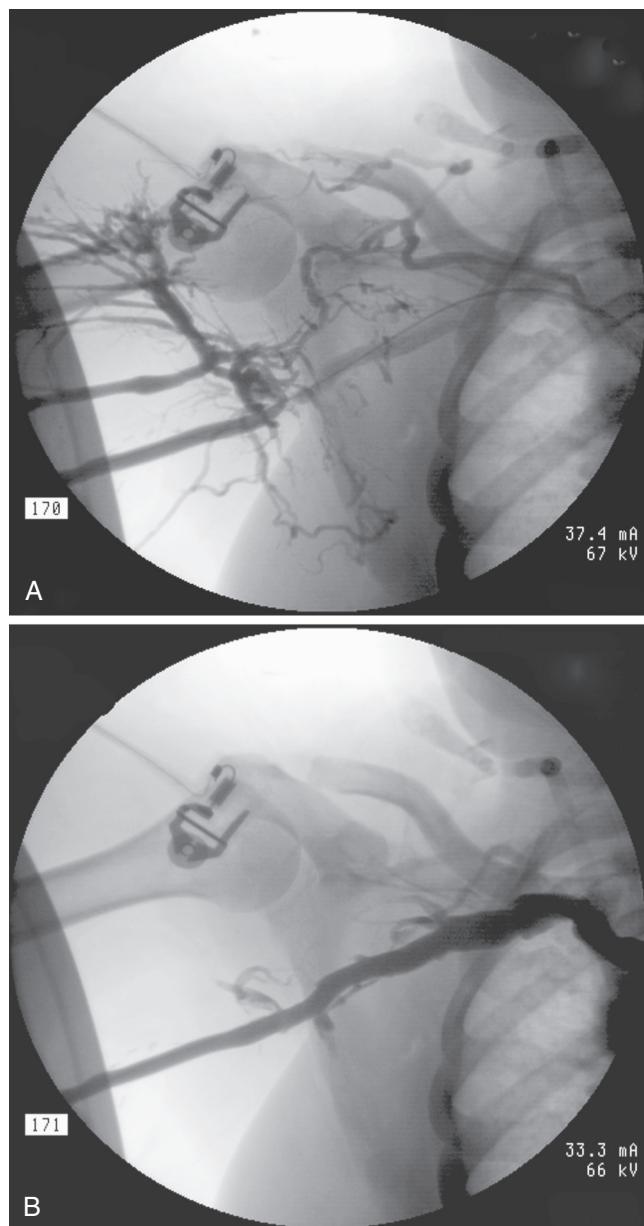


Figure 177.4 A stenosis in the axillary vein secondary to intimal hyperplasia is shown (A) before and (B) after successful treatment with an 8-mm high-pressure angioplasty balloon. Note the resolution of the venous collaterals.

to the access itself with repeated cannulations. Dialysis access-related steal syndrome may also lead to an inability to use the AV access due to discomfort and pain and may require further surgical intervention for inflow revision or ligation for limb ischemia.

Central venous stenosis may result from protracted use of devices residing in the central veins such as central venous catheter use, pacemakers, and defibrillators and it is commonly revealed once a high flow, ipsilateral autogenous or prosthetic access has been placed (Fig. 177.4). The higher volume flow associated with an ipsilateral dialysis access may exceed the venous outflow capacity depending on the adequacy of collateral vein development. Central venous stenosis can lead to chronic venous hypertension. Stenoses may be located anywhere in the

deep venous system from the subclavian vein to the superior vena cava, but is particularly common at sites of compression and turbulence, such as at the thoracic outlet (sometimes referred to as thoracic inlet in dialysis circles). Another unavoidable factor that contributes to access failure is the necessary puncture of the conduit that leads to IH. Finally, IH occurs at the venous anastomosis of prosthetic AV access, theoretically aggravated by the excess turbulence associated with the size and compliance mismatch between the prosthetic graft and the outflow vein (see Ch. 5, Intimal Hyperplasia).

Detection of Access Failure

History

Vascular surgeons are frequently asked to evaluate failing vascular access when dialysis cannot be effectively accomplished. The dialysis center may report difficulty sticking the access, elevated venous pressure, prolonged bleeding after decannulation, excessive recirculation, high negative inflow pressure or a combination of factors all resulting in ineffective dialysis. The vascular surgeon should obtain as much information as possible from the dialysis unit in order to more accurately determine the surgical cause and develop an appropriate remediation strategy.

Physical Examination

Following an appropriate history, assessment of the vascular access continues with the physical examination, which with practice can be a reliable indicator of access function. On inspection, skin integrity should be intact, without areas of discoloration or vitiligo, scabbing or infection, and there should not be swelling or collateral veins, which may indicate central venous stenosis. The presence of isolated ipsilateral chest wall, shoulder or arm/hand edema may be a sign of elevated venous pressures due to venous stenosis or occlusion.^{30–32} On arm elevation, an autogenous access should completely collapse, but when there is outflow stenosis, the access remains distended. When the outflow vein is compressed, the pulse in an autogenous access should augment. On palpation, a continuous thrill should be present near the arterial anastomosis, and continue several centimeters into the outflow vein. The outflow vein should be easy to compress. If the access is excessively pulsatile, then a venous outflow stenosis is likely. In most cases, a thrill distal to an area of pulsatility suggests the location of the stenosis. Pseudoaneurysms of the access may result in local pulsatility in the areas of enlargement, independent of venous outflow issues. On auscultation, the access should have a continuous low pitch systolic and diastolic bruit. In the presence of stenosis, the bruit is often high pitch, and noted during systole alone.

Clinical Indicators

Various clinical signs and symptoms may reflect access dysfunction and include difficult or painful cannulation, decrease in delivered dialysis dose, inability to achieve target blood flow, dialysis machine arterial or venous pressure alarming, and prolonged bleeding at the needle puncture sites upon decannulation. The

presence of a clinical indicator in conjunction with an abnormal physical examination of the access should prompt further evaluation with duplex ultrasound and/or angiography to treat any underlying stenosis and prevent thrombosis (see the section “Interventions for Failing Access”, below).

Failure to Mature

Following autogenous AV access creation, the process of fistula maturation is necessary to achieve usability and support the dialysis prescription. Hemodynamic alterations in the artery and vein of the AVF result in vessel remodeling, leading to a progressive increase in diameter and blood flow in the fistula. A physiologically mature fistula is defined as having an internal diameter ≥ 5 mm and an access blood flow of ≥ 500 mL/min, and often achieves this within 4–8 weeks.³³ Since fistula maturation failure rates are between 20% and 60%, and although many can be salvaged, it is important to allow time for referral, creation and treatment of dysfunction, as the average time to cannulation is 4.4 months in successful fistulae.³⁴

Evaluation of fistula maturation should occur 4–6 weeks after creation, and if not sufficient, the access should be interrogated for underlying cause. Inadequate inflow may be identified by a weak pulse/thrill, poor augmentation with venous outflow compression or a high-pitched bruit at the site of arterial inflow stenosis. Ultrasound can additionally help delineate vein diameter, flow volume and the presence of stenosis within the access circuit. Excessive number or size of tributary or branch veins may inhibit fistula maturation, by diverting blood from the main cannulation segment, making cannulation difficult and necessitating coiling or ligation.

Following corrective measures to address fistula maturation, successful fistula cannulation depends on avoiding excessive depth, a suboptimal location or inadequate cannulation segment length.³³ It is important to note that fragile, immature veins that lack sufficient arterialization may not withstand the trauma of repeated cannulations. Ideally, only an experienced technician should attempt cannulation of a new AV access, in order to avoid infiltration and hematomas, that may lead to further problems cannulating the access (both autogenous and prosthetic) and predispose to the development of a stenosis.

An open dialogue between the access surgeon and the dialysis center personnel is important to determine the cause of any cannulation difficulties to both optimize maturation and prolong the functional life of the access.

Access Surveillance Methods

It is important to note that routine surveillance has not been shown to improve the effective lifespan of dialysis access and is not currently recommended by KDOQI Guidelines.³⁵ In selected cases, however, there are several techniques that can be used to further evaluate dialysis access dysfunction and prevent access thrombosis.

Venous Pressure Measurement

Static venous pressure is perhaps the easiest of the surveillance techniques and the most widely used in dialysis centers.

Elevated static venous pressure is less predictive of access failure in autogenous fistulae compared with grafts.^{36–40} To measure this value, a manometer is connected to the dialysis needle while the dialysis pump is turned off, and normalized to systolic blood pressure. The ratio of intragraft to systemic pressure ≤ 0.4 is considered normal, while a ratio ≥ 0.5 is considered abnormal, and if reflected as a trend rather than a single measurement, is an indication for referral for a diagnostic angiogram.

Intra-access Flow Rate

Blood flow (mL/min) in the access can be quantified and may be more accurate in predicting access failure than clinical examination alone.⁴¹ There are several methods, including thermodilution,⁴² and ultrasound-dilution, the most commonly used method.^{43–45} Using this technique, a bolus of isotonic saline is injected into the blood stream and dilutes the blood and the corresponding ultrasound velocity. As the saline passes through the blood lines, a sensor registers an indicator curve that can be used to calculate the flow rate. There are several advantages of this technique. First, flow is measured by saline dilution with the dialysis lines reversed, producing a stable measure of access flow that is independent of the volume of the saline injected. Second, access recirculation can be assessed objectively at the same time with the same equipment using the needles in their normal orientation.^{36,39,46–48} Therefore, access flow and access recirculation can be assessed repeatedly over time to provide two independent measures of access function.

The development and progression of an access stenosis is highly variable. Generally, a flow rate of less than 600 mL/min predicts thrombosis in a prosthetic access, although the thresholds for autogenous accesses are typically lower but not precisely defined.^{15,45,49} However, it is important to note that current data does not support that surveillance with preemptive angioplasty decreases thrombosis rates or prolongs long-term patency in grafts. Consequently, the National Kidney Foundation Kidney Disease Outcome Quality Initiative (KDOQI) Clinical Practice Guideline for Vascular Access: 2019 Update suggests reliance primarily on clinical monitoring of grafts to detect stenosis, or referral for evaluation when the graft flow is ≤ 600 mL/min or $>25\%$ lower than baseline.³⁵

Duplex Ultrasound Access Surveillance

Duplex ultrasound can be used to identify a stenosis and to measure the peak systolic velocity on either side of the stenosis. A velocity ratio >2.0 indicates a clinically significant stenosis within an AV graft.^{50,51} There is limited data regarding the utility of duplex ultrasound in identifying significant stenotic lesions in autogenous fistulae. Duplex ultrasound can be useful in confirming any suspected abnormalities in access flow detected by physical examination, although it may not add much beyond a thorough examination by an experienced clinician. For these reasons, duplex ultrasound for AV access is generally reserved for those situations in which the clinical examination is unclear, such as in the setting of multiple aneurysms or identification of nonocclusive thrombus. Ultrasound can also be used to determine blood flow (mL/min) in the access.

Catheter-Based Contrast Imaging

Catheter-based contrast imaging is essential to maintaining or improving dialysis access function, but should not be considered part of surveillance, but rather intervention for suspected or known lesions. Contrast imaging is, by definition, invasive because needle or catheter access involves skin puncture. In general, contrast imaging provides anatomic information rather than physiologic data, although access flow can be inferred from the anatomic images. For this reason, surveillance and monitoring are complementary to contrast imaging, with anatomic contrast imaging providing supporting evidence for the alteration of access function identified by physiologic monitoring techniques.^{52,53} In addition, once the underlying anatomic defects are identified, intervention can be performed in the same setting as the diagnostic study. Performing the diagnostic and therapeutic procedures at the same time can avoid the risk of access failure during the intervening time associated with a staged approach.

