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Aortoiliac Disease: Endovascular Treatment

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BACKGROUND

Progress in endovascular surgery has resulted in a continued shift in the treatment of patients with aortoiliac occlusive disease to less invasive forms of therapy. Early pioneers such as Dotter and Gruntzig developed balloon angioplasty.¹ Subsequent work in stent development by Palmaz gradually improved the treatment of patients with aortoiliac disease.^{2–4} Improvements in technology such as higher resolution imaging, lower profile systems, premounted balloon-expandable stents, self-expanding stents, and stent grafts have resulted in better outcomes and lower complications. Vascular surgeons now incorporate these treatment modalities into much of their practice. Today the majority of patients with aortoiliac occlusive disease can be safely treated with either percutaneous endovascular procedures or, in patients with more advanced aortoiliac occlusive disease, by means of stent grafts and hybrid open endovascular approaches.

INDICATIONS

There are both patient- and lesion-specific indications for aortoiliac intervention. Patient-specific indications for treatment include lifestyle-limiting claudication, rest pain, and tissue loss. Less frequent indications include vasculogenic impotence and atheroembolization to the lower extremities. As for all vascular reconstructions, the expected benefits of the proposed procedure must be weighed against the potential risks in view of patient comorbidities.

Limb Ischemia

Patients with hip, buttock, thigh, or calf claudication constitute the largest group of patients who undergo aortoiliac endovascular revascularization. Patients with critical limb ischemia (CLI) manifesting as either rest pain or tissue loss frequently have multilevel occlusive disease. In this patient population, the aortoiliac disease is commonly diffuse and complex, often extending into the common femoral arteries (CFAs) and associated with infrainguinal occlusive disease. Patients in whom CFA occlusive disease does not cause significant obstruction can typically be treated with percutaneous approaches that improve perfusion to the lower extremities sufficiently to resolve the rest pain or heal ischemic ulceration. In patients with a significant CFA disease burden, combined femoral artery endarterectomy and patch angioplasty with simultaneous aortoiliac stenting or stent grafting often provides adequate perfusion to treat CLI and claudication.

Younger Patients

Patients younger than 50 years have worse outcomes following aortoiliac endovascular therapy. However, the same is generally true for open surgical approaches such as aortobifemoral bypass.^{5–8} Many younger patients cannot be absent from work for the 6- to 8-week recovery period required after open aortic

surgery, and as a result they may opt for the less invasive endovascular approach acknowledging a potentially less durable outcome when compared to open surgical reconstruction. In addition, many men are concerned about the relatively high incidence of erectile dysfunction that can occur following open aortobifemoral bypass surgery and thus choose an endovascular approach.

Embolization

Less frequently encountered are patients who present with spontaneous embolization to the lower extremity, or so-called blue toe syndrome, who may benefit from endovascular therapy. This is a controversial indication for endovascular therapy and usually involves placement of a bare or covered stent to trap the underlying pathogenic atherosclerotic lesion and prevent further embolization.^{9–11} Endovascular intervention is typically not indicated for patients whose atheroembolization is a result of arterial catheterization procedures. In the absence of subsequent catheterization procedures, the risk of recurrent embolization is low.

Improving Inflow for Concomitant Procedures

Endovascular therapy for aortoiliac disease is frequently required as an adjunct to various open infrainguinal procedures to provide adequate inflow. It may be performed simultaneously with lower extremity bypass or in conjunction with femoro-femoral bypass. Indications for treatment in this setting include a resting systolic pressure gradient proximal to the intended infrainguinal bypass procedure of greater than 10 mm Hg or a vasodilator-enhanced systolic gradient of greater than 20 mm Hg.

CONTRAINDICATIONS

There are no absolute contraindications to the endovascular treatment of aortoiliac occlusive disease. Relative contraindications are largely anatomic and include juxtarenal aortic occlusion, circumferential heavy (>1 mm) calcification, hypoplastic aortic syndrome, and juxtaposition to aneurysmal disease. Renal insufficiency is also a relative contraindication owing to potential contrast-induced nephropathy, although preventive regimens and minimal contrast techniques have reduced the impact of this complication.^{12–14}

RELEVANT ANATOMY: TASC CLASSIFICATION

Lesion-specific indications for the endovascular therapy of aortoiliac occlusive disease can be guided by the Trans-Atlantic Inter-Society Consensus (TASC) guidelines. The TASC classification system (Fig. 111.1) was revised in 2007 to offer more current guidelines on the use of endovascular therapy based on lesion anatomy.¹⁵ In general, endovascular therapy is the recommended first-line therapy for TASC A and B lesions and

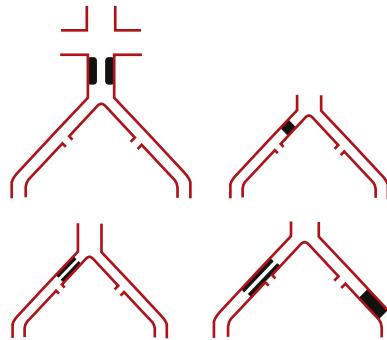
TYPE A LESIONS

- Unilateral or bilateral stenoses of CIA
- Unilateral or bilateral single short (≤ 3 cm) stenosis of EIA



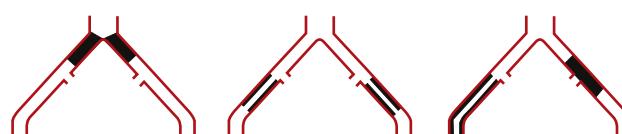
TYPE B LESIONS

- Short (≤ 3 cm) stenoses of infrarenal aorta
- Unilateral CIA occlusion
- Single or multiple stenoses totaling 3–10 cm involving the EIA not extending into the CFA
- Unilateral EIA occlusion not involving the origins of internal iliac artery or CFA



TYPE C LESIONS

- Bilateral CIA occlusions
- Bilateral EIA stenoses 3–10 cm long not extending into the CFA
- Unilateral EIA stenosis extending into the CFA
- Unilateral EIA occlusion that involves the origins of internal iliac artery and/or CFA
- Heavily calcified unilateral EIA occlusion with or without involvement of origins of internal iliac artery and/or CFA



TYPE D LESIONS

- Infrarenal aortoiliac occlusion
- Diffuse disease involving the aorta and both iliac arteries requiring treatment
- Diffuse multiple stenoses involving the unilateral CIA, EIA, and CFA
- Unilateral occlusions of both CIA and EIA
- Bilateral occlusions of EIA
- Iliac stenoses in patients with AAA requiring treatment and not amenable to endograft placement or other lesions requiring open aortic or iliac surgery

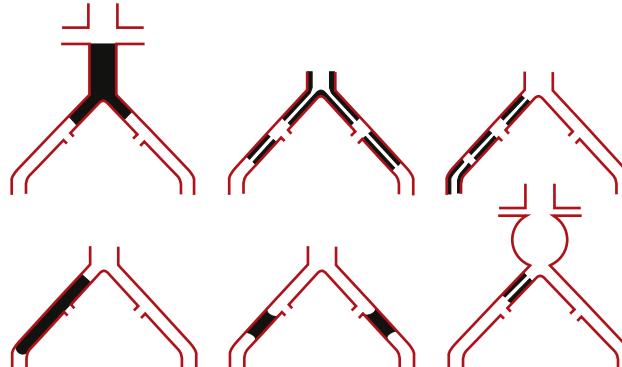


Figure 111.1 TASC Classification of Aortoiliac Lesions. AAA, abdominal aortic aneurysm; CFA, common femoral artery; CIA, common iliac artery; EIA, external iliac artery. (Redrawn from Norgren L, Hiatt WR, Dormandy JA, et al. TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg*. 2007;45(Suppl S):S5–S7.)

increasingly for TASC C lesions as endovascular techniques improve. Good-risk patients with TASC type C disease can also be treated with open surgery, depending on patient preference. Surgery is usually recommended for TASC D lesions, but advanced endovascular approaches are now being applied in these lesions as well, with good results.^{16–18} High-risk patients with TASC C and D disease, CLI, and advanced comorbidities such as severe chronic obstructive pulmonary disease, unreconstructable coronary artery disease, or a low cardiac ejection fraction may be treated with endovascular therapy, acknowledging that this approach will be less durable than open surgical options.

PATIENT EVALUATION AND OPERATIVE PLANNING

Primary Evaluation

Once a decision has been made that intervention is indicated (see Ch. 108, Lower Extremity Arterial Disease: Decision Making and Medical Treatment), information must be gathered to determine the location and extent of the atherosclerotic occlusive disease. This begins with a history and physical examination to determine whether the aortoiliac segment is involved. A history of hip, thigh, or buttock claudication;

impotence; the presence of a lower quadrant abdominal or CFA bruit; and diminished femoral pulses are all suggestive of aortoiliac occlusive disease. Patients should undergo noninvasive physiologic arterial studies, such as ankle–brachial index (ABI) and toe pressure measurements, if indicated. In patients with a history suggestive of vasculogenic claudication but a normal pulse exam or resting ABI, treadmill testing may help differentiate vascular from neurogenic symptoms.

Noninvasive Imaging

Just as when planning for an open aortobifemoral bypass, additional diagnostic studies are indicated before endovascular intervention to assess the location and extent of arterial occlusive disease and the degree of calcification. The use of arteriography as a purely diagnostic tool is infrequently indicated because of the widespread availability of less invasive imaging modalities that provide anatomic detail without the risks of an invasive procedure. A decision to proceed with endovascular treatment versus open revascularization can be made without the use of arteriography. Imaging modalities currently used to evaluate the aortoiliac segment include duplex arterial mapping, magnetic resonance angiography (MRA), and computed tomographic angiography (CTA). All these modalities have benefits and drawbacks.

Duplex Arterial Mapping

Duplex arterial mapping of the aortoiliac segment and CFAs can adequately assess the location of hemodynamically significant lesions (Fig. 111.2). It is particularly helpful to assess the burden of disease in the CFA which may potentially alter a planned percutaneous approach through the CFA to an open CFA endarterectomy and concomitant iliac stent/stent graft placement. This modality is especially useful in patients with renal insufficiency who are at risk for contrast-induced renal dysfunction.¹⁹ Drawbacks of duplex arterial mapping are that it provides only a semiquantitative assessment of the degree of iliac calcification, it may not adequately image the iliac system in certain patients owing to overlying bowel gas or body habitus, and it requires a significant time commitment and a highly

trained vascular technologist.^{20,21} These constraints have prevented duplex arterial mapping from becoming a more widely adopted imaging modality.

Magnetic Resonance Angiography

MRA can reliably assess the aortoiliac arterial segment, although there is institutional variability in its accuracy. The major drawback to MRA is its failure to provide an accurate assessment of the degree of calcification of aortoiliac lesions. It remains contraindicated in patients with renal insufficiency over concerns regarding increased risk of nephrogenic systemic fibrosis due to gadolinium.

Computed Tomographic Angiography

The presence of severe calcification has significant implications for operative or interventional planning. Circumferential calcification thicker than 1 mm is a relative contraindication to aortoiliac angioplasty and stenting because of the potential risk of fracture and rupture of the artery. In patients with significant comorbidities in whom intervention is mandated by CLI, use of a stent graft may be considered in an attempt to limit the incidence of clinically significant arterial perforation. In this setting, CTA has been used with success to assess calcification of the aortoiliac segment before intervention. The major disadvantages of this imaging modality include exposure to ionizing radiation and the need for iodinated contrast agent, with the risk of contrast-induced renal dysfunction. In appropriate patients, CTA can accurately assess lesion location and extent and degree of calcification. Based on CTA, the severity of aortoiliac and femoral disease can be classified according to TASC; this additional information regarding anatomy and severity of calcification allows the formulation of an appropriate procedural plan and the selection of either open or endovascular therapy.