INTERVENTIONS FOR FAILING ACCESS

Open Surgical Techniques

Revision for Stenoses

Open surgical revision of a stenotic segment within the AV access can improve both flow and function. The challenge is to define the underlying “target” lesion responsible for the diminished flow. As with all access interventions, complete fluoroscopic imaging from the arterial inflow to the right atrium is necessary, and this is generally done at the time of operative revision, and is compared with previous diagnostic imaging to determine the target lesion. The advantage of simultaneous imaging is that questions concerning the access can be answered in “real time.”

Surgical revision for stenosis is generally performed using an interposition graft or a patch angioplasty (Fig. 177.5). Both techniques have advantages and disadvantages, can be effective and are widely used. The use of an interposition graft to bypass a stenosis at the venous outflow of a prosthetic access proximalizes the venous anastomosis, thereby limiting the length of available outflow vein that can ultimately be used to construct any new permanent access. Patch angioplasty simply enlarges the area of stenosis without removing the local disease process (or consuming any available length of the vein), theoretically leading to a higher incidence of recurrent stenosis. However, results of these two techniques have comparable patency.^{54–56}

Revision for Other Problems

The presence of multiple outflow vein branches can limit venous cannulation length and can prevent sufficient dilation of the primary venous cannulation segment during the maturation period. The significance of collateral veins may not be obvious at the time of initial access placement, but may become apparent if the access fails to enlarge above a large branch. In this situation, ligation or coiling of collateral branches may promote augmentation of the main cannulation segment, enabling AVF usability.

Translocation or “elevation” of a deep, poorly palpable autogenous AV access may be necessary to allow successful needle



Figure 177.5 Collateral veins with venous hypertension due to central venous stenosis associated with a tunneled dialysis catheter.

cannulation. This is a common problem, particularly in obese patients. Overlying fat and subcutaneous tissue may make palpation and demarcation of the contours and margins of an autogenous access difficult, thereby limiting reliable cannulation, even in the presence of a mature AV access with sufficient diameter and flow. Transposition and/or superficialization to a more superficial location may allow access utilization that would otherwise be impossible.

The technique for superficial transposition is similar to that used in the second stage of a two-stage basilic vein transposition. In this situation, the depth of the vein from the skin is generally greater than its diameter. There are two basic approaches to making the vein accessible. The first is to remove the fat and subcutaneous tissues overlying the vein and then re-approximate the subcutaneous tissues, which produces a shallower tissue depth to cannulate the access. Bronder et al.²³ reported favorable results with this technique in a large series of patients.

The second technique involves transection of the vein, with superficial transposition and re-anastomosis. Although it may be possible to simply reattach the vein to its previous anastomosis, the access surgeon should be prepared to re-site the arterial anastomosis more proximally to accommodate the loss of vein length resulting from the new, superficial tunnel, taking care to leave a straight, superficial, and palpable segment with sufficient length for needle rotation. After transection of the vein, the longer segment is tunneled in a subcutaneous course. The vein is then carefully re-anastomosed to avoid unnecessary tension. As with the two-stage basilic vein transposition, the vein has already adapted to arterial pressure and flow, making the surgery safer and easier because the vein is somewhat easier to manipulate, although some venous hypertension is associated with the arterial communication. Any other abnormalities in the access can be addressed at the same time.

Percutaneous Techniques

Percutaneous techniques for failing and thrombosed accesses are similar to those used in other vascular distributions. Once

the complete circuit from the arterial inflow to the right atrium has been imaged, specific approaches to the underlying pathology can be performed. Despite the similarities, the lesions encountered in AV access are much different from arterial lesions, typically resulting from atherosclerosis. The fibrotic, rubbery stenoses characteristic of IH do not routinely dissect, like atherosclerotic stenoses, but more commonly tear or are disrupted as a result of the obligatory higher insufflation pressures applied during balloon angioplasty (Fig. 177.6).

Balloon Angioplasty

Of all the percutaneous interventions performed on AV accesses, plain old balloon angioplasty (POBA) is the most common.^{57–61} The balloon is placed within the area of stenosis and inflated to a pressure that will eliminate any focal stenosis or “waist” seen on the distended balloon. Treatment is repeated until all areas of presumed outflow stenosis are adequately treated. In contrast to arterial lesions, venous stenoses caused by IH routinely require high pressures to resolve, often 20 atmospheres or more. With these increased pressures, trauma to the vein can occur, which can stimulate the IH process, leading to recurrent stenoses. For this reason, some physicians advocate switching to a cutting balloon before high-pressure dilation,^{62–66} allowing subsequent balloon angioplasty to be performed at much lower pressures.

However, two randomized controlled trials comparing cutting balloon to high-pressure balloon angioplasty in fistulae showed no difference in clinical or treatment success, and no difference in 6-month patency.^{63,64,67} There are reports of drug-coated balloon use in dialysis access and a few trials with mixed results so far,⁶⁸ but there is ongoing investigation.

A technique termed “balloon-assisted maturation (BAM)” has been described to facilitate autogenous access maturation.^{69–72} In this technique, the outflow vein is serially dilated with progressively larger balloons until a target vein diameter is achieved. The vein is allowed to heal between the serial dilations (hopefully without the development of IH), resulting in a larger venous conduit once healing is complete. This approach was first described in 2001 by Turmel-Rodrigues et al.,⁷³ who reported a 97% success rate in 52 dysfunctional and 17 thrombosed forearm autogenous accesses with a mean age of 10 weeks. The corresponding primary and secondary success rates at 1 year were 39% and 79%, respectively. Subsequent authors have published similar results, advocating a policy of early intervention in patients with non-maturing forearm autogenous accesses.⁷⁴ However, the long-term functional outcome of accesses treated by these techniques remains undefined.

Stenting

An intraluminal stent may be used to treat any residual stenoses or dissections after balloon angioplasty. However, in-stent restenosis is quite common with the use of bare metal stents and their use in dialysis access conduits has increasingly fallen out of favor.^{75–77} Conversely, covered stents offer several advantages.^{75,78–82} These devices are essentially fabric-covered stents designed to prevent the ingrowth of hyperplastic tissue, and

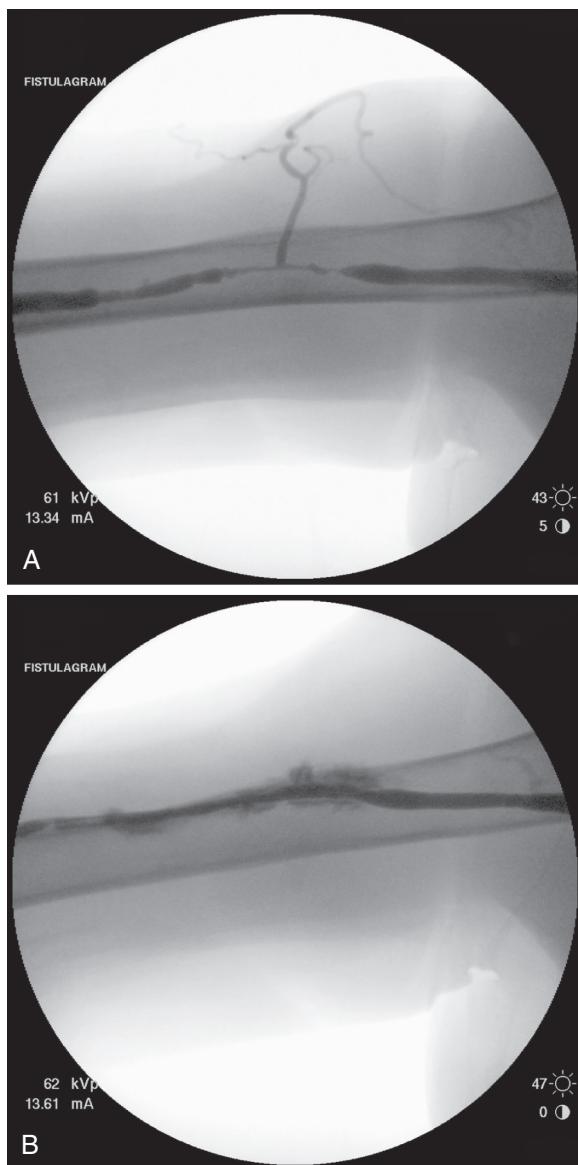


Figure 177.6 A diffuse, high-grade stenosis in an autogenous access (A) with disruption and contrast extravasation (B) after balloon angioplasty with a high-pressure balloon.

thus avoid the early failures seen with bare metal stents. Notably, covered stents have been shown to have a patency advantage when treating stenoses at the venous anastomosis of prosthetic AV accesses, and are limited only by their expense.^{58,78,83} Covered stents can also be used to prolong prosthetic AV access use in the presence of a large pseudoaneurysm or a degenerated graft.^{84–89} Although cannulation of this segment would be generally discouraged as off-label usage and have the potential to increase infection. The durability of this method is not yet established, but may serve as a temporary bridge until further access or formal access revision can be performed in certain clinical situations.^{90,91}

Hybrid Approach

Therapeutic endovascular procedures are often performed at the time of the diagnostic procedure, as outlined previously.



Figure 177.7 Patient with brachial–basilic autogenous arteriovenous access with stenoses at both the arterial anastomosis and within the outflow vein. A hybrid approach was performed, including (A) balloon angioplasty of the stenosis in the outflow vein and (B) open surgical revision of the arterial anastomosis.

Similarly, open, surgical revision can be performed at the same time as the diagnostic study if it is performed in an operating room, commonly a hybrid suite. The specific approach depends on the underlying pathology. A venous outflow stenosis may be treated by percutaneous techniques, whereas an arterial anastomotic stenosis may require open surgical revision. The catheter-based imaging can be performed in the operating room with either a portable C-arm or a fixed imaging system, and the choice of definitive intervention (open or endovascular) is dictated by the findings (Fig. 177.7). Thus, hybrid procedures are often the most efficient for patients and surgeons as all necessary treatments can be performed at the same session.

INTERVENTIONS FOR THROMBOSED ACCESS

Autogenous Arteriovenous Access

The treatment of thrombosed AV accesses may be difficult, particularly for autogenous accesses. In this case, the endothelial surface may be significantly compromised, because

thrombus does not usually form in native veins without some underlying abnormality. Thrombus removal (i.e., thrombectomy), without treatment of underlying lesion, often leads to recurrent thrombosis because the luminal endothelium is abnormal and the initiating reason for thrombosis remains untreated. For these reasons, open surgical thrombectomy was often avoided for autogenous AV accesses.^{92–96} Palmer et al.⁹⁷ reported technical success in 7 of 10 patients with thrombosed autogenous accesses treated with an open, surgical approach. However, the corresponding 6-month primary and secondary patency rates were only 51% and 69%, respectively, for the accesses that were initially treated successfully. More recently, Cull et al.⁹⁸ reported excellent results and described a detailed and efficient technique to remove thrombus. The secondary functional patency was $74\% \pm 5\%$ at 6 months and $61\% \pm 6\%$ at 12 months. Although the role for surgical thrombectomy remains unresolved, it certainly merits strong consideration, and it is likely to be most effective for limited or short-segment thrombotic occlusions. Additionally, it preserves an autogenous access which can be difficult to re-establish.

Other series reported good results with percutaneous mechanical thrombectomy, but long-term data are still lacking.^{99–102} Shatsky et al.¹⁰³ reported their experience using the Arrow-Trerotola device (Teleflex Medical, Research Triangle Park, NC) in a series of 44 thrombosed autogenous accesses. Their primary patency rates were 38% at 6 months and 18% at 12 months; secondary patency rates were 74% and 69% at 6 and 12 months, respectively. Although primary patency was limited, repetitive treatments seemed to be possible.

Prosthetic Arteriovenous Access

Prosthetic AV accesses tend to thrombose more frequently than mature autogenous accesses. As the most common failure mode is IH at the venous anastomosis, prosthetic accesses can usually be salvaged, providing long-term access without a significant disruption in a patient's dialysis schedule. In addition, prosthetic AV accesses tolerate balloon thrombectomy better than autogenous accesses because they do not have a viable endothelium, which is potentially susceptible to mechanical injury with thrombectomy. Segments of the prosthetic graft itself can also be replaced as necessary to remediate any graft degeneration or localized soft tissue infections, often continuing the dialysis schedule using the residual, unaffected segment. In fact, use of so-called "early cannulation" prosthetic access (compared with autogenous accesses) is worth considering as a catheter-sparing strategy in certain patients in accordance to their ESKD Life-Plan.^{35,104}

Open Surgical Techniques

The open, surgical treatment of a thrombosed AV access is predicated on the rapid removal of clot and definitive treatment of the underlying cause of failure. Most commonly, the access thrombosis is a result of venous outflow stenosis,

although there are other mechanisms of failure. For example, a large pseudoaneurysm at a cannulation site may result in pooling of blood within the dilated segment with the stagnant flow leading to thrombosis. Similarly, inadequate arterial inflow may lead to graft thrombosis in the absence of venous outflow issues. Therefore, the surgeon's first task is to determine the underlying cause of the thrombosis. The operative plan and the site of the incision are both dictated by the presumed underlying pathology.

The thrombus within an AV access can usually be removed using an appropriately sized balloon thromboembolectomy catheter; typically, a 4-F catheter is used for 6-mm diameter grafts. The location of the incision is based upon the anticipated revision approach. If the plan is for open revision, in the absence of any other obvious pathology, venous outflow stenosis is the probable cause and the focus of the likely revision. If the access has another significant obvious pathology, such as large pseudoaneurysms, it may be appropriate to incorporate this finding into the planning as well. If the plan is for hybrid approach, the apex of the graft is useful as it is rarely cannulated for dialysis and allows access to both arterial and venous ends.

Once the access is cleared of thrombus, it should be imaged from the arterial inflow to the right atrium, ruling out any draining or central venous lesion that may predispose to a recurrent thrombosis. All venous anastomotic or outflow lesions should be addressed. For an open surgical option, patch angioplasty may be used to manage typical venous outflow stenosis (Fig. 177.8). This approach has the advantage of preserving the outflow vein, but it requires an extensive dissection in a scarred operative field. As an alternative, an interposition graft can be used to essentially "proximalize" the venous anastomosis, avoiding scar tissue at the prior operative site and providing the best-quality outflow. In the era of endovascular availability, knowledge and skill, a hybrid approach is frequently used and favors complete thrombectomy and subsequent PTA or stenting of lesions avoiding further surgical dissection.

Prosthetic AV accesses can usually be used for dialysis after open, surgical thrombectomy because there is often a sufficient length of the graft left undisturbed. For example, if the

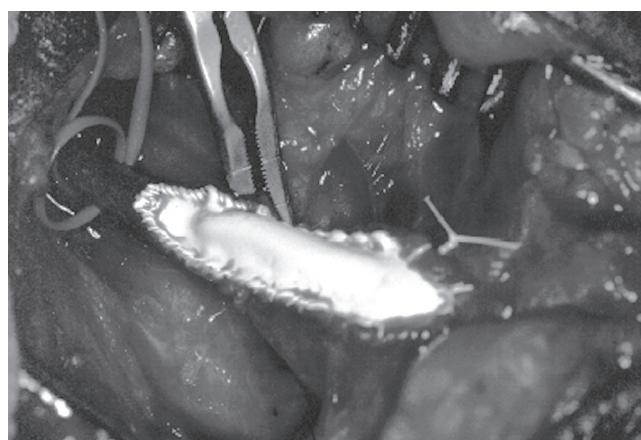


Figure 177.8 Surgical patch angioplasty using an expanded polytetrafluoroethylene patch at the venous anastomosis of a thrombosed prosthetic access.

access-related problem occurs near the arterial anastomosis of a C-shaped configuration (e.g., brachial–axillary configuration), a distal segment closer to the venous anastomosis can be used for cannulation. Similar options for immediate cannulation may exist after open, surgical thrombectomy of autogenous accesses, but the need for a temporary catheter is likely increased. Recently, early cannulation grafts (able to be used immediately after implantation) have been advocated by some to avoid catheter placement in revisions or even creation of new dialysis accesses.¹⁰⁵

Percutaneous Techniques

The use of percutaneous techniques for prosthetic access thrombosis was described in 1984 by Glanz et al.^{106,107} in an effort to both avoid the loss of vein associated with surgical revision and to allow outpatient treatment. Since that time, the use of balloon angioplasty for access circuit stenosis associated with AV access failure is now considered first-line treatment.

Percutaneous Mechanical or Chemical Thrombectomy

Several percutaneous techniques exist to treat a thrombosed prosthetic access. In most cases, crossed sheaths (typically 6F, one in direction of arterial and other venous) are placed within the clotted access. The approach can then be chemical, mechanical or a combination for removal of clot. In chemical, a thrombolytic agent is infused to remove the bulk of the thrombus and provide some antegrade flow (Fig. 177.9).^{108–114} Typically, 2 to 4 mg of tissue plasminogen activator is placed into the clot. The arterial and venous ends of the prosthetic access are intermittently occluded to allow the entire prosthetic graft (and thrombus) to be infused with lytic agent (Fig. 177.10). In the “lyse-and-wait” technique (chemical), the thrombolytic agent is given, and the patient is monitored in the holding area for a “return of flow.”^{110,113–116} In the “lyse-and-go” technique (chemical and mechanical), the patient is immediately taken to the operating room or interventional suite for further percutaneous intervention. Typically an 8-mm by 8-cm high-pressure balloon (i.e., 8 × 80 balloon) is introduced through a sheath

within the prosthetic access, and balloon angioplasty of the entire graft, including venous outflow, is performed. Any areas of residual stenosis are treated with balloon angioplasty. If there is a residual thrombus or “plug” at the arterial end, a balloon catheter is used to facilitate extraction (Fig. 177.11). Any residual, partially lysed clot is further fragmented by repeat balloon angioplasty. Ultimately, the residual debris is released into the pulmonary circulation, although this is not usually associated with any systemic effects or complications.^{117–121}

Alternatively, a mechanical thrombectomy device can be used alone or in combination with the lytic agent to debulk

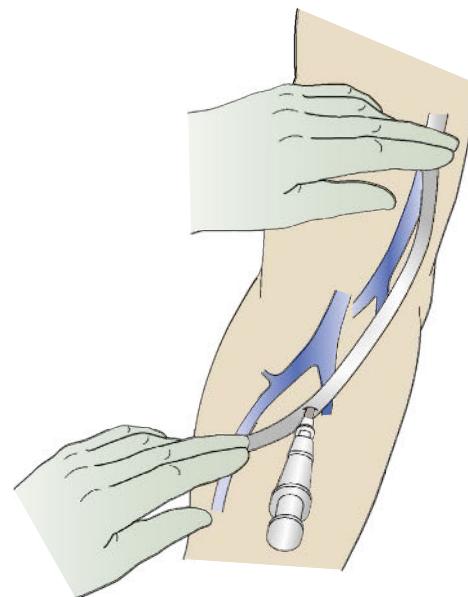


Figure 177.10 Thrombolytic agent is infused into the thrombosed prosthetic access, and both the arterial and venous ends are serially occluded to diffuse the agent throughout the thrombus.

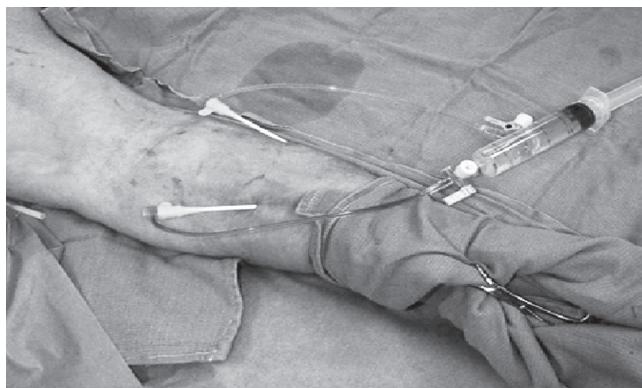


Figure 177.9 The crossed sheaths, typically used for endovascular treatment of a thrombosed prosthetic access, are shown with sheaths directed toward the arterial and venous ends.

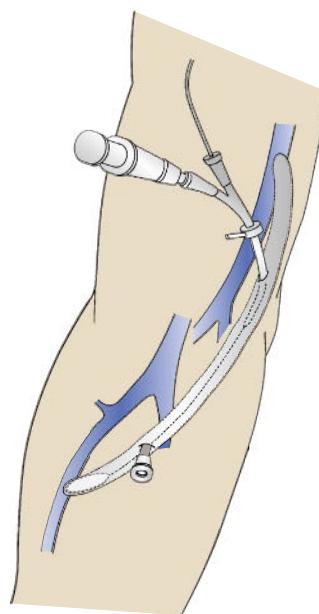


Figure 177.11 If a thrombus or plug persists at the arterial anastomosis, a conventional thromboembolectomy catheter can be passed through the sheath to facilitate removal.

or remove thrombus within the prosthetic access. The most common devices used for this purpose are the Fogarty catheter, Cleaner (Argon Medical) AngioJet,^{122–126} the Arrow-Trerotola device,^{114,127,128} and the Hydrolyser (Cordis Corp, Bridgewater, NJ).^{129–132} All these devices have their proponents, but none has proved superior in clinical settings.

Stenosis Treatment

Once the prosthetic AV access is cleared of thrombus, the next challenge is to treat the underlying cause of failure. Again, complete fluoroscopic imaging from the arterial inflow to the right atrium is necessary to fully define the potential problems leading to the failure. Once the cause or causes have been defined, treatment is focused on the offending lesion(s). In general, a 6-mm prosthetic graft can easily tolerate balloon dilation to 8 mm. The fibrotic nature of IH may cause the offending lesion to recoil significantly, and thus prolonged high-pressure insufflations are often needed. Although ultra-high-pressure balloons may allow dilation of stubborn lesions in the venous outflow, tearing or disruption of the vein can occur. Some physicians advocate the use of cutting balloons followed by balloon angioplasty for refractory stenoses in an effort to better control the applied force (discussed previously).