Evaluation for Common Femoral Artery Disease

The determination whether to proceed with percutaneous endovascular therapy or an open femoral approach is based on the presence of significant CFA disease. Patients with greater than 50% CFA stenosis on duplex arterial mapping, MRA,

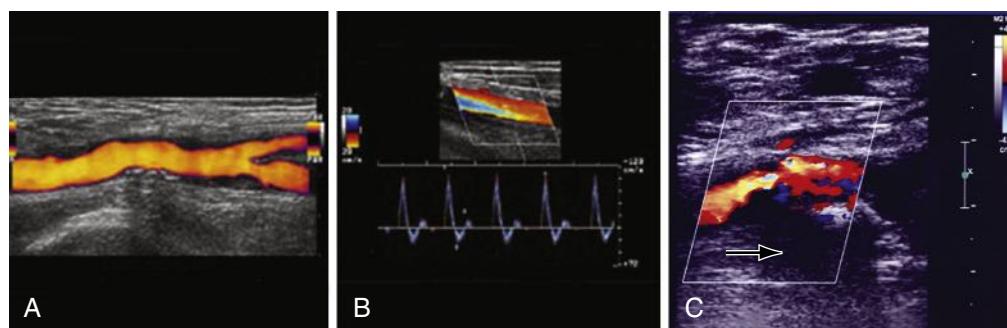


Figure 111.2 Duplex Mapping of the Common Femoral Artery. (A) Longitudinal view of the common femoral artery (power imaging) and the bifurcation of the superficial and deep femoral arteries. (B) Doppler spectral waveform from a normal right femoral artery. The Doppler signal was obtained from a longitudinal view with the Doppler sample volume placed in the middle of the lumen. The characteristic triphasic Doppler signal shows a brisk upstroke to peak systole, reversal of blood flow during early diastole, and a forward flow component during late diastole. (C) Longitudinal view of the common femoral artery with greater than 50% stenosis due to posterior plaque.

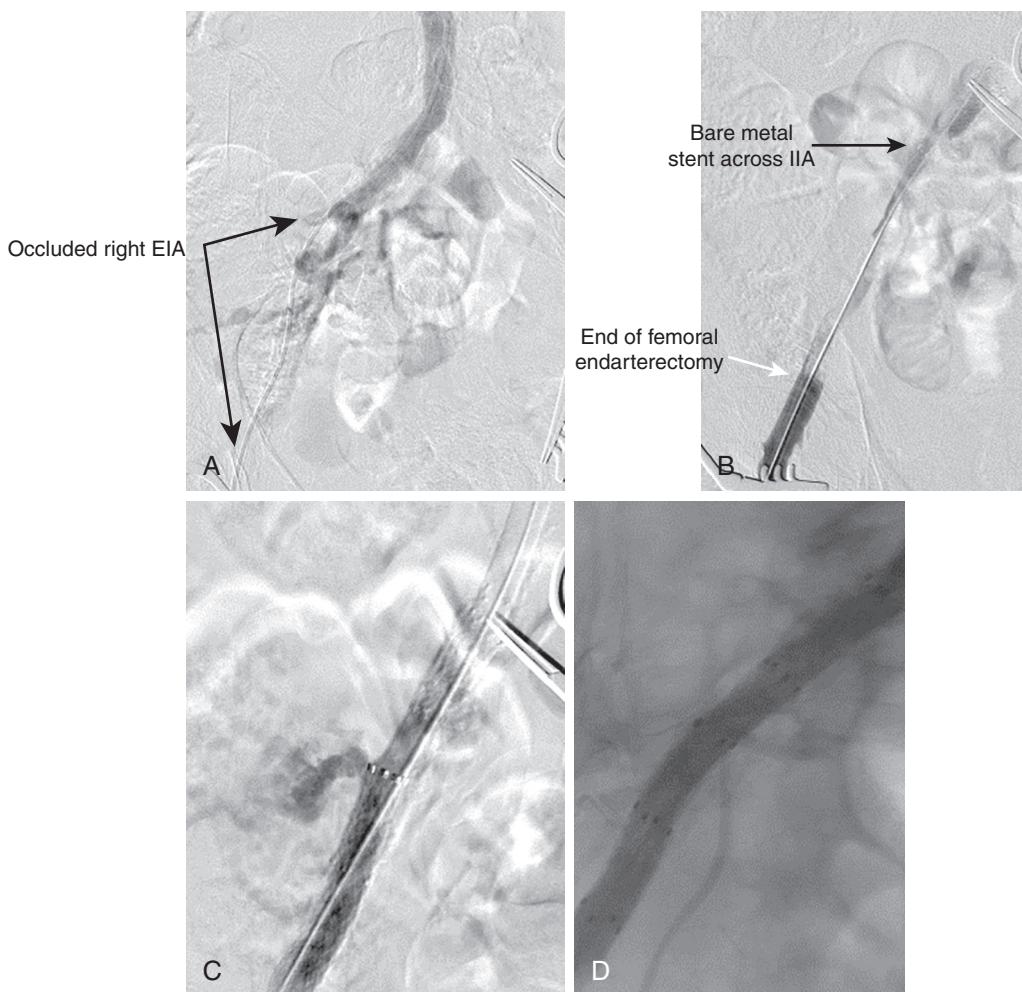


Figure 111.3 Ruptured External Iliac Artery Treated with a Stent Graft. (A) Heavily calcified external iliac occlusion. (B) After completion of femoral endarterectomy and placement of bare stent across proximal external iliac artery – hypogastric. (C) Extravasation from external iliac. (D) Stent graft placed to achieve hemostasis.

or CTA are usually treated with a hybrid approach that entails open ileo-femoral endarterectomy, patch angioplasty, and simultaneous stent or stent-graft placement. In general stent grafts are frequently used in conjunction with open endarterectomy especially in the presence of calcific external iliac artery disease due to the risk of arterial rupture and bleeding with bare metal stents (Fig. 111.3). In patients with less severe CFA disease, a percutaneous approach can be undertaken.

Concomitant Aortic Disease

Aortic angioplasty and stenting for lesions proximal to the aortic bifurcation warrant special consideration because these lesions are frequently exophytic and calcific. When treating such lesions, emphasis should be placed on obtaining an adequate hemodynamic response; acceptance of an imperfect angiographic completion image is critical to avoid aortic rupture. Because of the exophytic nature of these lesions, primary stent or stent-graft placement to trap potential atheroembolic debris should be considered. Primary stenting or stent grafting should also be considered for lesions suspected of being the source of atheroembolization to minimize the potential for embolic complications.

TECHNIQUE

Pretreatment Considerations

Before the intervention, the patient's history and all pertinent imaging studies are reviewed, and informed consent is obtained. Patients' medications typically include an antiplatelet agent and a statin. Recent data from the COMPASS and VOYAGER trials suggests that patients not on dual antiplatelet therapy should be treated with an antiplatelet agent such as 81 mg aspirin per day and low dose rivaroxaban 2.5 mg BID. Patients treated with aspirin and low dose rivaroxaban had significantly lower long-term major cardiovascular events and lower acute limb events compared to aspirin alone.^{22,23} Laboratory tests of coagulation status and renal function are essential.

Determination of Approach

Common iliac artery (CIA) disease is generally treated through an ipsilateral, retrograde approach. If the CIA is occluded, contralateral flush catheter placement should be considered so that a complete diagnostic study can be performed before

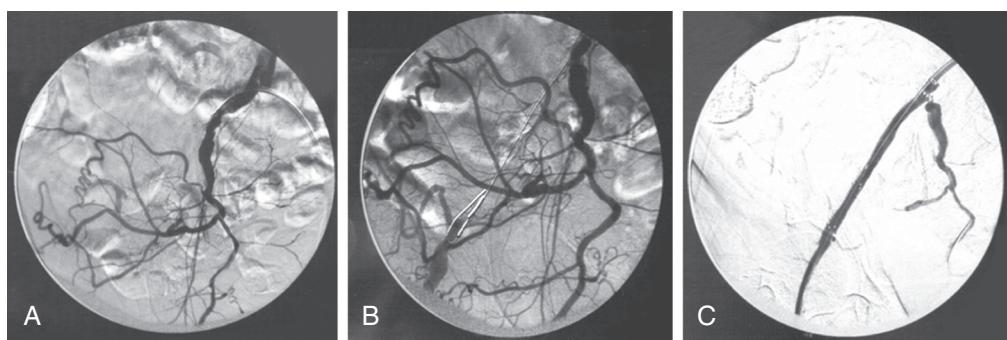


Figure 111.4 (A) External iliac artery occlusion approached through the contralateral common femoral artery. (B) Subintimal crossing of the complete occlusion with a reentry catheter. (C) Contralateral placement of a bare metal stent into the external iliac artery, allowing for placement in the proximal portion of the common femoral artery.

any intervention. This technique also provides access to protect the contralateral CIA from injury during ipsilateral CIA intervention. A complete diagnostic arteriographic examination includes a study of the pararenal aorta to exclude abdominal aortic aneurysm, oblique pelvic imaging of the iliac bifurcations to determine internal iliac artery patency and origin, and adequate views to evaluate CFA bifurcation disease. In general, the contralateral oblique projection shows the iliac artery bifurcations, whereas the ipsilateral oblique projection best displays the profunda origins at the femoral artery bifurcations. Finally, complete imaging of the infrainguinal runoff is requisite before inflow intervention. If imaging of the runoff is done only after completion of the intervention, differentiating preexisting distal occlusive lesions from emboli may be problematic. External iliac disease is generally better approached from the contralateral side because it permits more extensive treatment of the external iliac artery (EIA) into the proximal portion of the CFA if needed (Fig. 111.4).

The procedure begins with placement of an arterial sheath to facilitate catheter exchanges. The lesion is crossed with the use of a catheter-guide wire combination. An angle-tip catheter with a floppy-tipped guide wire is used to cross the lesion first, followed by the catheter. In difficult cases, hydrophilic guide wires may be used (see Fig. 111.4B). After advancing the catheter across the lesion, the wire is removed, and free aspiration of blood ensures that the catheter tip is intraluminal.

Determination of Hemodynamically Significant Lesion

Pressure measurements across the lesion should be obtained by connecting the hub of the catheter and/or the side arm of the vascular sheath to the intra-arterial pressure monitor. Alternative options include the “pullback method,” in which an end-hole catheter is withdrawn from proximal to distal across the lesion over a 0.014-inch wire. Most consider a peak-to-peak systolic pressure gradient of 10 mm Hg or greater at rest to be hemodynamically significant. In the absence of a resting gradient, intra-arterial nitroglycerin (100 to 200 µg) or papaverine (25 mg) can be administered distally to reveal the significance of a lesion. The maximal increase in pressure gradient occurs 20 to 40 seconds after vasodilator injection. If the mean pressure

gradient increases to above 10 mm Hg, the lesion may be considered for treatment.

Techniques to Recanalize Chronic Totally Occluded Iliac Arteries

Contralateral Approach

When attempting to recanalize an occluded common iliac artery in a retrograde fashion, the guide wire frequently follows a subintimal path. Once this has occurred, it may be difficult to redirect the guide wire into the lumen. An antegrade approach from the contralateral CFA is frequently successful, especially if there is a CIA stump and the CIA is not flush-occluded. A hooked catheter is used to probe the occlusion. The lesion can then be crossed with the use of hydrophilic guide wire and a supporting catheter. As soon as the guide wire has crossed the obstructive lesion and lies within the ipsilateral EIA lumen a catheter can be advanced over the wire and intra-arterial placement can be confirmed. Depending on the proximity of the occlusion to the aortic bifurcation a cross-over sheath can be placed over a stiff guide wire or the wire can be snared from the ipsilateral CFA and a sheath can be placed in a retrograde fashion.

Brachial Approach

In the presence of a flush CIA occlusion, a contralateral femoral approach to cross the lesion is frequently unsuccessful; transbrachial or ipsilateral retrograde femoral approaches are more likely to achieve success. A brachial approach reduces the risk of creating or extending an aortic dissection and provides better “pushability.” The presence of significant subclavian artery occlusive disease obviously limits this approach.