Balloon angioplasty is appropriate for any significant and symptomatic central vein stenosis. Although balloon angioplasty alone in this situation is commonly associated with early recurrence, bare metal stents do not provide any significant patency advantage because of recurrent IH within the stented segment or “in-stent” stenosis. Alternatively, covered stents may be considered for recurrent central venous lesions that have limited response to PTA, taking care to avoid “jailing” of outflow or contralateral veins during stent placement. Covered stents may also be beneficial in anastomotic venous outflow stenoses, which are more traditionally treated by balloon angioplasty alone. Haskal et al.¹³³ showed that covered stents dramatically improved patency (51% in the covered stent group vs. 23% of those with balloon angioplasty alone at 6 months) in patients with failing hemodialysis grafts. Although this overall patency difference is significant, the cost-effectiveness of these relatively expensive devices is less clear.¹³⁴ Further studies also seem to support this concept,^{80,85,135–137} but additional experience is needed to define their specific roles. Open surgical revision for central venous stenosis or occlusions with the Hemodialysis

Reliable Outflow (HeRO, Merit Medical, Salt Lake City, UT) graft, a subcutaneous outflow component which is connected to prosthetic graft, has also been reported.¹³⁸ In their multi-center report, Gage reported 24-month primary patency of 42.9% and secondary patency of 86.7%. Central venous stenosis is particularly challenging and will continue to receive attention as the availability and use of central venous catheters and devices continue to increase.

Hybrid Techniques

The two components of successful AV access thrombectomy and restoration of AV access flow are removal of the thrombus and treatment of the underlying cause of access failure. Removal of thrombus can be achieved by percutaneous methods or open balloon thrombectomy. Either approach can often be performed with the patient under local anesthesia with sedation and, in the case of open, using a small incision over the prosthetic graft (Fig. 177.12). Once the thrombus is removed, complete imaging from the arterial inflow to the right atrium can be performed. With this approach, treatment of any remote, underlying lesion can be accomplished. The potential advantage of open thrombectomy is avoiding the potential to embolize residual thrombus into the pulmonary circulation, which may occur with the total percutaneous approach. Finally, any venous anastomotic stenoses can be treated with balloon angioplasty, thereby preserving the available length of the outflow vein, frequently compromised with the open, surgical approaches. In many ways, this hybrid procedure has the potential for improved results with reduced morbidity. Unfortunately, the published results of this hybrid technique are limited.^{99,139,140}

TREATMENT OUTCOME

Unfortunately, there are few long-term studies comparing these various approaches. The majority of the studies compare open, surgical thrombectomy for prosthetic access with the percutaneous approach.¹⁴¹ Despite limitations in the quality of the evidence, the outcomes for the two approaches appear to be comparable. The two variables that appear to have the most impact on outcome include the effectiveness of the thrombectomy and the treatment of the underlying cause of



Figure 177.12 Hybrid technique for thrombectomy and angioplasty of a prosthetic arteriovenous access. (A) A thromboembolotomy catheter is passed proximally and distally through a small incision in the graft near the venous anastomosis. (B) Conventional balloon catheters are used for thrombectomy. (C) A sheath is then placed through the arteriotomy to facilitate imaging and potentially perform an endovascular intervention.

thrombosis rather than the specific approach. Each center has unique skills and resources that will determine the optimal approach whether it be open, percutaneous or hybrid. Until alternative approaches are better validated, the “best” treatment will remain a topic of debate.

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Hemodialysis Access: Nonthrombotic Complications

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The National Kidney Foundation Kidney Dialysis Outcomes Quality Initiative (KDOQI) has updated guidelines for 2019. Recognized complications are: bleeding, infection, aneurysm/pseudoaneurysm, seroma, access-related hand ischemia (ARHI) or steal syndrome, venous hypertension, neuropathy, and cardiopulmonary complications.^{1–3}

BLEEDING

The most frequent bleeding complications are prolonged access-site bleeding and easy bruising. Needle dislodgement is extremely rare.⁴ End-stage renal disease (ESRD) is associated with increased gastrointestinal bleeding, spontaneous retroperitoneal bleeding, and hemorrhagic transformation of stroke.^{5–11} Contributing factors include anemia, acquired defects of primary hemostasis, thrombocytopenia, repeated procedures, and medications.

Etiology

At normal hematocrit levels, platelets and plasma reside at the vessel periphery, facilitating activation and aggregation at injury sites. In anemia, rheology changes.^{12–14} As hematocrit declines, nitrous oxide (NO) activity increases, causing vasodilation and platelet inhibition.^{15,16}

Moderate thrombocytopenia is common in ESRD. Increased bleeding is predominantly due to uremia-induced platelet dysfunction.^{15–18} Risk increases markedly when BUN is >100 mg/dL (35.7 mmol/L). Uremia is associated with multiple defects of platelet function.^{13,18–21}

Many medications increase chronic kidney disease (CKD) bleeding risk. Beta-lactam antibiotics cause platelet dysfunction at high levels, and are only partially cleared by dialysis.²² At extremely high levels, penicillins alter antithrombin III activity, causing heparin-like abnormalities.²³ Antiplatelet agents are common among HD patients due to high rates of cardiovascular disease (CVD). Su et al.'s meta-analysis of antiplatelet effect on major cardiovascular events in patients with CKD noted a beneficial effect on prevention of access failure (OR 0.52; 95% CI, 0.31–0.73), 15% reduction of odds of cardiovascular events, 23% reduction of MI.²⁴ Antiplatelets are recommended for high risk patients by the National Kidney Foundation.²⁵ A recent meta-analysis showed increased bleeding risk (RR = 2.78; 95% CI 1.63–4.76) with dual antiplatelet agents, but no increased risk with monotherapy (RR = 1.08; 95% CI 0.53–2.19),²⁶ suggesting reserving dual antiplatelet therapy for secondary prevention of CVD following intervention.

Oral anticoagulation is also common in CKD, as almost 20% have atrial fibrillation.²⁷ Most receive warfarin, however novel oral anticoagulation (NOAC) use is increasing.²⁸ NOACs are renally cleared in varying degrees, and initial trials excluded dialysis patients.^{29–33} Fresenius Medical Care North America ESRD database demonstrated that dabigatran and rivaroxaban are associated with higher risks of bleeding than warfarin and can result in hospitalization or death. Apixaban (5 mg BID) has the same^{34,35} or decreased bleeding risk,^{36,37} decreased embolism/stroke risk, and decreased mortality in comparison to warfarin.³⁷

Persistent or recurrent access-site bleeding requires evaluation for causes other than coagulopathy. At least 40% of fatal vascular access hemorrhages are preceded by a herald bleed or access infection within the prior 6 months.³⁸

Treatment

Active Bleeding and Emergent Surgery

Rapid and short-term treatments include platelet transfusion and desmopressin (1-desamino-8-D-arginine vasopressin, DDAVP). Platelet transfusions work immediately, lasting 4 to 5 hours.¹⁵ DDAVP (0.3–0.4 µg/kg administered intravenously or subcutaneously) induces rapid release of autologous vWF and factor VIII transiently decreasing protein C activity.^{39–41} Tachyphylaxis typically develops after a second dose.⁴²

Prolonged effects occur with cryoprecipitate, a plasma derivative rich in fibrinogen, vWF, and factor VIII, works within minutes, maximal effects 4–12 hours, lasting up to 24 hours.^{15,43} Anaphylaxis and hemolysis are rare.¹⁵ If ACT is elevated, protamine (up to 1.5 mg/100 units of heparin) can be administered. Recombinant factor VIIa may be used "off label" as rescue,^{44–46} but carries risk of systemic thromboembolic complications.⁴⁷

Elective Surgery

Preoperative planning should minimize platelet dysfunction and correct anemia. Hemoglobin <10 g/dL is present in at least 20% of ESRD patients.²⁷ Adequate hematocrit facilitates platelet function. Recombinant human erythropoietin induces erythropoiesis,¹⁵ but takes several weeks. Erythropoietin increases expression of GP-IIb/IIIa and enhances platelet aggregation.^{18,48} Platelet function can also be improved by scheduling surgery 24 hours after dialysis. Aspirin should be continued, but other antiplatelet medications held 1 week prior.²⁵

Conjugated estrogens, transdermal estrogen administered 2 weeks prior (50 µg/24 hours) for elective, 25–50 mg orally, or 0.6 mg/kg per day IV for 5 consecutive days for urgent interventions decrease bleeding by increased vWF synthesis, protein S and NO reduction, and bleeding time correction.^{15,16,49–53} Transdermal estradiol can be used long term in patients with chronic uremic bleeding as well,⁵⁴ with less incidence of VTE than oral estrogens.⁵⁵

Postoperative Bleeding

Postoperative bleeding warrants prompt re-exploration for surgically correctable causes. Pharmacologic adjuncts, particularly protamine sulfate, should be considered if the procedure involved heparin. DDAVP may also be useful.

INFECTION

Infections are the second most frequent cause of death and access loss (20%),⁵⁶ more commonly with prosthetics.^{57–60} Risk of sepsis-related death is markedly increased in CKD.⁵⁹ The Society for Vascular Surgery reporting standards recommend classifying infections as early (<30 days) or late (>30 days), culture-positive or culture-negative, and by site of infection.

Local signs include: erythema, skin breakdown, purulence, and exposed graft material.

Bacteriology

Most access-related infections are single-organism Gram-positive bacteria, predominantly *Staphylococcus aureus*, with up to 40% methicillin resistant,⁶¹ followed by solitary Gram-negative organisms, and fewer polymicrobial.^{62,63}

Catheter Related

Temporizing catheters are associated with higher mortality and infection and lower patency.⁶⁴ Catheters are the source of two-thirds of all infections and more than 80% of all bloodstream infections in hemodialysis patients.^{59,65} In a Centers for Disease Control and Prevention study, use of a catheter, specific dialysis units, and malnutrition (albumin <3.5 g/dL) were independent risk factors for sepsis.⁶⁶ Multiple trials have attempted to identify specific lock solutions to decrease infection risk but results are varied. Some show improved results,^{67,68} while others show similar infection rates, but increased antibiotic-resistant species.⁶⁹

Epidemiology

Most infectious complications are local (61%). Access type is the most important factor with infections occurring in 11% of catheters, highest with temporary (RR 32.6), 9.3% of grafts, and 5.5% of fistulas.^{59,70,71} More recently Dialysis Outcomes and Practice Patterns Study showed HR for systemic infections of graft to fistula, 1.36, and catheter to fistula, 2.47.⁷⁰

Other factors include repeated cannulation, cannulation technique, poor hygiene, repetitive hospitalizations, duration of prosthetic AV access use, increased age, lower extremity location, and diabetes mellitus.^{65,72} Gram-negative bacteria and associated remote infections or complications are more common with lower extremity prosthetic accesses.^{51,52} The buttonhole technique is also implicated in higher infection rates.⁷³⁻⁷⁵

Treatment

Suspicion of AV access infection can be evaluated with duplex, CT, PET and nuclear medicine scans, but does not replace physical exam.³ Broad-spectrum antibiotics should be initiated and tailored to appropriate organisms. Most commonly, vancomycin and gentamicin are chosen because of dosing ease and spectrum. In centers with a low prevalence of methicillin-resistant *S. aureus*, nafcillin, oxacillin, or cefazolin may be used.^{76,77}

Autogenous Access

Most autogenous AV access infections are associated with cannulation issues or hematomas, with bacteriology similar to prosthetic infections. They may present with cellulitis or abscess. Most respond to 2–4 weeks of antibiotics, rarely requiring surgery. Fistulas with intraluminal endovascular devices requires a prolonged course (4–6 weeks) of parenteral antibiotics and/or resection of prosthetic material.⁵⁹

Prosthetic Access

Prosthetic access infections are more complex. Greater than 50% of such infections involve only a discrete portion of the access.⁷⁸ Attempts at salvage are reasonable for limited infections, allowing uninterrupted dialysis, site preservation, decreased catheter days and surgical complexity. Failure to improve with local resection may necessitate full graft excision. Thigh graft infections are more likely to involve Gram-negative bacteria (OR 10.22) and distant seeding (OR 5.24) including endocarditis, spinal abscess and septic arthritis.⁷⁹

Graft salvage is feasible when infection involves the mid-graft, allowing segmental resection following exposure of uninfected graft, tunneling through clean tissue planes and resection of involved segment. Early success is 90%.⁸⁰⁻⁸² Unfortunately, recurrent infection occurs in up to 20%. Vacuum-assisted closure after open surgical debridement is an alternative.⁸³

Anastomotic Infection

Anastomotic infections require prompt complete graft excision to prevent disruption and hemorrhage.⁸⁴ Low-virulence organisms may be amenable to subtotal graft excision, leaving a small arterial cuff to decrease dissection and complexity, but risks recurrent cuff infection (17%).⁸⁴ In critically ill patients with grossly infected grafts, brachial artery ligation is a last resort.⁸⁵ Cryopreserved grafts may allow site preservation with 1-year primary patency (PP) and secondary patency (SP), 42% and 68%, and recurrent infection rates of 2.3%.⁸⁶ Early infections, within days of access creation, require complete graft excision.^{59,80}

Thrombosed Grafts

Although removal of thrombosed AV grafts is usually unnecessary,⁸⁷ several studies demonstrate the potential infectious source.^{84,87} Thrombosed AV graft removal decisions should be based on signs of inflammation combined with absence of alternate sources.

PSEUDOANEURYSM AND ANEURYSM

While some dilation is expected with fistulas, >18 mm or 3× the matured diameter is considered aneurysmal.⁸⁸ Both pseudoaneurysms and true aneurysms create issues with cannulation and cosmesis, as well as increased risk of thrombosis, pain, bleeding, and infection.⁸⁹ Progressive enlargement can compromise overlying skin, which may lead to rupture (Fig. 178.1).

Pseudoaneurysm

Pseudoaneurysms occur in 2%–10% of polytetrafluoroethylene (PTFE) grafts.⁹⁰ They develop from repeated punctures, with perigraft hematoma formation. They are associated with outflow stenosis, with increased intragraft pressures, often in older grafts. Surrounding tissue ingrowth limits development, with poorly incorporated grafts at higher risk. Autogenous fistula pseudoaneurysms are less frequent, mostly related to cannulation.⁹¹ Asymptomatic pseudoaneurysms should prompt a change in cannulation, but is not a reason for intervention.³



Figure 178.1 Symptomatic pseudoaneurysms with early skin erosion that appeared several years after creation of an autogenous proximal radiocephalic arteriovenous fistula.

Treatment

Open

Open repair is recommended.³ Prosthetic graft pseudoaneurysm requires resection of involved segments with interposition graft or bypass with tourniquet for control. While new segments become incorporated, dialysis continues in preexisting incorporated segments. Extensive degeneration requires near-complete excision while maintaining anastomoses, with temporary catheter placement. Staged, segmental replacement is an option to avoid catheter placement, but requires two procedures.

Treatment of autogenous fistula degeneration options include conversion to a graft, maintaining only the arterial anastomosis or fistula reduction surgery (“aneurysmorrhaphy”). This involves resection of excess skin and a portion of the vein wall. Anastomosis is typically performed along lateral wall to prevent issues with cannulation along the suture line.

Endovascular

Endoluminal repair avoids use of catheters and allows identification and treatment of concomitant venous stenosis, present in up to 73%.^{89,92–96} Cannulation difficulty may occur due to need to puncture stent graft through the pseudoaneurysm and persistent cosmetic issues. Although minimally invasive techniques are appealing, higher cost, risk of infection (7%–37%), skin erosion (OR 5.0), thrombosis (17%–35%),⁹⁴ and potential difficulty with access without good long-term patency remain concerns.

True Aneurysm

Aneurysm formation occurs adjacent to the anastomosis associated with hemodynamically significant stenosis, within cannulation areas, adjacent to mid-access stenoses, next to vein junctions and valves, or scarring from prior catheters.

Treatment

The preferred treatment for post-anastomotic aneurysms is relocation of the anastomosis. Comparable SP has been achieved for small dilations with angioplasty of stenotic anastomosis,

but increases resolution time and may necessitate a catheter. Partial resection and patch angioplasty are alternatives. For mid-access aneurysms, fistulogram and treatment of associated stenoses are recommended. For diffuse degeneration partial aneurysmectomy is preferred,^{97,98} with 6–10 mm catheter used as a dowel. Stapled repair has also been described, with good technical success.^{99–101} A modified technique is dissecting and resecting only the lateral wall and preserving an incorporated area to access which decreases the need for catheters.¹⁰¹ Treatment for aneurysms along the venous outflow tract is angioplasty, with selective stenting.

Aneurysmal Degeneration of Inflow Artery

Although rare, arterial aneurysms occur and may present as painless pulsatile masses or with distal embolization, ischemia, compressive neurologic symptoms, pain, or swelling.^{102–104} Ligation, renal transplant with immunosuppression, and high flow have been associated with arterial degeneration.^{105–107} Decision to intervene depends on symptoms, size, comorbidities, and life expectancy. Radial artery aneurysms can be treated by ligation, whereas brachial or axillary aneurysms require repair or bypass.

SEROMA

A perigraft seroma is a sterile, clear, ultra-filtered serum surrounded by a non-secretory fibrous pseudocapsule. Early seromas frequently resolve¹⁰⁸ and are common with prosthetic grafts. Chronic seroma is rare, mostly occurring near the arterial anastomosis.¹⁰⁹

Etiology and Incidence

Seromas have been reported with both PTFE and polyester grafts^{108,110,111} with incidence <2%,^{112–114} but are highest with gel-coated PTFE grafts, at 36%.

Proposed mechanisms include increased graft porosity, failure of graft incorporation, and lymph disruption. Several studies have suggested presence of a fibroblast growth inhibitor in patients' serum.^{115–117} Histologic studies support this, noting immature fibroblasts lining the graft.¹¹⁰ Other theories include immunologic reaction, graft damage at implantation, and occult infection.

Presentation

Ultrasound can help distinguish from aneurysm or hematoma. Seromas generally appear within 1 month and may lead to cannulation difficulty or thinning skin.¹¹⁴

Treatment

Surgery is warranted if seroma interferes with cannulation, or compromises skin. Aspiration should be avoided, as it increases risk of graft infection and loss. Graft replacement yields the highest cure (92%) vs. observation (68%). Aspiration

and cyst removal were similar (69% vs. 72%), but increased infection or thrombosis (8% aspiration; 12% cyst removal). Incision and drainage had worst results (53% success), with infection or thrombosis, 7%.¹¹¹ Graft and capsule excision is recommended, with rerouting and changing prosthetic material.^{109,111,112,115,118}

Several reports show adequate results with access preservation^{113,114,119,120} using microfibrillar collagen (Avitene; Bard Davol Inc., Warwick, RI)¹²¹ or fibrin glue (84% success)¹¹³ in the perigraft space. Borrero and Doscher report salvage by pseudocapsule excision.¹¹⁴ Gargiulo et al. reported success with percutaneous Dacron-covered stents and closed suction drainage.¹²⁰

ACCESS-RELATED HAND ISCHEMIA

ARHI, initially described in 1969,¹²² is uncommon but devastating. Access construction reduces digital blood flow in up to 80%; however, few develop symptoms.¹²³ Coolness and tingling is present in up to 10%.¹²⁴ Most resolve within weeks. Significant ischemia occurs in 1%–2% with autogenous access at the wrist^{125–128} and 4%–8% with brachial-based access.^{125,127–129} ARHI must be promptly evaluated. Treatment may be indicated for claudication, or pain on dialysis, and is mandatory for ischemic rest pain or tissue loss.¹³⁰

Pathophysiology and Risk Factors

Creation of an access substantially alters flow dynamics and resistance. Arterial inflow supplies two competing circuits – the low-resistance access and the higher-resistance peripheral vessels. Relative resistances and collateral circulation determine the amount and direction of flow. A “physiologic steal” is common, noted in up to 73% of autogenous accesses and 91% of prosthetic accesses.¹³¹ Reversal is neither necessary nor sufficient to cause distal ischemia.^{132,133} Ischemia results from inadequate collateral circulation and inability to meet increased demand via increased cardiac output (CO) and vasodilatation,^{134,135} leading to decreased distal perfusion pressure. Hypotension in dialysis further decreases perfusion causing symptoms during treatment. ARHI is locoregional hypoperfusion secondary to inadequate arterial compensation.¹³⁶

Risk factors include advanced age, diabetes, peripheral artery disease, coronary artery disease, distal brachial-based access, female gender, large conduits, history of ARHI, and multiple previous access.^{3,133,137–140} Hyperglycemia decreases shear-induced vasodilation, which is critical to collateral recruitment and inflow artery remodeling.^{135,141,142} Atherosclerosis increases likelihood of flow-limiting inflow lesions and peripheral resistance. Brachial-based accesses increase flow relative to wrist accesses¹⁴³ and decrease resistance to flow in the AV access.

Prevention

The ideal strategy is prevention. No test reliably predicts development of ARHI. Patients with a preoperative digital brachial

index (DBI) <1.0 are more likely to develop steal, but there is no cutoff below which steal is inevitable.¹³⁸ Similarly, intraoperative DBI <0.6 has 100% sensitivity and 18% PPV for predicting eventual ARHI.¹⁴⁴ Alternately, patients with preoperative DBI >1 have increased cardiovascular mortality (HR 2.09).¹⁰¹

Preoperative examination includes bilateral upper extremity blood pressures and an Allen test. Patients with radial-dominant incomplete palmar arch should not undergo radial artery-based access creation. Questionable Allen tests should be assessed by continuous-wave Doppler.¹⁴⁵ Routine testing is not justified.¹⁴⁶ In patients with blood pressure differential >20 mm Hg,¹⁴⁶ the low pressure extremity should be avoided unless the problem can be corrected.

Operative strategy should be adjusted in high-risk patients. Distal brachial-based accesses should be avoided,^{105,106,128,134,138,140,147} with preference for radial or axillary artery inflow.¹⁴⁸ Prosthetic grafts in diabetics should be tapered, 11% ischemia vs. 55% with straight grafts.¹⁰⁷

Diagnosis

Clinical Presentation

Symptoms vary depending upon severity. Although rare, onset may occur within hours,¹²⁹ and is more common with prosthetics.^{149,150} Most develop over weeks to months and occasionally years after creation.^{151–153} Symptoms can include coolness, paresthesias, rest pain/tissue loss and weakness. Physical examination reveals cool extremity with pallor, cyanosis, delayed capillary refill, absent pulses/signals, diminished sensation, weak grip, or ulceration/gangrene. Mean handgrip and Disability of Arm, Shoulder, and Hand (DASH) questionnaire are decreased in access arms even without clinically relevant ischemia,^{154,155} whereas dexterity and sensation are unchanged.¹⁵⁵ Improvement with access compression confirms the diagnosis and predicts good response to revision.¹⁵⁶ Ischemia should be suspected until proven otherwise, except immediately after creation when ischemic monomelic neuropathy must be considered.