Reentry Wires and Catheters

The development of reentry wires and catheters has greatly increased the technical success of crossing complete arterial occlusions. Crossing wires and catheters designed to cross chronic total occlusions (CTOs) typically involve a wire that, based on a mechanical drive system, potentiates passage of the wire through the true lumen of the CTO either through a vibration or rotating action. The majority of these devices have been tested in the femoral-popliteal vascular bed and their utility in the iliac vessels is uncertain.

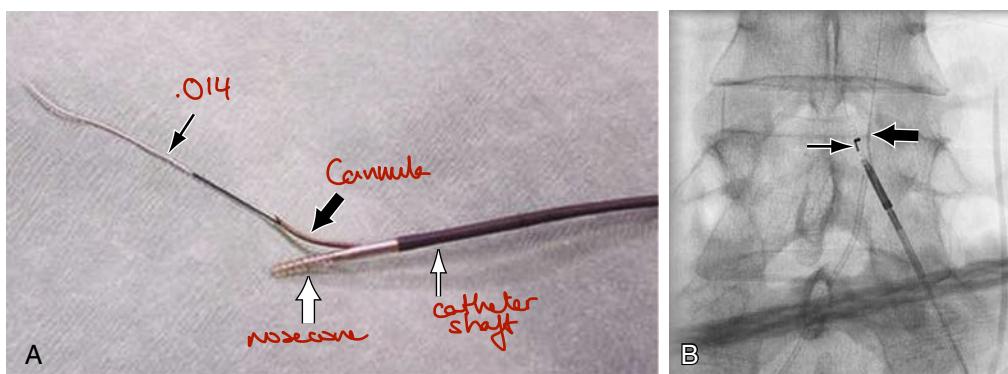


Figure 111.5 Reentry Catheters. (A) Outback LTD catheter. The cannula (large black arrow) is deployed, and the 0.014-inch guide wire (small black arrow) is advanced through it. The nosecone (large white arrow) has the radiopaque “LT” orientation marker. The catheter shaft is indicated by the small white arrow. (B) Outback catheter. The cannula is deployed (large arrow), with free passage of the guide wire into the true lumen of the aorta. Note the “L” configuration (small arrow).

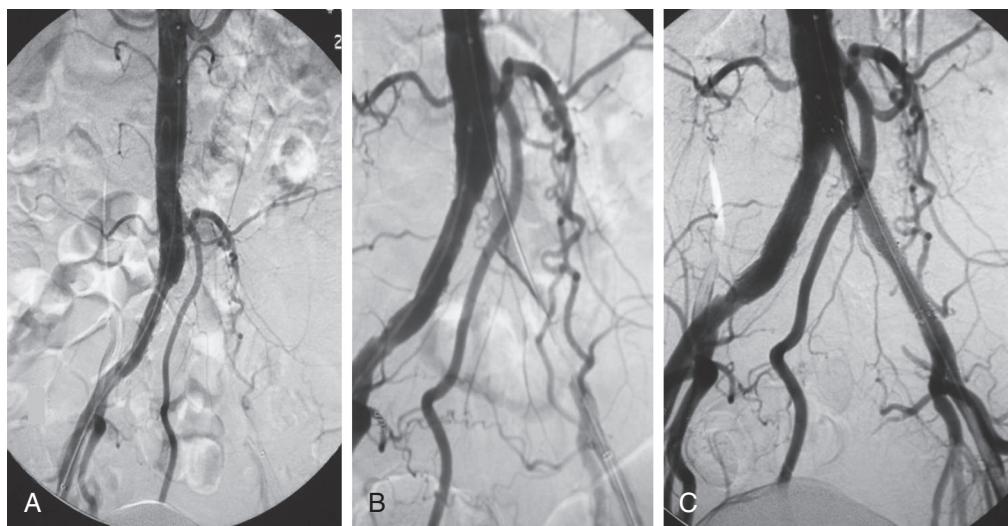


Figure 111.6 Results using a reentry catheter. (A) Pelvic arteriogram showing complete occlusion of the left common and external iliac arteries. (B) Glide catheter advancement into the aorta after reentry at the aortic bifurcation. (C) Retrograde stent-graft placement into the common iliac artery. Note the contralateral bare metal common iliac stent.

The reentry catheters facilitate crossing CTO by a subintimal approach. There are no data to suggest any advantage to crossing an iliac CTO either through the native lumen or subintimally. The Outback reentry catheter (LuMend Inc., Redwood City, CA) is a single-lumen catheter designed to facilitate access and positioning of a guide wire within the peripheral vasculature from a remote vascular entry site using a retractable needle to pierce the intima and gain access to the true lumen (Fig. 111.5). The Pioneer catheter (Medtronic, Minneapolis, MN) works by a similar mechanism but contains an intravascular ultrasound probe in the distal portion that assists in orienting the reentry needle toward the flow lumen. To use this catheter a 300-cm-long, 0.014-inch guide wire is passed subintimally beyond the CTO. Usually a 0.035 wire is used to make the initial subintimal plane and then exchanged for the 0.014 wire. The reentry catheter is then advanced beyond the CTO under continuous fluoroscopy. An angiogram is performed via the contralateral access to confirm traversal of the occlusion and positioning of the lateral exit port of the catheter at the aortic bifurcation proximal to the occlusion. In the case

of the Pioneer catheter this is done with IVUS. The precise location and orientation of the lateral exit port are confirmed by aligning the fluoroscopic guide. The nitinol cannula is then advanced forward through the lateral exit port under continuous fluoroscopy. Applying firm but guarded forward pressure while deploying the cannula may contribute to a successful puncture. Free passage of the 0.014-inch wire indicates true lumen access. This is confirmed by contrast injection through a catheter placed over the wire. The catheter can be exchanged for a 3-mm-diameter angioplasty balloon that is used to dilate the subintimal tract and puncture site. This step enables a catheter to pass and allows exchange for a standard 0.035-inch guide wire to facilitate stenting. Stenting can then be performed in a conventional manner (Fig. 111.6).

Aortic Bifurcation Lesions

Technical Approach

Lesions at the aortic bifurcation have been traditionally treated using the “kissing balloons” technique. Simultaneous balloon

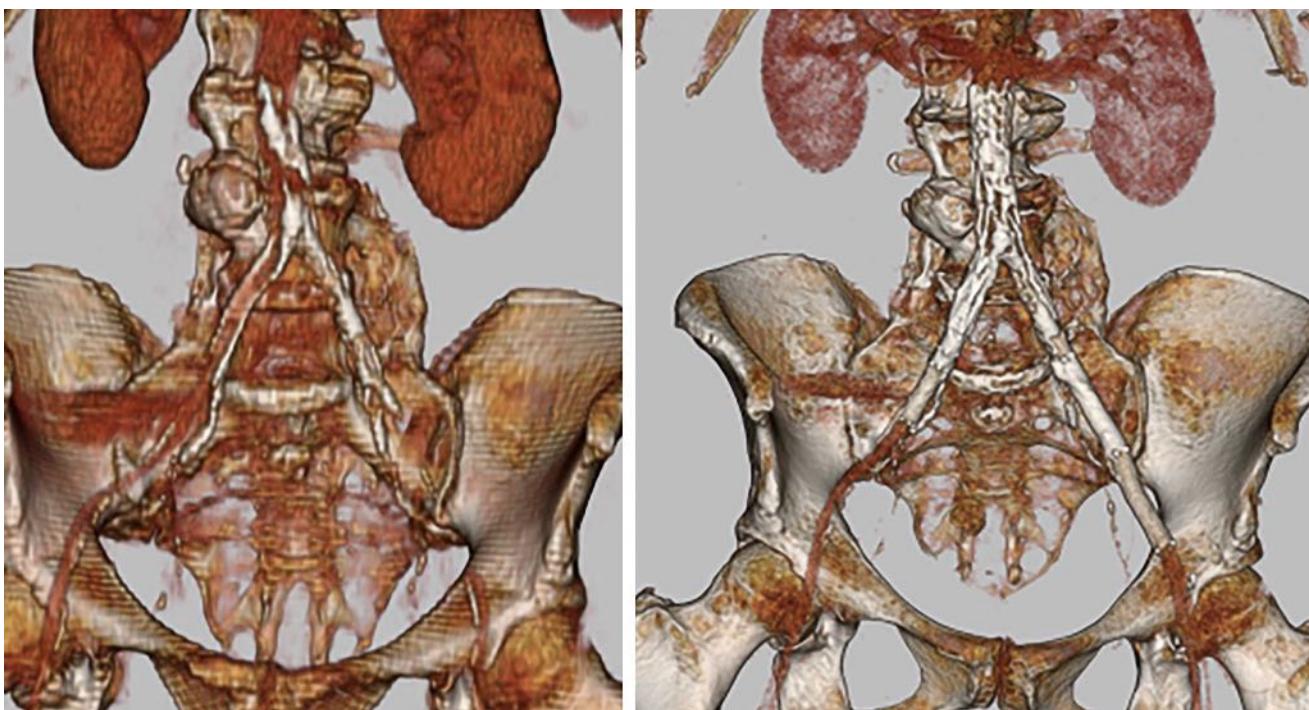


Figure 111.7 Severe aortoiliac occlusive disease treated with Endologix uni-body bifurcated stent graft and bilateral iliac balloon-expandable stent grafts.

dilatation at the origins of both CIAs is advocated, even in the presence of a unilateral lesion, to protect the contralateral CIA from dissection, plaque dislodgement, or subsequent embolization. A retrospective review of patients undergoing percutaneous treatment for unilateral CIA occlusive lesions by Smith and associates challenged this long-established practice.²⁴ In this report, 175 patients with unilateral ostial iliac artery lesions were treated with percutaneous transluminal angioplasty (PTA) or stenting without contralateral protection; in only two patients did the contralateral unprotected CIA develop mild stenosis (17% and 24%, respectively). The authors concluded that protection of the contralateral CIA during PTA or stenting of the ipsilateral proximal CIA is not mandatory.

Aortic Bifurcation Advancement

Because calcified lesions at the aortic bifurcation are not amenable to balloon dilatation alone, the “kissing stents” or “aortic reconstruction” technique is applied.²⁵ The aortic bifurcation reconstruction technique is technically successful; however, some have expressed fear that extension of the proximal ends of the stents into the distal aorta (“aortic advancement”) may serve as a nidus for thrombus formation. More recently reconstruction of the aortic bifurcation and iliac arteries using covered stent grafts has gained increasing acceptance. Early reports are promising with primary patency rates of 82% at 3 years for TASC C and D bifurcation disease. The procedure, termed covered endovascular reconstruction of the aortic bifurcation (CERAB), can be performed with aortic cuffs and iliac limbs or a uni-body bifurcated stent graft.¹⁷ The appeal of the uni-body bifurcated stent graft is that it allows for a contralateral iliac approach should further endovascular therapy be needed (see Fig. 111.7).

Concomitant Femoral Endarterectomy

As previously discussed, patient evaluation through duplex ultrasound, CTA, or MRA can help determine which CFA should be used for percutaneous access. If such studies identify significant CFA disease, an open femoral approach with combined endovascular iliac therapy and femoral endarterectomy should be strongly considered.^{26,27} The CFA is exposed from the circumflex femoral branches down to the femoral bifurcation. The CFA is punctured under direct vision, and the iliac lesion is crossed prior to endarterectomy. This technique allows complete assurance of intraluminal wire placement distally at the endarterectomy site. For cases in which retrograde guide wire passage is not possible as previously described, a percutaneous approach from the contralateral femoral artery or brachial artery can be used to cross the iliac lesion or a reentry catheter can be used at the completion of the endarterectomy. The guide wire can then be brought out through the femoral artery. Wire access is left in place, proximal and distal control is obtained, and a longitudinal arteriotomy is created, allowing for standard endarterectomy and patch angioplasty. Before completion of the patch angioplasty, the center of the patch is punctured with an 18-gauge needle, and the guide wire is brought out through the needle. Patch closure is then completed, and flow is restored. An appropriate sheath can then be passed over the wire to allow iliac stenting. Stents may be extended down to the proximal endpoint of the endarterectomy and patch if necessary (Fig. 111.8).