Diagnostic Testing

Multiple studies, including digital pressure measurement, pulse oximetry, photoplethysmography (PPG), color duplex ultrasound, and angiography (all with/without compression) have been described. PPG is preferred. While few are symptomatic, many patients demonstrate both reduction in digital pressure and flow reversal in distal arteries.^{123,131,132} Modaghagh et al. found DBI of less than 0.7 was 100% sensitive, but only 73% specific; a threshold of 94% was identified for pulse oximetry.¹⁵⁷ Lazarides et al. utilized postoperative systolic pressure index (SPI, postoperative forearm pressure/contralateral forearm pressure) to identify patients at risk. 14% had mild to moderate ischemic symptoms with SPI <0.4. 50% improved over time, as did SPI. Serial SPI and nerve conduction studies (NCS) are recommended, with NCS deterioration considered an indication for revision.¹²⁹

Angiography and duplex ultrasound (DUS) help determine the mechanism of ARHI (Fig. 178.2). Inflow stenosis is a

factor in 15%–20%,^{128,146,158,159} therefore imaging is imperative (Fig. 178.3). DUS allows flow measurements and should also be obtained to determine flow rates –high (autogenous >800 mL/min, prosthetic >1200 mL/min¹⁵²) or low – to facilitate intervention.

Treatment

Transient, mild symptoms can be managed expectantly with reassessment, warming, and blood pressure management.¹⁶⁰ Patients with claudication or pain during hemodialysis need



Figure 178.2 Pseudoaneurysm of AV access with skin compromise and pending rupture.

close monitoring. If severe symptoms are present (progressive numbness, pain or hand pallor, diminished sensation, ulcers/dry gangrene, decreased motor function, or atrophy), swift intervention is critical.¹⁶¹ Gradual tissue loss can rapidly deteriorate.

The goals of treatment are symptom resolution and access preservation. There are two basic strategies: access-flow reduction and augmentation of distal arterial flow. Options include banding, revision using distal inflow (RUDI), proximalization of arterial inflow (PAI), distal revascularization with/without interval ligation (DRIL), and arterial angioplasty. Ligation is a last resort in those with limited life expectancy, severe tissue loss, or a poorly-functioning access.

Reduction of Access Flow

Banding or flow-limiting procedures

Stenosis is created near the arterial anastomosis via suture plication, a single tie, or wrapping a constrictive prosthetic cuff. Relative resistance of the access increases and directs a higher proportion of arterial flow toward the hand. Determining the precise degree of stenosis needed is difficult. Consequently, results are variable, both in terms of symptomatic improvement and access preservation.

Many early series based the degree of banding on intraoperative assessment of distal perfusion alone with high rates of access loss.^{125,158} Improved results have been achieved with access flow monitoring, particularly in prosthetic grafts.¹⁵² On final analysis, access flow of 700 mL/min is an important cutoff

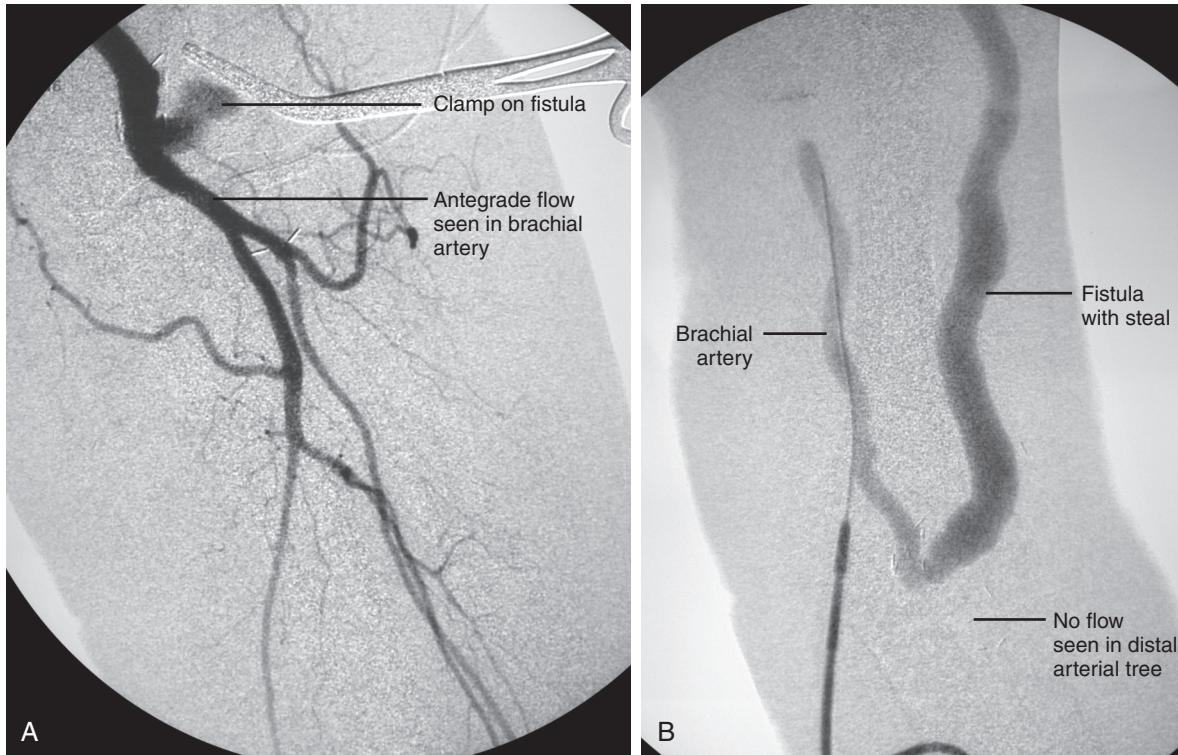


Figure 178.3 Arteriogram of a patient with steal syndrome (A) with and (B) without arteriovenous access compression. Note visualization of the distal brachial artery and forearm arteries with compression (B).

for maintenance of AVG access patency (38% vs. 74%), suggesting the reason for earlier failures with banding.^{125,158,162,163}

Despite favorable results utilizing intraoperative monitoring, anesthesia-induced changes can impact these results. Consequently, many now advocate using minimally invasive limited ligation endoluminal-assisted revision (MILLER).¹⁶⁴ This method uses a percutaneous 4- to 5-mm endoluminal balloon placed as a sizing dowel, with a suture placed around access with the balloon inflated via a small incision. Significant clinical improvement occurred in 89% of 114 patients, early thrombosis rate 4.4%.¹⁶² Hong recently described a complete percutaneous “corset” technique deploying 5 × 25 mm stent followed by 10 × 60 mm stent graft distal to the arterial anastomosis, decreasing flow by 40% with symptom improvement.¹⁶⁵

Revision using distal inflow

RUDI involves ligation of the fistula at the arterial anastomosis with reestablishment of flow from a more distal artery via bypass or translocation of a vein side branch (Fig. 178.4).^{166,167} This technique is useful for high flow fistulas. Native arterial flow is preserved, risking the fistula over the extremity.

Recent studies demonstrate good symptom resolution and access patency.¹⁶⁸ A systemic review of 130 patients, 11 articles, noted 82% (95%CI, 74.4%–89.6%) successful outcome, median 12 months; 10.7% required ligation for continued symptoms, and 7.6% thrombosed.¹⁶⁹ Recurrence noted in nearly 50% within 3 years,¹⁷⁰ hypothesized to be associated with brachial arterial damage,¹⁷¹ therefore continued surveillance is recommended.

Direct Augmentation of Peripheral Flow

Arterial angiography

Arterial occlusive disease is common in dialysis patients and requires evaluation. Inflow disease, subclavian or brachial artery, is less frequent than distal disease but responds better to intervention. Cheun et al. showed 91% clinical 30-day success

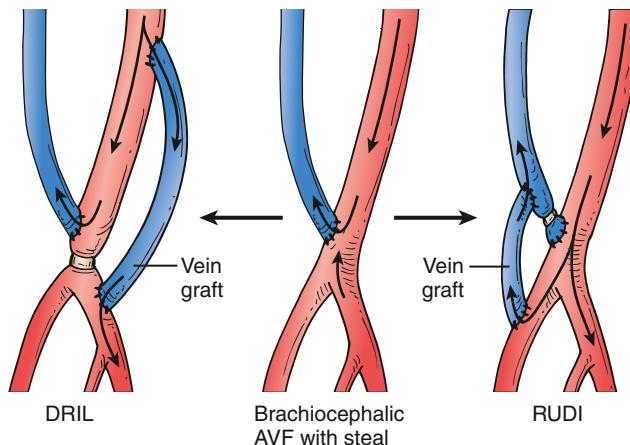


Figure 178.4 The anatomic configurations of the distal revascularization and interval ligation (DRIL) and revision using distal inflow (RUDI) procedures are illustrated for the treatment of hand ischemia or steal syndrome after an autogenous brachiocephalic arteriovenous access. *AVF*, arteriovenous fistula.

following inflow treatment compared to 51% for forearm disease.¹⁷² Endovascular morbidity and mortality are low and is therefore a good initial option to be evaluated in patients presenting with ARHI.

Proximalization of arterial inflow

Zanow et al.¹⁷³ described ligation of the anastomosis and conversion to a more proximal inflow using a 4- to 5-mm prosthetic interposition (Fig. 178.5). Uninterrupted dialysis continues via the vein. The proximal artery's diameter and higher capacity, creates lower pressure drop across the anastomosis at similar flow rates. The primary advantage is preservation of the native artery's continuity. Symptom resolution occurred in 84%; the remaining significantly improved. Access PP was 87%, 12 months, and 67%, 36 months.¹⁷³ Thermann et al. confirmed similar results but found that patients with severe tissue loss did poorly.¹⁷⁴ Autogenous conduits have shown comparable results.¹⁷⁵

Distal Revascularization–Interval Ligation

Many consider DRIL, first described in 1988¹⁷⁶ the gold standard.^{146,163,177–180} DRIL entails creation of a bypass originating 7–10 cm proximal to the access anastomosis and terminating distal to it, with ligation of the artery distal to access anastomosis (Fig. 178.4). Retrograde flow is prevented and the new bypass creates a low-resistance pathway to the peripheral vascular bed. This avoids the “pressure sink” near access anastomosis.^{181,182} Recent data suggest that the pressure augmentation from ligation contributes only 10% and may be avoided if circulation is adequately improved with bypass.¹⁸³

Long-term results are excellent for both symptom resolution and access patency.^{124,146,179,182} A recent meta-analysis found best results with saphenous vein conduit with resolution of symptoms in 81% and patent fistula at mean of 22.2 months.¹⁸⁴

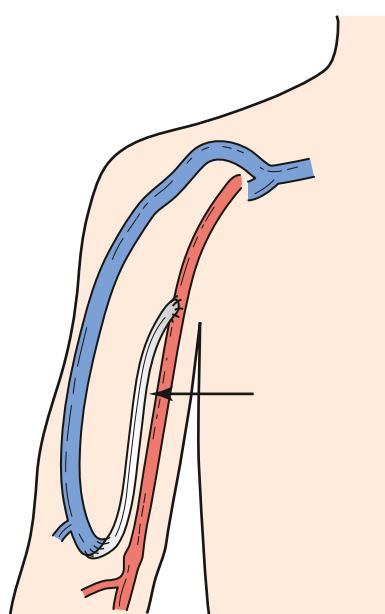


Figure 178.5 Proximalization of Arterial Inflow. The arterial inflow is proximalized with a synthetic interposition graft (arrow).