Stent Sizing

Selection of the appropriate balloon or stent diameter is of utmost importance for a successful intervention. Slight oversizing

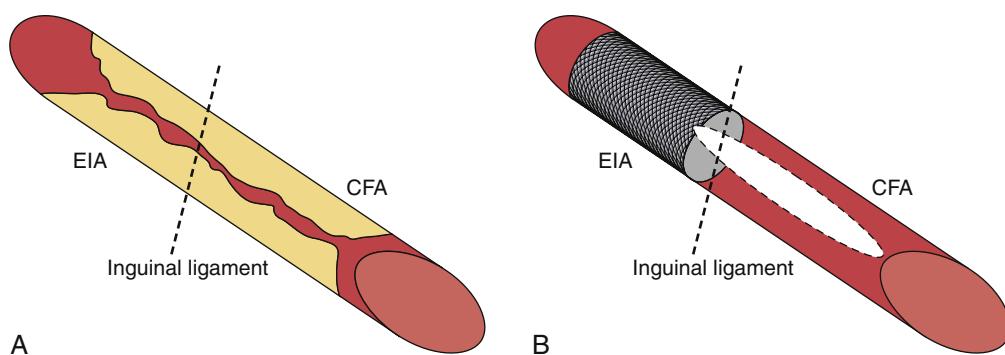


Figure 111.8 Operative technique for an open femoral approach to the diseased common femoral artery (CFA) and external iliac artery (EIA). (A) The common femoral artery is exposed from the circumflex femoral branches, distal to the femoral bifurcation. The common femoral artery is punctured under direct vision, and the iliac lesion is crossed before endarterectomy. Wire access is left in place, and a standard subintimal endarterectomy with patch angioplasty is performed. Before completion of the patch angioplasty, the patch is punctured in the center with an 18-gauge needle, and the guide wire is brought out through the center of the patch. After patch angioplasty is complete and flow is restored, a short sheath can be placed over the wire and through the center of the patch. (B) Iliac stenting can be performed such that the distal endpoint of the stent is just proximal to the endarterectomy and patch angioplasty.

of 5% to 10% is recommended, except in the case of heavily calcified lesions that may rupture. The optimal vessel diameter can be estimated from the adjacent normal arterial segment or by comparison to the same vessel on the contralateral side. A calibrated catheter inserted into the vessel allows measurement of the artery. The length of the balloon or stent should cover the diseased area without damaging the normal vessel. If in doubt when balloon-dilating a lesion, it is wise to undersize. A larger balloon can be used if the initial result is not satisfactory. With balloon expandable stents, this rule does not apply, because an undersized stent usually cannot be exchanged for an optimal one. Balloon inflation should be gradual to avoid trauma to the adjacent normal vessel. A waist on the balloon indicates the lesion location; the waist disappears after successful dilatation. Mild pain during dilatation is acceptable and indicates stretching of the adventitia; excessive pain may indicate impending arterial rupture (see Fig. 111.3A and B). The technical success of the intervention is judged not only by the angiographic appearance but also, and more importantly, by the measurement of any residual pressure gradient. Less than 20% residual stenosis and a less than 10 mm Hg systolic pressure gradient is considered a technical success. The determination of the angioplasty's success should be based on the translesional pressure gradient measurement; angiographic criteria are not reliable.²⁸ Intravascular ultrasound may also be used to assess the technical result following iliac or aortic stent placement. The IVUS will better demonstrate stent–arterial wall apposition and gives a three dimensional assessment of the stented iliac artery.

Stent Selection

Commercially available stents are numerous and fall into four main categories: balloon-expandable bare metal stents, self-expanding bare metal stents, balloon-expandable stent grafts, and self-expanding stent grafts. Features of balloon-expandable stents and stent grafts include precision of placement, good radio-opacity, and high hoop strength. However, they are less

flexible than self-expanding stents and become permanently deformed if external force is directly applied to them.

Placement of a balloon-expandable stent generally requires the sheath to be advanced beyond the lesion, especially in severe stenoses, to avoid dislocation of the stent on the balloon. The stent mounted on the balloon is inserted into the sheath and positioned across the lesion using bone landmarks or road mapping. The sheath is then retracted, and the balloon is inflated to expand the stent. Self-expanding stents and stent grafts are mounted on a carrier device and constrained by an outer sheath. The introducer sheath does not need to cross the lesion. Stent deployment is achieved by holding the carrier device with one hand and retracting the outer sheath with the other. Selection of an iliac artery stent depends on availability and the operator's familiarity with specific devices. In addition, iliac artery tortuosity, introducer sheath diameter, and intrinsic lesion characteristics influence the selection of an appropriate stent type. Short, eccentric, calcified lesions, typically occurring at the aortic bifurcation, are best treated with balloon-expandable stents owing to the ability to place them with great precision. In contrast, whenever the stent must follow a tortuous path or is to be placed from the contralateral side over the aortic bifurcation, self-expanding stents are advantageous because of their flexibility. A frequent scenario for occlusion of the iliac system while performing endarterectomy is to place a balloon-expandable stent graft at the aortic bifurcation and a self-expanding stent graft into the CFA artery patch. If need be, a bare metal stent can be placed across the hypogastric artery to maintain hypogastric artery patency.

RESULTS

Percutaneous Angioplasty versus Selective Stenting

PTA of focal iliac artery stenoses has demonstrated acceptable success rates (Table 111.1). The reported 4-year success rates

TABLE 111.1 Review of Outcomes in Interventional Treatment of Aortoiliac Occlusive Disease

Series	Year	Number of Patients	Indication	Type of Intervention	Primary Patency (%)
Parsons et al. ³²	1998	45		PTA	74 (5-yr)
Klein ³³	2006	279		Primary stenting vs. selective stenting	83 (5-yr)
Bosch and Hunink ³⁴ (meta-analysis)	1997	1300	Claudication vs. CLI	Selective stenting vs. primary stenting	70 (5-yr)
	1997	1300		Primary stenting	77 (4-yr) 67 (4-yr)
Murphy ³⁵ (meta-analysis)	1998	2058		Primary stenting	73 (5-yr)
Schurmann et al. ³⁶	2002	110	93% claudication	Primary stenting	66 (5-yr)
Galaria and Davies ³⁷	2005	276	TASC A and B	Primary stenting	71 (10-yr)
Leville et al. ¹⁶	2006	92	TASC C and D	Primary stenting	76 (3-yr)
Rzucidlo et al. ³⁸	2005	34	TASC B, C, and D	Stent-grafting	80 (5-yr)
Chang et al. ²⁶	2008	171	TASC B,C, and D	Stent graft 41%, bare metal stent 59%	60 (5-yr)
Mwipatayi ³⁹	2011	40 24	TASC C and D	Stent graft Bare metal Stent	95 (18-month) 50 (18-month)
Psacharopulo ⁴⁰	2015	11	TASC D	Stent graft	91 (2-yr)
Zavatta ⁴¹	2018	1472	TASC C and D	Stent graft and bare metal stent	79% (1-yr)

CLI, critical limb ischemia; PTA, percutaneous transluminal angioplasty; TASC, Trans-Atlantic Inter-Society Consensus.

for iliac angioplasty are approximately 44% to 65%. Complications associated with angioplasty include vessel dissection, abrupt closure, spasm, and thrombus formation. Moreover, several studies evaluating the use of PTA alone for total iliac artery occlusions showed a significant embolization incidence, which led some to question the usefulness of PTA in this patient subset.^{29,30} In another study of 106 patients, kissing iliac stents showed good results in aortic bifurcation disease (a location that can be problematic for balloon angioplasty), with primary and secondary patency rates of 78% and 98%, respectively, at 3 years.³¹

Several randomized studies have compared stenting with stand-alone PTA. The Dutch Iliac Stent Trial Study Group performed a randomized comparison of primary balloon-expandable stent placement with primary angioplasty followed by selective stent placement in patients with iliac artery occlusive disease. Iliac patency ranged from 97% (122 of 126 patients) at 3 months to 83% (90 of 109 patients) at the final mean follow-up of 5 years in the patients with primary stent placement; it ranged from 94% (113 of 120 patients) to 74% (67 of 90 patients) in the patients treated with PTA and selective stent placement. This difference was not significant. The study also showed that selective stent placement was more cost-effective than primary stenting of iliac artery stenosis.^{28,42} However, nearly half the patients (43%) randomized to balloon angioplasty underwent stent placement for a suboptimal result during the primary procedure. Twenty-five of 143 patients (17%) treated with primary stent placement needed re-intervention in the iliac artery segment because of the development of symptomatic or hemodynamic (by noninvasive testing) restenosis. In the PTA and selective stent placement

group, 28 of 136 patients (21%) needed re-intervention. Complication rates were nearly double (4% versus 7%) in the angioplasty group.⁴²

Primary Stenting versus Selective Stenting

Randomized trials have shown primary stenting to be superior to selective stent placement in terms of both hemodynamic parameters and Rutherford classification (see Table 111.1). These include a meta-analysis comparing the results of PTA versus stent placement for iliac occlusive disease.³⁴ This meta-analysis of more than 1300 patients compared selective to primary iliac artery stenting and found significantly higher initial technical success (>90%) and improved primary patency rates (>70% at 2 and 5 years) in both claudicants and those with limb-threatening ischemia among patients treated with primary stenting.³⁴ Because critical ischemia was considered an independent risk factor for failure, the authors stratified patency rates for claudication versus critical ischemia. The 4-year primary patency rate for claudication, with technical failures excluded, was 68% (range, 65% to 74%) after PTA, compared with 77% (range, 72% to 81%) after stenting. The 4-year primary patency rate for critical ischemia, with technical failures excluded, was 55% (range, 48% to 63%) after PTA, versus 67% (range, 55% to 79%) after stenting. The authors concluded that stent placement reduced the risk of long-term failure by 39% compared with PTA alone. Disease severity (claudication versus critical ischemia) was an independent predictor of long-term failure. However, whenever initial success was achievable, no statistically significant difference in long-term patency was found between stenoses and occlusions.

1° stent > PTA alone → better 4yr patency

Patency Based on TASC Classification

TASC Types A and B Lesions

Outcomes of iliac intervention depend on TASC lesion classification. Galaria and associates examined reported 10-year patency results for patients with TASC types A and B lesions.³⁷ Indications for intervention were claudication (77%) or critical ischemia (23%). Altogether, 276 patients (all men; average age, 64 ± 11 years; range, 32 to 87 years) underwent 394 interventions. Sixty-two percent of the lesions were TASC type A, and the remainder were type B. Of the 394 primary interventions, 51% included the placement of stents. Technical success (defined as <30% residual stenosis) was achieved in 98% of treated vessels. The procedure-related mortality rate was 1.8% at 30 days and 4.7% at 90 days; the procedure-related complication rate was 7%. Hemodynamic success (defined as a rise in the ABI >0.15) was achieved in 82%. The average Society for Vascular Surgery symptom score was 3.4 + 0.9 before intervention; this improved to 1.9 ± 0.8 following intervention. Within 3 months, 84% of patients demonstrated clinical improvement. The cumulative assisted patency rate was $71\% \pm 7$ at 10 years. The presence of two-vessel femoral runoff, two or more patent tibial vessels, or both was associated with improved patency. Limb salvage rates were $95\% \pm 2$ and $87\% \pm 9$ at 5 and 10 years, respectively. By Cox proportional hazards analysis, hypertension, hypercholesterolemia, and chronic renal insufficiency were associated with increased risk of primary failure, whereas the presence of immediate hemodynamic improvement was associated with increased long-term patency. Use of a stent did not influence outcome. These results approach those reported for surgical aortoiliac bypass grafting. For comparison, in a meta-analysis of 23 studies of aortoiliac or aortofemoral bypass grafts published between 1970 and 1996, de Vries and Hunink calculated limb-based patency rates of 91% and 86.8% at 5 and 10 years, respectively, for patients with claudication, and patency rates of 88% and 82%, respectively, for patients with critical ischemia (Fig. 111.9).⁴³