Drawbacks to DRIL include its invasiveness and perioperative mortality as high as 6.8%,¹⁶³ with wound complication rates of 9%–19%.^{168,177,178,185} ARHI patients are particularly frail, with a 1-year mortality of 30%,^{146,177,178} higher than typical ESRD patients,¹⁸⁶ reflecting advanced comorbid conditions. The second issue is dependence of the hand on the bypass. In rare instances of bypass occlusion, limb salvage is achievable via repeat bypass or access ligation.^{177,178,185,187}

Distal Radial Artery Ligation

Palmar arch steal syndrome (PASS) occurs when retrograde flow through intact palmar arch results in inadequate digital flow in those with radial–cephalic AV accesses. Treatment is ligation or coil embolization of the distal radial artery.^{188–190} It is critical to evaluate ulnar artery and palmar arch patency prior to ligation.¹⁸⁹

Treatment selection

Treatment should be individualized based on symptoms, life expectancy, access flow rate and utility, future access options, and conduit availability. RUDI, DRIL, and PAI have similar outcomes,¹⁹¹ but require extensive surgery, with higher morbidity and mortality.¹⁶³ Ligation or banding are better suited to those with limited life expectancy. Banding may require repeat interventions to be effective.^{159,163} With more severe ischemia and risk of limb loss DRIL is preferred.^{179,180,192}

Access-specific factors

Flow rate. Most ARHI are high flow (autogenous >800 mL/min, prosthetic >1200 mL/min). Less than a third of patients have low/normal flow ARHI,^{133,160} often due to poor collateral circulation or atherosclerotic disease. Treatment is with DRIL, PAI, or angioplasty.

Conduit. Both RUDI and DRIL traditionally require autogenous conduit, whereas PAI typically uses PTFE.

VENOUS HYPERTENSION

Venous hypertension affects access patency and function and can cause disabling edema, mostly secondary to central venous stenosis (CVS) or occlusion.^{193,194} CVS is identified in 17%–26% of venograms for failing access but many patients with CVS are asymptomatic due to adequate collateral flow.^{195–198} CVS threatens access and risks loss of extremity for future access. Prevention, early recognition, and definitive treatment are crucial.

Etiology

CVS is primarily caused by catheters, longer durations correlating with increased stenosis,^{199,200} but may occur within 1 month.^{201–203} Despite efforts by Fistula First Catheter Last Workgroup Coalition, 80.2% of patients begin hemodialysis with catheters.²⁰⁴ CVS is highest with subclavian access, 40%–50%, less with jugular <10%.^{205–207} Presumed etiology is chronic endothelial trauma from catheter motion,^{205,208} resulting in fibrous tissue and neointimal fibromuscular

hyperplasia.²⁰⁹ Caution should be exercised in placing access ipsilateral to cardiac devices with intravenous wires for similar reasons.^{210–213}

Although catheters account for most CVS, up to 10% occur in its absence.^{214,215} It is thought to be due to increased blood flow, natural anatomic narrowing, and valves, most often in the region of the thoracic outlet, leading to smooth muscle cell proliferation and eventual stenosis.^{197,216}

Diagnosis

Clinical Presentation

Presentation is dictated by degree of collateral flow, site of obstruction, and status of peripheral venous valves. Patients with robust collaterals and competent valves may be asymptomatic,¹⁹⁹ so a high index of suspicion is needed when creating access in patients with prior catheters. Physical signs include scars and dilated shoulder collaterals (Fig. 178.6). In many cases, declining access function, increased recirculation or high venous pressures, and prolonged needle-hole bleeding are indications of CVS after access creation.

Symptomatic venous hypertension, swelling, tenderness, and pain, may manifest immediately after creation or in delayed fashion.¹⁹⁶ Severe cases may present with cyanosis, stasis, and ulceration.²¹⁷ Some edema is normal after AV access creation. Persistent swelling beyond 2 weeks requires additional assessment, as up to 25% will be associated with central stenosis.¹⁹⁶ Atypical venous hypertension can also occur. Bleeding

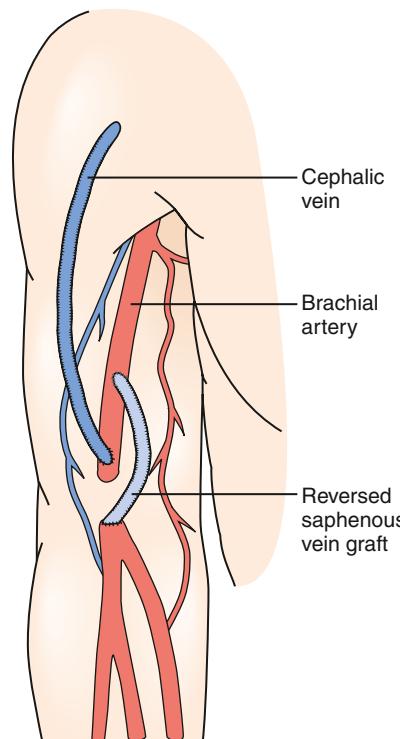


Figure 178.6 Diagram of brachiocephalic arteriovenous access and brachial artery bypass with interval brachial artery ligation and division. (Redrawn from Knox R, Berman SS, Hughes JD, et al. Distal revascularization–interval ligation: a durable and effective treatment for ischemic steal syndrome after hemodialysis access. *J Vasc Surg*. 2002;36:250–256.)

esophageal varices,²¹⁸ increased intraocular pressure,²¹⁹ and venous congestive encephalopathy²²⁰ have been described.

Diagnostic Testing

Duplex ultrasound may be helpful¹⁴⁵; however, more proximal lesions may be inadequately visualized.^{145,221–223} KDOQI 2019 guidelines consider it reasonable to perform venography before access creation in patients with prior subclavian lines.³ If CVS is confirmed, placement of AV access in the limb should be avoided.

Duplex is preferred for early-onset edema after access creation to avoid cannulation and damage to thin-walled veins, or bleeding from unincorporated grafts. If edema persists/develops after 2 weeks patients should undergo venography, with IVUS if stenosis is not clearly identified.

Treatment

Management is controversial. Ligation is effective and well tolerated, but sacrifices the access. Given the finite number of access options, attempts at salvage should be made when possible.

Endovascular Intervention

KDOQI recommends intervention only for symptomatic patients with initial preferred therapy being high pressure, low compliance percutaneous transluminal angioplasty (PTA) generally for >2 minutes (Fig. 178.7).³ Histologic analysis demonstrates recurrent venous lesions have more aggressive

neointimal hyperplasia (NH).²²⁴ Consequently, the natural history of central venous angioplasty and stenting is frequent restenosis and reintervention. Renaud et al. noted better patency after withholding intervention in asymptomatic high-grade (>70%) CVS than treated symptomatic cases without decreased access patency supporting this guideline.²²⁵

PTA's technical success is 82%–89%,^{197,198,226} with poor long-term outcomes. PP rates drop to 23%–55% at 6 months and 12%–43% at 1 year.^{197,198,226,227} With multiple reinterventions, assisted PP (APP) improves to 64%–82%.^{226,228–230} Stenting increases immediate technical success^{195,226,231,232} but 1-year PP ranges from 11% to 56%, with majority <25%.^{195,226,227,229,230,232} Kovalik et al. noted degree of elastic recoil predicts angioplasty response, with lesions >50% recoil having poor long-term patency (2.9 months), which improved with stenting (8.6 months). If recoil <50%, angioplasty results were better (7.6 months) and worse after stenting (4.2 months). He concluded stents should be avoided in nonelastic lesions.²³³

The most frequent cause of stent failure is NH, which is particularly robust in the hemodialysis outflow tract,²²⁴ therefore stent grafts have been evaluated. Results are promising, with 12-month PP 40%–67% and APP 80%–86%.^{234–237} KDOQI 2019 guidelines recommends stent-graft placement for AVG venous anastomosis stenosis after two multicenter prospective randomized control trial results showed improved 6-month PP and longer time to reintervention compared to PTA.^{3,238,239} In central veins, caution must be used to avoid coverage of major venous confluences and collaterals. Verstandig et al.

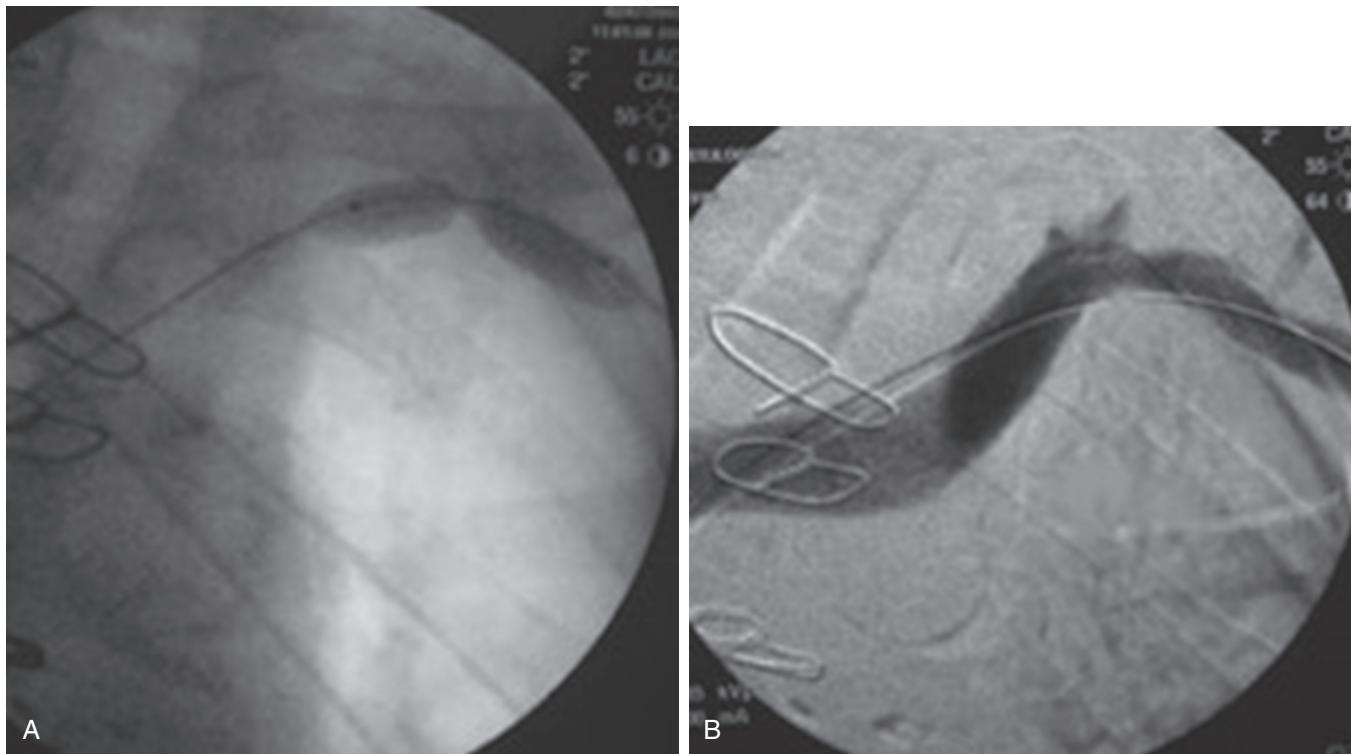


Figure 178.7 (A) Angioplasty of subclavian vein stenosis in a patient with an ipsilateral autogenous AV access and venous hypertension. (B) Completion venogram after subclavian vein angioplasty demonstrating no residual stenosis.

reported internal jugular (IJ) vein exclusion in 77%.²³⁵ Stent graft placement has also been proposed when stenosis occurs within the cephalic arch, improved PP compared to bare metal stents (BMS) and PTA,^{240–242} leading to KDOQI recommendations to avoid BMS.³ In-stent restenosis also responds best to stent grafting. The RESCUE study 2-year results show higher stent-graft access PP compared to PTA at 6-month (18.6% vs. 4.5%, $P < 0.001$), 12-month (6.2% vs. 1.5%), and 24-month PP (15.6% vs. 2.2%).²⁴³