TASC Types C and D Lesions

Although iliac angioplasty and stenting of TASC types A and B common iliac lesions achieve a patency similar to that of open surgical reconstruction, patients with diffuse aortoiliac occlusive disease (TASC types C and D lesions) have markedly inferior patency with bare metal stenting when compared with aortobifemoral bypass. Recently, several authors have documented more promising results in the treatment of more complex TASC types C and D iliac lesions. Jongkind and coworkers recently reported a meta-analysis of the late results of the endovascular treatment of complex iliac occlusive disease.⁴⁴ Five-year primary patency, secondary patency ranged from 60% to 86%, with secondary patency rates of 80% to 98%. In a series of 105 patients with chronic iliac occlusions, estimated 60-month primary, assisted primary and secondary patency and survival rates in this group was 92%, 92%, 96% and 82.5%, respectively.⁴⁵ More recently stent

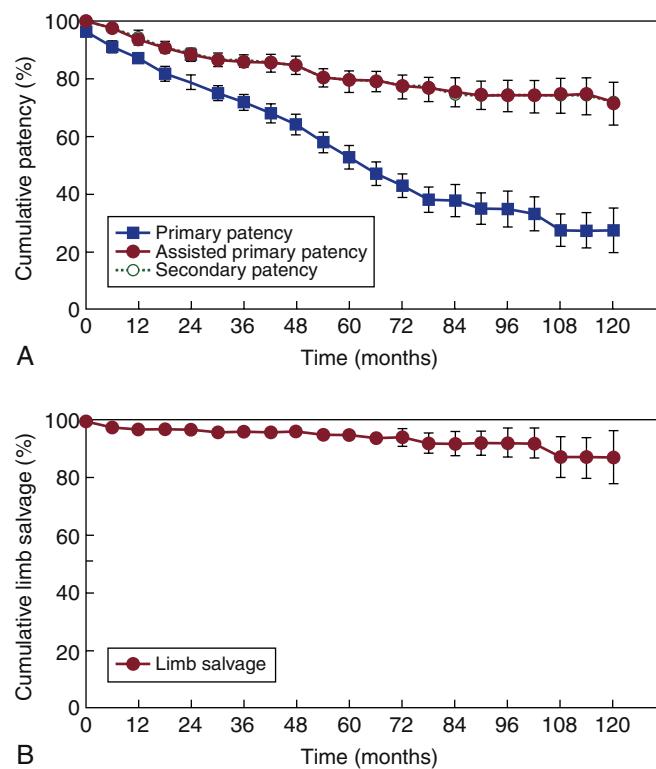


Figure 111.9 (A) Cumulative primary patency, assisted primary patency, and secondary patency (superimposed in assisted primary patency) intervals for all vessels. (B) Cumulative limb salvage for all patients. In both A and B, the values are the mean \pm a standard error less than 10% for all data points by life-table analysis. (From Galaria II, Davies MG. Percutaneous transluminal revascularization for iliac occlusive disease: long-term outcomes in Trans-Atlantic Inter-Society Consensus A and B lesions. *Ann Vasc Surg.* 2005;19:352–360.)

graft placement has been shown to improve outcomes in patients with TASC C and D lesions. This will be subsequently discussed below.

Patency Based on Global Limb Anatomic Staging System (GLASS) Classification

The Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia (CLTI) have developed the GLASS classification system which also addresses aortoiliac inflow disease in patients with CLTI.⁴⁶ Disease staging of aortoiliac disease in GLASS consists of two stages.

- Stage 1: Stenosis of the common and/or external iliac artery. Chronic total occlusion of either the common or external iliac artery (not both), stenosis of the aorta; any combination of these.
- Stage 2: Chronic total occlusion of the common and external iliac artery; severe diffuse disease and/or small caliber (<6 mm) common and external iliac arteries. Concomitant aneurysm disease. Severe diffuse in-stent restenosis in the AI system.
- A: no significant CFA disease; B: significant CFA disease (>50% stenosis)

The authors suggest using an endovascular first approach for patients with GLASS stage 1A disease and surgical reconstruction for average risk patients with GLASS 2 disease.

Patency with Concomitant Common Femoral Artery Disease

Chang and colleagues have reported their long-term results of combined endovascular and open treatment of iliofemoral occlusive disease.²⁶ One hundred and seventy-one patients underwent 193 CFA endarterectomies and iliac stent or stent-graft placement. Indications were rest pain (32%), tissue loss (22%), and claudication (46%). EIA lesions were present in 39%, combined CIA and EIA lesions were seen in 61%, and complete CIA–EIA occlusions were present in 41% of patients. Stent grafts were used in 41% of patients. Technical success was reported in 98%, and clinical improvement was seen in 92% of patients. Five-year primary, primary assisted and secondary patency rates were 60%, 97%, and 98%, respectively. Endovascular re-intervention was required in 14% of patients; inflow surgical procedures were required in 10%. By logistic regression analysis, use of stent grafts compared with bare stents was associated with significantly higher primary patency ($87\% \pm 5$ vs. $53\% \pm 7$; $P < 0.01$). In a study by Zavatta and coworkers analyzing data from the Vascular Quality Initiative, they compared aortobifemoral bypass to hybrid endovascular repair consisting of open femoral endarterectomy and iliac stent placement. The authors found that the hybrid approach was associated with lower 30-day mortality and comparable 1-year primary patency (ABF 81% vs. hybrid 79%) but increased 1-year mortality (8.6% vs. 6.3%, $P = 0.04$).⁴¹ In a meta-analysis performed by Premaratne and coworkers, the authors compared outcomes of endovascular revascularization vs. direct surgical reconstruction.⁴⁷ TASC C and D lesions were present in 69% of endovascular patients and 79% of direct surgical-treated patients. Direct surgical repair had improved primary patency compared to endovascular repair (HR 0.51; CI 0.36–0.73; $P = 0.0002$); however, endovascular procedures combined with femoral endarterectomy had improved primary patency compared to endovascular procedures without femoral endarterectomy (HR 0.43 vs. 0.88, $P = 0.0002$). This study again shows the advantage of the hybrid approach to endovascular repair of iliac occlusive disease in appropriate patients.

Predictors of Failure

Extension of disease into the EIA increases procedural complexity and decreases the durability of the intervention. The presence of external iliac disease has been shown to be a predictor of decreased primary and primary-assisted patency rates.^{48–50} In a study by Powell and coworkers, patients with severe EIA disease treated with bare metal stents had a 1-year primary patency rate of only 47%.^{48,51} These patients also had poor rates of hemodynamic and clinical improvement after intervention. Many required surgical inflow procedures or subsequent endovascular re-intervention to maintain aortoiliac patency. Other reported predictors of worse outcome after iliac artery angioplasty are female gender,⁵² renal insufficiency, and CLI and non-Caucasian race.^{49,50} Timaran and associates concluded that women with EIA stents had the poorest outcomes.⁵³ Work by Danczyk and coworkers failed to find a difference in

outcome between patients treated with bare metal stents for EIA versus CIA lesions.⁵²

Stent Grafting

Stent grafting has in the past been used to treat patients with isolated iliac aneurysms, iatrogenic perforations or ruptures, arteriovenous fistulae, and on occasion severe aortoiliac occlusive disease, especially those with small calcified EIAs, who are not candidates for open surgical intervention. These devices are stainless steel, nickel–cobalt–titanium–steel alloy (Elgiloy), or nitinol stents covered with Dacron or polytetrafluoroethylene (PTFE).^{39,40,54,55} More recently stent grafts have become more frequently used to treat patients with aortoiliac occlusive disease, especially TASC C and D lesions.

Stent-Graft Patency

Stent-graft treatment of patients with severe aortoiliac occlusive disease (85% TASC types C and D lesions) was reported by Rzucidlo and colleagues.³⁸ The use of stent grafts increased the primary and primary-assisted patency at 1 year to 70% and 88%, respectively, compared with patients treated with bare metal stents alone, and led to 100% early hemodynamic and clinical success. There was a trend toward improved primary iliac artery patency in patients who underwent concomitant common femoral endarterectomy compared with patients who did not. At 6 and 12 months, the primary patency rates in patients who underwent concomitant common femoral endarterectomy were 94% and 94%, respectively, compared with 79% and 53% in patients who did not undergo endarterectomy.

Others have reported the use of stent grafts to treat diffuse iliac occlusive disease. Nevelsteen and coworkers placed 29 stent grafts in 24 patients to treat claudication ($n = 7$) or limb-threatening ischemia ($n = 17$).⁵⁵ Mean primary and secondary cumulative patency rates after 1 year were 85% and 95%, respectively. All patients in this series underwent outflow procedures – that is, profundaplasty or femoral distal grafting. Psacharopulo has demonstrated 91% 2-year primary patency in patients treated with self-expanding stent grafts for TASC D lesions.⁴⁰ These patients also underwent concomitant femoral endarterectomy.

Data from the multicenter ILIACS registry demonstrated no difference in primary patency when comparing bare metal stents to stent grafts in the treatment of iliac TASC C and D lesions. Primary patency at 36 months was 93% for each group. However stent-graft treatment had a lower incidence of arterial rupture (0% vs. 3.5%, $P = 0.013$) and improved patency in moderately to severely calcified iliac lesions when compared to bare metal stents.⁵⁶

The COBEST trial was a randomized trial comparing bare metal stent placement to stent grafts in patients with TASC B–D lesions. At 5 years the primary patency for patients receiving stent grafts was superior to bare metal stent placement (75% vs. 63%, $P = 0.01$, Fig. 111.10).⁵⁷ This improvement in patency was more dramatic in patients with TASC C and D lesions. Use of a stent graft and Rutherford class were the only predictors of patency.

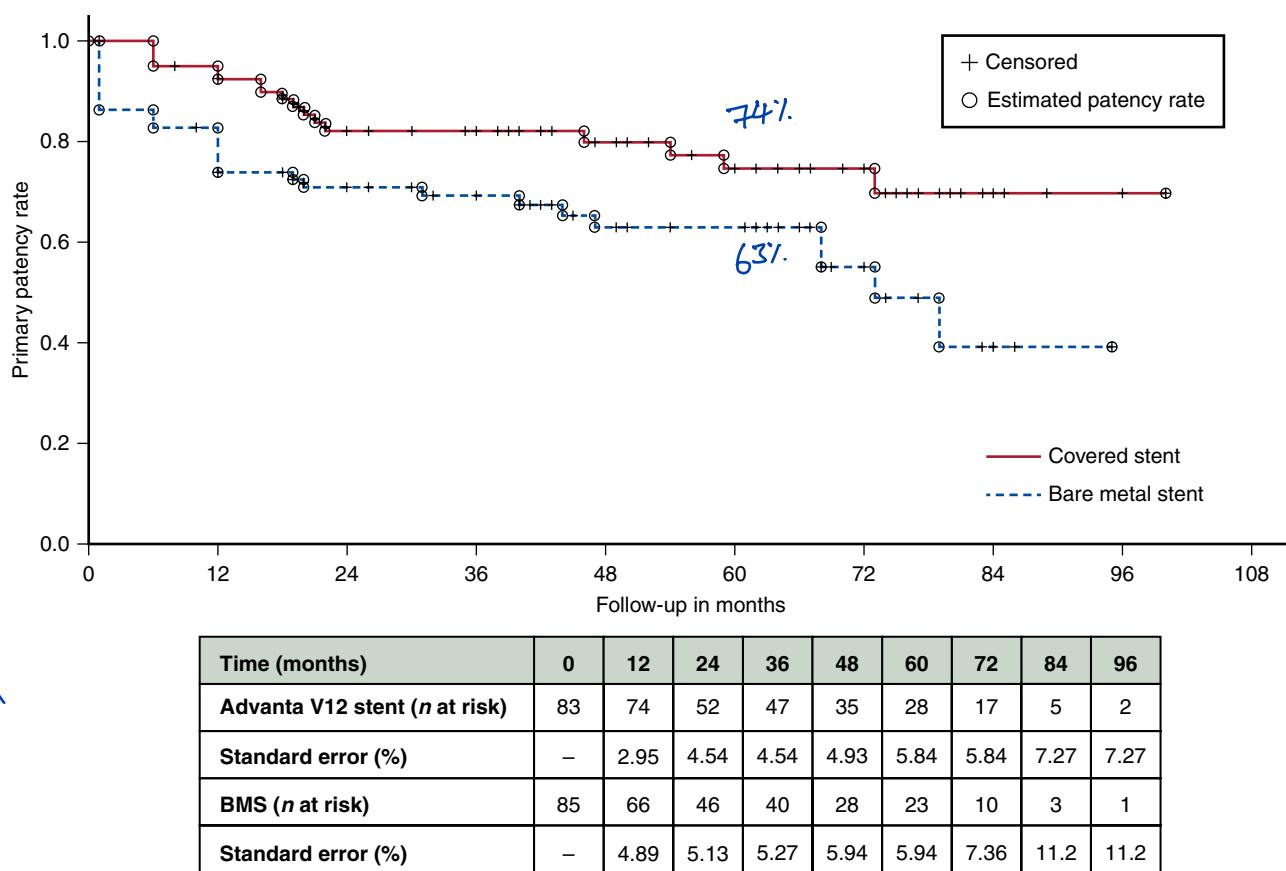


Figure 111.10 Kaplan–Meier curve of overall primary patency rates of both stent groups. The overall patency rate was 74.7% in the covered stent (CS) group vs. 62.9% in the bare metal stent (BMS) group at 60 months of follow-up (log-rank test, $P = 0.01$). *n* at risk, number of stents at risk of severe restenosis.³⁷

Predictors of Failure for Stent Grafting

CFA disease has been shown to be a significant predictor of failure at long-term follow-up. In a study by Chang and co-workers, 5-year primary patency rate was 88% for patients who had concomitant CFA endarterectomy and iliac stent grafting, versus 66% for stent grafting alone ($P = 0.04$; relative risk, 8). This finding has prompted more intense evaluation of the CFA plaque burden before proceeding with iliac intervention (Fig. 111.11). *if CFA endarterectomy*

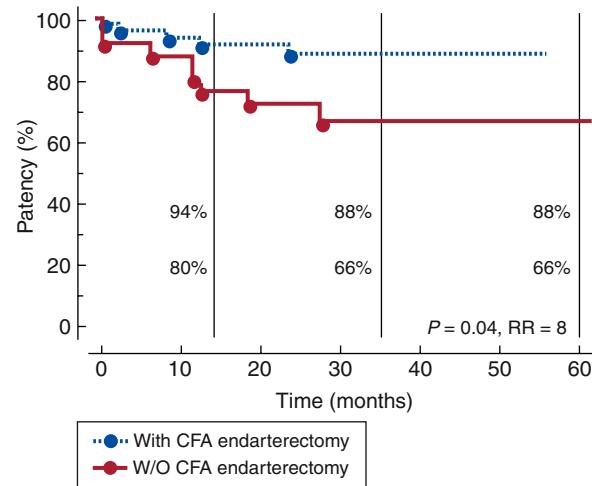


Figure 111.11 Kaplan–Meier primary patency curves for patients with common femoral artery (CFA) disease as a variable. Patients with concomitant CFA endarterectomy had significantly better patency than those without (W/O) endarterectomy (88% vs. 66% at 60 months; $P = 0.04$). RR, relative risk.²⁶

COMPLICATIONS

Bypass surgery has the best long-term durability, with 5-year patency in excess of 80%, but it has been associated with a perioperative complication rate of up to 30%.^{58–63} Recovery from aortobifemoral bypass typically requires weeks of absence from work, a financial burden that many patients cannot absorb. Thus, less invasive endovascular treatment for aortoiliac occlusive disease has largely supplanted aortobifemoral bypass because focal iliac disease is well treated with angioplasty or stent placement. These less invasive options are not without complications, however. These complications can be categorized as contrast related, sheath site related, and remote.

Sheath-Site Related

The incidence of local wound complications related to sheath insertion is 1% to 3%, but this can be reduced by accurate placement of the puncture site in the CFA, avoiding high and low punctures. Most sheath sites can be closed with closure

devices to decrease the incidence of hematoma and CFA pseudoaneurysm.⁶⁴

Iliofemoral arteriography is performed to determine the suitability for closure device use. If the femoral artery is less than 5–6 mm or if significant calcification is present, the sheath is removed after the activated clotting time has decreased to less than 200 seconds and manual pressure is applied. If CFA disease is not well defined before intervention, posterior plaque disruption by means of the initial needle puncture can cause acute CFA occlusion. Femoral artery occlusion is obvious on physical examination by the loss of color and pulses; immediate operative intervention with groin exploration is necessary.

Remote

Arterial Rupture

Arterial rupture is an uncommon (<1%) but potentially serious complication. In most instances, arterial rupture occurs in the setting of angioplasty or stenting of small, heavily calcified EIAs. When the procedure is performed under local anesthesia, patients typically have significant flank or back pain before the artery ruptures. If such pain occurs, further dilatation should not be performed. Patients under regional or general anesthesia do not exhibit these symptoms. Arterial rupture can usually be treated with the placement of stent grafts to seal the ruptured iliac artery (see Fig. 111.3A to C). A balloon occlusion catheter may be needed to stabilize hypotensive patients. This must often be placed from the contralateral femoral artery to allow for upsizing of the ipsilateral femoral sheath to a size sufficient to allow placement of a stent graft.

Arterial Dissection

Arterial dissection has been described as a complication of PTA. Proximal or distal progression of iliac dissection can occur beyond the site of intervention. The typical cause is over-dilatation of a small calcified artery. Treatment consists of the extension of stenting to stop flow-limiting occlusion due to the dissection.

Embolization

Distal embolization is uncommon in the absence of aggressive pre-dilatation prior to iliac stent placement. Appropriate assessment by pre- and postprocedural arteriography, physical examination, and Doppler evaluation is important to detect this complication.

POSTOPERATIVE MANAGEMENT

There are well-accepted criteria for reporting procedural success, clinical improvement, and patency, and the proper use of these standards for outcomes is critical. Initiation of a program of ongoing care to monitor and treat modifiable risk factors is also an important aspect of postoperative management. Risk factor management is critical and is discussed in Chapter 108 (Lower Extremity Arterial Disease: Decision Making

and Medical Treatment). In general, patients should be on an antiplatelet therapy and statin. Regular follow-up should be performed at 1 month, 6 months and yearly to assess patient outcome. This should include a history, pulse examination and hemodynamic evaluation such as ankle-brachial index measurements.

Medical Therapy Following Aortoiliac Endovascular Intervention

All patients who undergo revascularization should continue with best medical therapies. In addition patients should be maintained on a statin and antiplatelet agent such as aspirin. In addition recent evidence suggests that if not otherwise contraindicated patients may be considered for secondary prevention low dose rivaroxaban in order to prevent late major adverse cardiovascular events.^{22,23}

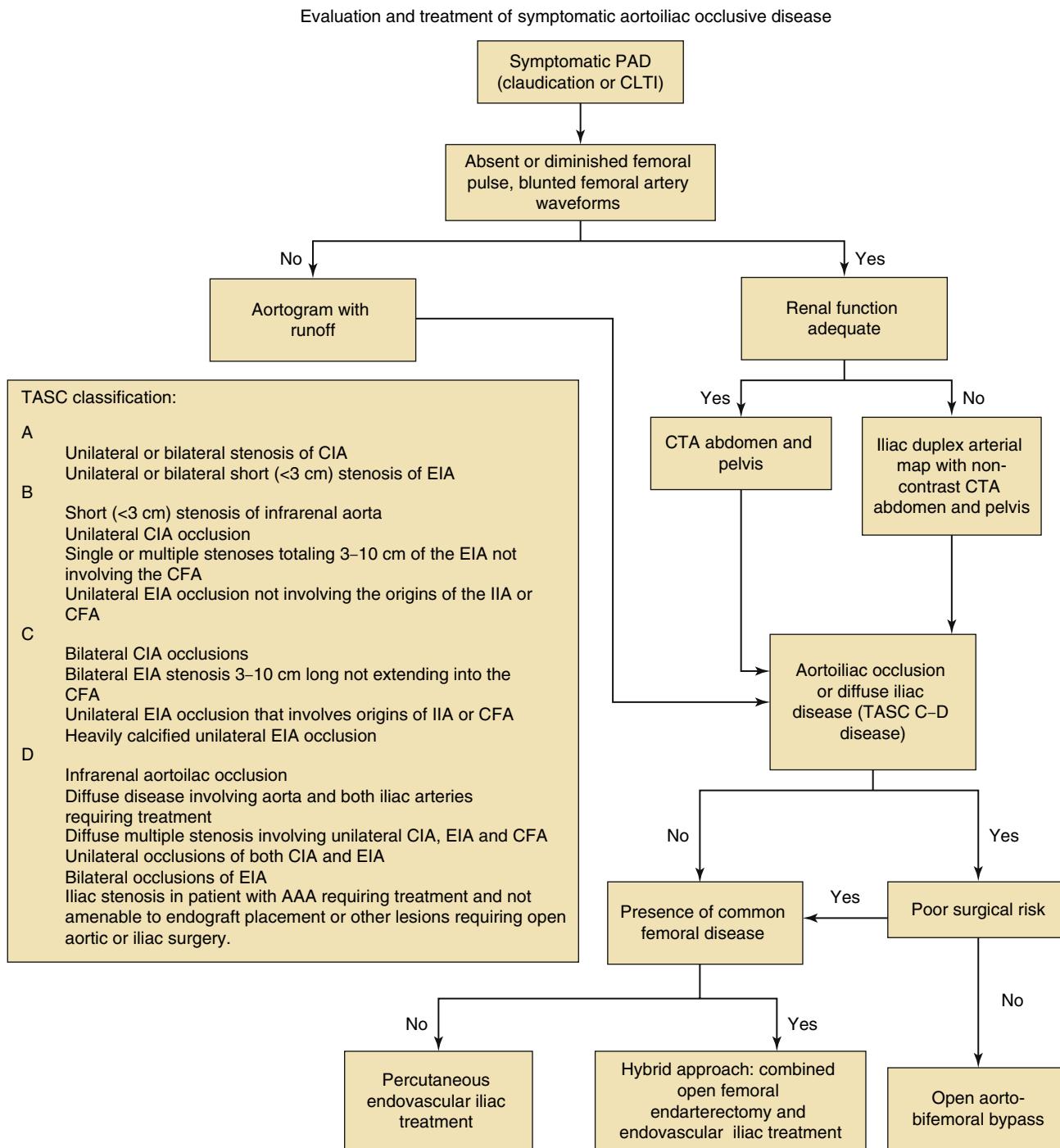
Criteria for Reporting Significant Change in Clinical Status

Clinical assessment expressed grossly in terms of “symptomatic relief” is notoriously unreliable because it lacks objectivity. Combining standard clinical categories with objective noninvasive testing can overcome this weakness. For reporting purposes, the designation “clinically improved” requires an upward shift by at least one clinical category (see Ch. 107, Lower Extremity Arterial Occlusive Disease: Epidemiology and Natural History, Table 107.3), except for those with actual tissue loss (category 5), who must move up at least two categories and reach a level of claudication to be considered improved. In addition, to claim a cause and effect and attribute the improvement to treatment, some objective evidence of hemodynamic improvement must be documented; an increase of more than 0.10 in ABI is recommended. In patients in whom the ABI cannot be accurately measured (e.g., those with diabetes and medial calcinosis), the systolic toe pressure (which is less commonly affected by vessel incompressibility) or any measurable pressure distal to the revascularization can be substituted.