Generally, stents should be extended more peripherally than centrally to prevent displacement. Placement of a guide wire in the IVC prevents embolization to the heart or pulmonary artery if undersized and facilitates removal by snare when necessary. Although most CVS are due to intrinsic lesions, a subset are from extrinsic compression.^{214,244,245} These have a poor response to endovascular therapy and are prone to stent fracture and collapse. It is crucial to maintain a high index of suspicion, particularly for lesions at the costoclavicular junction.²⁴⁵

KDOQI guidelines state insufficient evidence for drug-coated (DCBA) or cutting balloon angioplasty. A recent meta-analysis, 908 patients, showed improved patency in autogenous access with DCBA compared to PTA at 3, 6, 12, and 24 months.²⁴⁶ Another 2019 meta-analysis of 1113 patients showed similar results with improved patency at 6 (RR 0.57) and 12 months (RR 0.73). This study found benefit for CVS as well.²⁴⁷ In AVGs, a small RCT noted improved target lesion patency at the anastomosis with DCBA at 6 (41% vs. 9%) and 12 months (23% vs. 9%) whereas PP benefit was only maintained through 6 months.²⁴⁸

Open Interventions

Surgical treatment has substantial morbidity and is reserved for patients untreatable with angioplasty/stenting.²⁴⁹ Open reconstruction improves symptoms with 1-year patency of 75%–88%.^{250–254} Techniques include direct reconstruction, decompression, and bypass. Bilateral venography is essential to planning. Surgical repair was first described with a spiral saphenous vein graft,²⁵⁵ with 87.5% patency, mean 10.9-year follow-up.²⁵⁶ In modern series, interventions include prosthetic bypass, with outflow including right atrium, femoral vein, saphenous vein, ipsilateral internal jugular vein, and contralateral jugular vein.²⁵⁷ Symptom resolution has been achieved in 89%–100% with graft patency of 86%–100%.^{253,258,259} Another option is jugular turndown; IJ is divided high in the neck and anastomosed to the ipsilateral subclavian vein.²⁶⁰ Disadvantages are clavicle resection and inability of future IJ temporary access. With high-flow access, adjunctive banding can improve the inflow–outflow balance.^{214,258,261} A final option is the HeRO graft, which does have a high complication rate but may be used as a final resort.²⁶²

NEUROPATHY

Peripheral neuropathy is present in 2/3 of patients at initiation of dialysis.^{263–265} Diabetes is predictive for development after access creation.²⁶⁶ Access-related neuropathy has four grades of severity²: Grade 0: Asymptomatic, Grade 1: Mild

– intermittent changes (pain, paresthesia, numbness with sensory deficit), Grade 2: Moderate – persistent sensory changes, Grade 3: Severe – sensory changes, progressive motor loss (motion, strength, muscle wasting).

Types of Neuropathy and Management

CKD neuropathy is categorized into three groups: (1) systemic disease neuropathies, which develop gradually and involve painless, progressive, symmetrical sensorimotor polyneuropathy¹⁹²; (2) mononeuropathies, related to compression, compartment syndromes, and entrapment; and (3) ischemic mononeuropathy, which occurs acutely after access creation.

Systemic Disease Neuropathy

Diabetic polyneuropathy

In the United States, 46% of dialysis patients are diabetic (Dialysis Outcomes and Practice Patterns Study [DOPPS]). Diabetic neuropathy with large fiber demyelination typically affects lower extremities with numbness, paresthesias, and pain. Peripheral neuropathy is present in 79% of diabetic dialysis patients with foot ulceration.²⁶⁷

Uremic polyneuropathy

Uremia is the most common neuropathy in dialysis patients; 50%–70%, and more common in men.^{268,269} It improves with hemodialysis and may resolve with transplant.^{269–272} Axonal degeneration with secondary segmental demyelination is seen and is most severe distally.^{268,273–276} Hyperkalemia affects symptom severity.²⁷⁷ Physical findings include lower extremity impaired vibratory sensation, loss of Achilles deep tendon reflexes, and loss of distal touch and position sense.

Compressive Mononeuropathies

Carpal tunnel syndrome (CTS) is 10x more frequent in hemodialysis patients, prevalence of 0.6%–30%.^{278,279} Time since hemodialysis initiation is associated with CTS, 46%–50% at 5 years, 50% at 10 years.^{280–282} The etiology of increased risk is not understood but thought to be due to serum β_2 -macroglobulin deposition as amyloid in periarticular tissues.^{279,281,283,284} Koçyigit et al. identified early onset CTS without amyloid deposition, but with venous hypertension,²⁸⁵ suggesting a role for venous hypertension with chronic irritation and thickening of the carpal ligament. There are conflicting data as to whether access side impacts CTS development.^{281,286} Systemic factors include uremia, expanded extracellular fluid volume, and nerve ischemia.^{210,211}

Pseudoaneurysms and hematomas also cause nerve compression.²⁸⁷ Symptoms include tingling dysesthesias in the median nerve distribution, worse at night or during dialysis.²⁶⁸ Dialysis exacerbation is related to relative ischemia with venous hypertension and tunnel edema.^{281,288} Early intervention causes rapid improvement,^{289,290} delays have poor outcomes.²⁹¹ Ulnar nerve compression, elbow/wrist, presents with pain or sensory changes in the ulnar aspect of the hand, adductor pollicis weakness, and finger adduction/abduction weakness.^{279,292–294}

Ischemic Monomelic Neuropathy

IMN is rare, 0.5% of access, and results from acute vascular compromise of neurologic structures.^{295–301} Delayed intervention leads to irreversible, profound neurologic deficits.²⁹⁵ Most occur in older diabetics with preexisting peripheral neuropathy, peripheral arterial disease, and brachial-based accesses. It has never been reported in forearm-based accesses.^{299,302,303}

Presentation can be confounded by anesthesia. Within hours of surgery, patients develop acute pain out of proportion to clinical findings, weakness, or hand paralysis, often with prominent sensory loss and dysesthesias. Arterial signals and pulses are normal.^{268,299,302–304} Digital pressure index is >0.3.³⁰⁵ Symptoms are frequently misattributed to anesthesia, patient positioning, or surgical trauma.³⁰⁵ Patients with acute symptoms immediately postoperatively should also be assessed for direct nerve injury or hematoma compression. Most nerve injury from anesthesia occurs more gradually and is more focal.³⁰⁶

IMN is related to preexisting marginal nerve perfusion, compromised by additional flow diversion by the access.³⁰⁵ Prevalence of brachial artery involvement suggests that IMN is due to inability of this vessel to vasodilate and compensate for increased access demands. The resultant low-level ischemia does not translate to muscle or skin viability issues, nor does it present as ARHI. However, it results in irreversible ischemic nerve injury if not promptly treated. Dyck et al. found the antecubital area to be a “watershed” for the vasa nervosum of the three nerves of the upper limb. Nerve conduction studies done 1 hour after AV access creation demonstrate acute, reversible changes with motor conduction block and conduction slowing due to myelin retraction from the node of Ranvier.²⁹⁹ Axonal loss occurs late, consistent with degenerative types of polyneuropathy, and sensory amplitudes are more severely affected.²⁹⁶ Evidence of denervation is more severe distally, with a proximal gradient.³⁰⁵ Because IMN is a form of ARHI limited to the nerves, treatment is access ligation or emergent augmentation of flow. Even with rapid intervention, symptoms may only partially resolve or may become permanent.^{303–307}

CARDIOPULMONARY COMPLICATIONS

Cardiovascular complications, including CHF, pulmonary hypertension (PH), and coronary steal remain the leading causes of morbidity and mortality in patients with ESRD. Patients with CKD also have accelerated atherosclerosis related to comorbidities. AV access construction itself is associated with an increased risk of cardiovascular death.

Congestive Heart Failure

CHF is present in one-third of new dialysis patients.³⁰⁸ Associated factors include chronic volume overload, arterial hypertension, cardiovascular calcification, valvular disease, increased arterial stiffness, anemia, inflammation, high access flow, and arrhythmias.³⁰⁹ High access flow (Qa) may predispose to CHF

in patients with marginal cardiac function. Left atrial (LA) diameter and CO increase within 3–14 days of fistula creation,³¹⁰ and LV mass and LA area within 3 months.³¹¹ Abassi et al. found a 40% increase in CO, suggesting a Qa/CO ratio >0.3 increases risk for high-output CHF.³¹² The Qa/CO ratio is significantly higher in patients with upper arm access, with 1 in 10 patients at risk for developing CHF.³¹³ Not all studies find a relationship between AV access and cardiac issues. A review of the U.S. Renal Data System saw no association between AV access and CHF or acute coronary syndrome.³¹⁴

Treatment includes banding, ligation, or flow restriction if the access contributes. Access is lost with ligation and banding jeopardizes access. RUDI for high-flow accesses noted 77% access PP and 100% CHF resolution with a decrease in CO from 8 ± 3.1 to 5.6 ± 1.71 L/min.³¹⁵

Coronary Steal Syndrome

The internal mammary artery (IMA) is frequently utilized in coronary revascularization. Ipsilateral access may steal from IMA bypass. Proximal subclavian stenosis or high-flow access without stenosis predispose to coronary steal. CTA is recommended to assess subclavian artery prior to CABG to avoid potential complications. Flow directionality can be assessed by DUS or angiography. Kato et al. showed retrograde IMA flow by angiography.³¹⁶ Minami found correctable reversal of flow by fistula compression at coronary revascularization, mitigated with free grafting IMA.³¹⁷ Multiple studies have found increased risk of cardiac events with ipsilateral AV access (HR 2.92, $P = 0.008$).^{318,319} If coronary steal is detected with ipsilateral AV access and patent IMA graft, evaluation of the subclavian artery is mandatory. Stenosis correction may result in symptom resolution without access sacrifice.

Embolization of Stents to Heart and Pulmonary Arteries

Physiologic variations in vein wall diameter, stent undersizing, and lack of adherence to the wall may lead to embolization. Complications include tricuspid regurgitation, acute MI, pulmonary infarction, and cardiogenic shock from embolization to the right atrium, right ventricle, and pulmonary arteries.³²⁰

Pulmonary Hypertension

PH is a progressive, fatal disease with significant decrease in survival (mortality 30.8% vs. 3.5%) associated with increased CO, which increases in prevalence soon after access creation (40%) and regresses after access closure.³¹²

PH is precipitated by volume overload, left ventricular failure, arterial hypertension, high-flow from the access, and metabolic changes. Recurrent embolization from the access and salvage procedures is also a potential cause. CKD patients have acquired endothelial cell dysfunction, reducing ability to tolerate the elevated CO. Nakhoul et al. found elevated endothelin in all HD patients, with 48% having PH, and greater

CO. Temporary access closure resulted in systolic pulmonary artery pressure (PAP) and CO decrease, suggesting increased venous return is a factor.

Haylucu et al. had a correlation with systolic PAP and AVF flow, reversible with compression from 36.8 ± 10.7 to 32.8 ± 10.5 mm Hg.³²¹ Yigla et al. noted PH in 37% of AV access, no peritoneal dialysis patients, and 1 patient with renal insufficiency. CO was significantly higher in patients on hemodialysis (6.9 L/min vs. 5.5 L/min). PAP increased in 66% of patients after beginning HD, concluding that long-term HD and access creation are associated with PH by affecting CO and pulmonary vascular resistance. Recurrent embolization has not been proven to impact PH.^{322,323}

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A complete reference list can be found online at www.expertconsult.com

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