Criteria for Patency

The determination of patency for iliac stents should be based on objective findings. Although physical examination can detect the presence of a palpable femoral pulse, iliac stent patency should be demonstrated by an accepted vascular imaging technique such as arteriography, duplex ultrasound color-flow scan, or magnetic resonance imaging. A diameter reduction within the stented segment of greater than 50% indicates significant restenosis. A biphasic or triphasic Doppler waveform should be noted at the CFA level. No clear duplex criteria for the iliac segment exist; however, most would consider a doubling of the peak systolic velocity indicative of restenosis, especially with an ABI drop greater than 0.1.³

CHAPTER ALGORITHM



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

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Infrainguinal Disease: Surgical Treatment

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Lower extremity arterial reconstruction is most commonly performed in patients with moderate to severe limb ischemia due to atherosclerotic peripheral artery disease (PAD). Although the techniques described below may also be applied to patients with traumatic, aneurysmal, and nonatherosclerotic conditions, this chapter focuses exclusively on patients with PAD.

Infrainguinal bypass is defined as any major arterial reconstruction using a bypass conduit, either autogenous or prosthetic, that originates at or below the inguinal ligament. Inflow sites therefore include the common, deep, and superficial femoral arteries as well as the popliteal or even the tibial arteries. The bypass insertion site may be the femoral, above- or below-knee popliteal, tibial, peroneal, or pedal artery. During the past two decades, progress in patient evaluation and selection and in the conduct of infrainguinal bypass operations has resulted in a more aggressive and generally more successful approach to distal arterial reconstructions, especially for patients with chronic limb-threatening ischemia (CLTI), many of whom would otherwise face major limb amputation. CLTI is a spectrum of disease. Determining whether revascularization is required for wound healing and, if performed, whether open bypass or endovascular therapy is the best initial option is still contentious due to observer bias, widely variable levels of technical expertise and lack of prospective, randomized data to support any given approach. Although graft patency and limb salvage rates have demonstrated continuous improvement, there remains a critical need for detailed clinical studies examining the cost-effectiveness of infrainguinal bypass as well as patient quality of life (QoL) outcomes to ensure the appropriate use of these procedures and to permit meaningful comparison with less invasive endovascular therapies.

INDICATIONS

The two primary indications for infrainguinal bypass are CLTI and claudication.

Claudication

Patients who are truly disabled by claudication, such that they are unable to perform their primary occupations or comfortably carry out the activities of daily living, and those whose lifestyles are significantly limited are potential candidates for infrainguinal bypass. A trial of smoking cessation, lifestyle modification, and exercise, with or without medical therapy, is usually indicated before operative intervention (see Ch. 108, Lower Extremity Arterial Disease: Decision Making and Medical Treatment). There is consensus that bypass is preferable to angioplasty in patients with TransAtlantic Inter-Society Consensus (TASC) type D lesions, that is, complete common femoral artery (CFA) or superficial femoral artery (SFA) occlusions or complete popliteal and proximal trifurcation occlusions; however, bypass may also be applied to patients with types B and C lesions.¹ Operation should be offered only if the benefit-to-risk ratio is high and if anatomic characteristics suggest a favorable and durable result. The primary reason for intervention in claudicants is to improve lifestyle or QoL, given

that the risk of severe clinical deterioration (20%) or major limb amputation (5%) during a 3- to 5-year period is low.^{1,2} In most centers with extensive infrainguinal bypass experience, claudicants constitute only 15% to 30% of patients, with the majority of patients undergoing bypass for CLTI. These data reflect practice patterns in tertiary referral centers and may not reflect the realities of community-based practices.³

Chronic Limb-Threatening Ischemia

Patients with advanced CLTI generally require intervention. Such patients previously fell into Fontaine III and IV⁴ and Rutherford 4 to 6 categories (see Chs. 107, Lower Extremity Arterial Occlusive Disease: Epidemiology and Natural History and 108, Lower Extremity Arterial Disease: Decision Making and Medical Treatment).⁵⁻⁷ The most recent European consensus document defines CLI as follows: persistent, recurring ischemic rest pain requiring opiate analgesia for at least 2 weeks and ankle systolic pressure lower than 50 mm Hg or toe systolic pressure lower than 30 mm Hg; or ulceration or gangrene of the foot or toes and ankle systolic pressure lower than 50 mm Hg; or toe systolic pressure lower than 30 mm Hg (or absent pedal pulses in diabetics).⁸ Wolfe and Wyatt⁹ further subdivided patients meeting the longstanding definition of CLI into critical or subcritical ischemia on the basis of subsequent, observed amputation risk. Subcritical ischemia is present in patients with rest pain and ankle pressure higher than 40 mm Hg. Critical ischemia is defined as rest pain and tissue loss or ankle pressure lower than 40 mm Hg. This distinction is based on a retrospective analysis of 20 publications analyzing 6118 patients. At 1 year, 27% of patients with subcritical ischemia achieved limb survival without revascularization, in contrast to only 5% in the group of patients with critical ischemia. In practice, these data indicate that certain extremely high-risk patients with subcritical ischemia might be managed medically (nonoperatively) but that virtually all patients who are expected to live more than 1 to 2 years with true "critical ischemia" require either bypass or major limb amputation. Because of inconsistencies with terminology and the inappropriate application of the term critical limb ischemia to patients with diabetes, the Society for Vascular Surgery Lower Extremity Guidelines Committee created a more comprehensive threatened limb classification system intended to stratify amputation risk in patients across the spectrum of CLTI.¹⁰ This system is based on objective grades Wound (W), Ischemia (I) and Foot Infection (FI) to calculate a threatened limb clinical stage from 1 to 4 and has been validated in multiple studies to be highly predictive of 1-year major limb amputation risk, including a recent systematic review and meta-analysis.¹¹ This classification has subsequently been incorporated into the Global CLTI Guidelines, which also include a new anatomic classification system, known as GLASS. GLASS has yet to be validated for infrainguinal bypass.¹²

PREOPERATIVE ASSESSMENT

It is broadly recognized that patients requiring infrainguinal bypass frequently have medical comorbidities, which may include diabetes mellitus, chronic obstructive pulmonary disease,

and renal insufficiency; there is a particularly high prevalence of associated coronary artery disease (CAD). The incidence of perioperative myocardial infarction ranges from 2% to 6.5% after lower extremity arterial reconstruction; approximately 70% of both perioperative and late mortality in these patients is due to concomitant CAD.^{13–15} Significant CAD is a nearly universal accompaniment of PAD. What remains controversial is determining which individuals are most likely to benefit from a detailed preoperative cardiac assessment and possible coronary intervention before undergoing infrainguinal bypass. Proposed algorithms have ranged from routine cardiac evaluation of all PAD patients to an almost nihilistic approach.¹⁶

Patients with CLTI pose a more complex problem because, especially for WIFL Stage 3 and 4 patients, there is a high anticipated amputation rate without lower extremity arterial reconstruction.⁹ CLTI patients have an even greater prevalence of CAD than claudicants do as well as a significantly reduced 5-year mortality, primarily due to associated CAD. However, because CLTI patients also tend to be older and have more comorbidities, cardiac intervention in such individuals has higher reported morbidity and mortality rates than in the general population of patients with isolated CAD targeted for intervention.¹⁶ My approach in CLTI patients is to assume they all have significant CAD. Perioperative blood pressure control, anti-anginal regimens, and treatment for congestive heart failure are optimized.^{17–20} I would recommend postponement of infrainguinal bypass in CLTI patients to allow further cardiac evaluation only in the presence of frequent or unstable angina, recent myocardial infarction, poorly controlled congestive heart failure, critical aortic stenosis, or symptomatic/untreated arrhythmia. Even in these instances, the cardiac evaluation should be focused and expeditious. Invasive coronary intervention should be pursued only if patient and anatomic characteristics are favorable, the benefit-to-risk ratio is high, and the delay to perform the limb intervention is not prolonged. In the absence of such cardiac instability, CLTI patients are best treated with meticulous perioperative medical care and expeditious lower extremity revascularization.^{21,22} Prolonged delays before limb revascularization in CLTI patients increase morbidity and amputation risk.²³ In patients requiring vascular reconstruction, the focus has turned sharply toward maximizing medical therapy rather than performing multiple, expensive, and sometimes ambiguous preoperative cardiac tests so that the patient can be “cleared for surgery.” A large, well-designed prospective randomized trial failed to show a benefit of cardiac revascularization before vascular surgery in patients with stable cardiac symptoms (see Ch. 34, Preoperative Evaluation and Management).²⁴ McFallas - NEJM 2004

PREOPERATIVE IMAGING

Infrainguinal bypass requires a careful assessment of arterial disease extent as well as detailed anatomic characterization of the inflow and outflow arteries (see Chs. 27, Arteriography and 108, Lower Extremity Arterial Disease: Decision Making and Medical Treatment). Standard arteriography remains the “gold standard” for most patients. Computed tomographic angiography has improved and is now the dominant preoperative imaging modality for aortic

aneurysm disease; however, in the periphery, the small caliber of the infrainguinal arteries and the presence of calcification in multiple vessels (associated with increasing age and diabetes) limit the applicability of computed tomographic angiography, especially in CLTI patients.²⁵ Magnetic resonance angiography²⁶ is continually improving,^{27–31} and particularly for patients with claudication, preoperative duplex imaging, also referred to as duplex arterial mapping (see Ch. 22, Vascular Laboratory: Arterial Duplex Scanning),^{32,33} may provide sufficient anatomic information to proceed directly to the operating room without formal arteriography. In this circumstance, immediate pre-bypass arteriography in the operating room is a reasonable approach. For most patients, however, especially for those with CLTI, I prefer to perform the initial diagnostic angiography in a separate setting, for several reasons. One reason is that for an increasing number of CLTI patients, endoluminal techniques are a reasonable initial option.

On the basis of a careful assessment before angiography, including the indications for intervention, anatomic considerations (based on duplex imaging), and the patient's functional status, comorbidities, and availability of vein conduit (see Ch. 108, Lower Extremity Arterial Disease: Decision Making and Medical Treatment), I try to determine whether a given patient with GLASS III (TASC type C or D) disease would be best served by endoluminal therapy or open bypass. If endoluminal therapy is the preferred option, I vigorously pursue endoluminal treatment at the time of diagnostic arteriography. If open bypass is preferable, I focus on optimal visualization of potential target arteries and obtain multiple views, as required, to ascertain that no unexpected inflow disease is present that would require treatment before proceeding with infrainguinal bypass. Detailed high-quality diagnostic arteriograms can be obtained and reviewed carefully before proceeding with bypass. In some patients, selection of outflow arteries may be difficult, and this area of decision making can be improved if films are reviewed and discussed with colleagues. Confining the initial procedure to diagnostic or therapeutic angiography obviates time constraints and scheduling difficulties that arise in the operating room when trying to perform angiography and open reconstruction in one sitting. I reserve that approach for carefully selected patients whose arterial anatomy has already been fairly well delineated by preoperative magnetic resonance angiography or duplex scanning. This confines the “one-stop approach” primarily to claudicants undergoing bypass for isolated, single-level femoropopliteal disease.

Defining Bypass Target Arteries

In the vast majority of patients in whom infrainguinal bypass is indicated, suitable target arteries can be identified (Fig. 112.1) if diagnostic angiography is properly performed.^{34,35} Only a tiny fraction of individuals, usually those following multiple failed reconstructions, have no identifiable target artery.³⁶ Detailed runoff views are necessary, including magnified lateral views of the foot. Such films can be obtained in nearly all patients with adjunctive techniques such as foot warming, local administration of intraarterial vasodilators, and proper positioning of the diagnostic catheter. It is frequently helpful to advance the catheter selectively into the SFA or popliteal

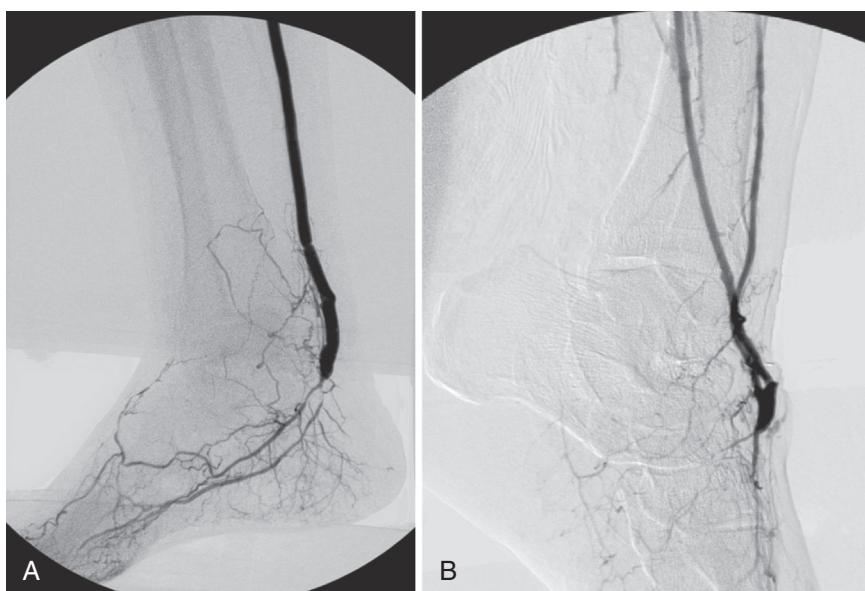


Figure 112.1 Detailed diagnostic arteriography with fixed imaging, proper timing, and appropriate catheter placement almost always identifies suitable target arteries. Each of the patients depicted had popliteal artery occlusion and extensive trifurcation and long-segment tibial disease, but diagnostic studies identified suitable target arteries in the foot. (A) Completion arteriogram after inframalleolar posterior tibial bypass in a patient with diabetes and forefoot gangrene. Despite a small-caliber outflow vessel, the bypass remains patent, and the ischemic foot ulcers healed and have not recurred at 2 years. (B) Completion arteriogram after bypass to a diseased dorsal pedal artery. Despite poor outflow and diseased arch and pedal vessels, the graft remains patent at 1 year. This patient with diabetes healed and ambulates with a transmetatarsal amputation.

artery to obtain adequate views of the infrapopliteal and pedal circulations, especially in patients with diabetes mellitus. Intraarterial runoff films with bolus injections performed while the diagnostic catheter is positioned in the aorta may fail to adequately define the runoff. If percutaneous access has been achieved from a contralateral, retrograde femoral approach, selective films can be obtained by advancing a wire and an appropriate diagnostic catheter over the aortic bifurcation and selectively down the affected extremity. In selected patients with normal inflow based on physical examination and noninvasive studies, an ipsilateral antegrade approach may be more expeditious to identify suitable runoff vessels, with the additional advantage of requiring a reduced contrast load (Fig. 112.2). Such an approach is especially useful in diabetic patients with renal insufficiency and noninvasive studies that suggest isolated infrapopliteal disease.

Despite optimal angiographic techniques, there may be a small number of patients in whom no suitable target can be identified. Selective exploration of dorsal pedal or distal posterior tibial arteries with flow detectable by Doppler or duplex imaging may identify a graftable recipient artery. Pomposelli et al.³⁶ reported a surprisingly high success rate under these circumstances, although I believe that this situation is relatively uncommon if diagnostic angiography has been optimally performed. In short, there are relatively few patients who are truly unreconstructible from an anatomic standpoint owing to the lack of a suitable outflow target vessel.

Autogenous Vein Assessment

Since Kunlin's first description of the successful use of autogenous femoropopliteal vein bypass for arteriosclerosis obliterans,^{37,38} there has been universal agreement that autogenous vein is the best conduit for infrainguinal bypass at all levels.^{39,40} Great saphenous vein (GSV) is the most readily available and durable conduit. Assessment of vein availability and quality is critical and should be carried out before embarking on the

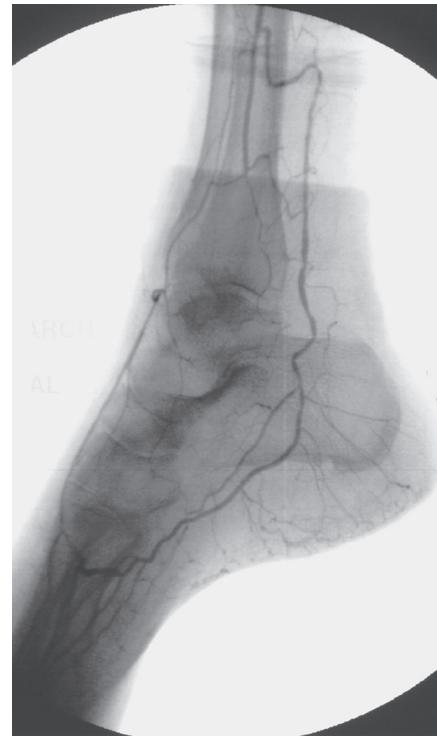


Figure 112.2 Lateral foot view obtained by distal selective superficial femoral arterial catheter injection identifies excellent collaterals from the distal peroneal artery to both the dorsal pedal and posterior tibial circulations.

operation.^{41–43} I routinely perform preoperative duplex mapping of the GSV (see Chapter Algorithm). If ipsilateral GSV is absent, unsuitable, or of insufficient length for the anticipated bypass, I also scan the ipsilateral small saphenous vein, the contralateral great and small saphenous veins, and the upper extremity veins, to locate a suitable vein and to be able to deal with any extenuating circumstances that might arise during the conduct of the operation. Patients are scanned with a light tourniquet in place and with the limb dependent, as described by Blebea et al.⁴⁴ I prefer to use veins that are soft,

compressible, and at least 3 mm in diameter. Calcified or sclerotic veins are rejected. Soft, compressible veins between 2 and 3 mm in diameter are worthy of exploration, but if they do not distend appropriately, the operation should be modified either by harvesting a better-quality vein (based on preoperative duplex studies) or by shortening the length of the proposed bypass, if possible, by selecting alternative inflow or outflow sites. The type and quality of the bypass conduit are the most important determinants of infrainguinal bypass success; efforts to maximize conduit quality will be rewarded.

Vein harvesting can be performed through long continuous incisions, skip incisions, or endoscopically. Endoscopic vein harvest has become common in cardiac surgery. Although there are a few enthusiasts, it has not been widely adopted by vascular surgeons for leg bypass, likely owing to equipment costs, learning curve issues, and concerns about damaging vein segments when a long conduit is needed. There are no convincing data to support any specific harvesting technique.^{45–49} Regardless of the harvesting technique, poor-quality or marginal vein should be rejected. The search for high-quality vein is worth the time and effort, even if vein splicing or bypass shortening is required. Every effort should be made to perform all infrainguinal bypasses with vein conduit (all-autogenous policy). Long-term results should not be sacrificed for the sake of expediency at the initial operation. Saphenous vein performs well in the reversed,^{50–54} nonreversed,⁵⁵ and *in situ*^{56–64} configurations; the technique chosen is dictated primarily by conduit availability, anatomic considerations, and surgeon preference and experience.

OPERATIVE PLANNING

Operative planning for infrainguinal bypass requires complex decision making by the vascular surgeon. More than any other operation, infrainguinal bypass taxes one's ingenuity, and requires the surgeon to anticipate and carefully consider numerous alternatives and potential complications both during preoperative evaluation and in the conduct of the reconstruction itself. Foremost, the major anatomic lesions and their hemodynamic significance must be identified.^{65–67}

Concomitant Inflow Disease

Adequate inflow should be ensured before commencing with infrainguinal bypass. Selected inflow lesions can be treated either percutaneously in advance, at the time of preoperative diagnostic arteriography, or at the same operative sitting (hybrid procedure). Iliac artery lesions of hemodynamic significance should be addressed in nearly all claudicants before proceeding with infrainguinal bypass. For patients with CLTI, an iliac lesion with a resting gradient of less than 5 to 10 mm Hg may be acceptable if the pulse and Doppler waveform at the selected inflow site (e.g., femoral artery) are normal. In patients with claudication or CLTI presenting with rest pain alone in the absence of tissue loss (WIFL: W0, I3, fl 0), an isolated iliac angioplasty without concomitant infrainguinal bypass may suffice if the iliac lesion is of sufficient hemodynamic importance.

In such patients with tandem lesions, the profunda–popliteal collateral index may be helpful in predicting whether an inflow procedure alone will be sufficient to alleviate the patient's symptoms.⁶⁵ An index greater than 0.25 indicates a large pressure gradient across the knee joint and suggests that inflow disease correction and profundaplasty alone are unlikely to be adequate.^{68–70}

Proximal Anastomotic Site

Before operation, the surgeon must define the inflow source; it need not be the CFA. There is abundant evidence that originating shorter bypasses from the deep femoral, superficial femoral, popliteal, or, in rare cases, one of the tibial arteries results in patency rates equivalent to those achieved when the CFA serves as the bypass origin. Short bypasses are frequently useful in patients with diabetes mellitus and primary infrapopliteal arterial occlusive disease as well as in individuals with limited available vein conduit who present after failure of a previous reconstruction. Based upon hemodynamic data and anatomic imaging, the surgeon should commence the operation with the optimal inflow site in mind. However, if unanticipated arterial disease is identified or vein quality and length are worse than anticipated once the operation is under way, the surgeon should have alternative bypass origins in mind that can be used to shorten the bypass length without compromising hemodynamics. If there is uncertainty about the appropriateness of the inflow site at exploration, its hemodynamic suitability can be assessed by direct intraarterial pressure measurements that can be compared with the transduced radial artery pressure. A resting gradient exceeding 10 mm Hg is significant, as is a drop in pressure exceeding 15% after the administration of intraarterial papaverine.^{66,67,71} If a significant gradient is identified at the selected inflow site, a more proximal inflow site above the culprit lesion should be selected, or the responsible lesion should be addressed by local endarterectomy or angioplasty. This problem occasionally arises with iliac or common femoral lesions whose hemodynamic significance was not appreciated at the time of preoperative arteriography, particularly lesions consisting primarily of posterior plaque that may have been masked if appropriate oblique projections were not obtained.

Associated Femoral Endarterectomy

Whenever the CFA is used as the site of origin for bypass, significant occlusive disease involving the origin and proximal deep femoral artery should usually be addressed concomitantly. The endarterectomy often begins in the CFA. After the division of veins that cross the anterior surface of the deep femoral artery, the femoral arteriotomy is carried out beyond the posterior tongue of disease that extends a variable distance down the deep femoral artery, usually at least to its first or second portion. Tacking sutures may or may not be needed at the distal endpoint. The arteriotomy can be closed with a vein patch or a segment of endarterectomized SFA. This patch can then be opened longitudinally to serve as the origin for the infrainguinal bypass (modified Linton patch technique; Fig. 112.3).

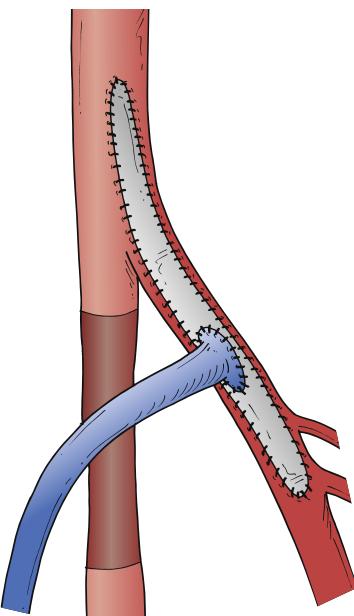


Figure 112.3 Linton vein patch technique after endarterectomy of the distal common and proximal deep femoral arteries, with anastomosis of the reversed vein graft to the patch.

Alternatively, if the vein caliber is excellent (>4 mm), a longer venotomy can be made in the vein conduit, which then serves simultaneously as a profundaplasty patch and the bypass origin; this technique should not be used if the arterial wall is markedly thickened or if the caliber of either the native donor artery or the vein conduit is small to avoid compromising the origin of the vein graft at the proximal anastomotic heel. Incorporation of a venous side branch as part of the anastomotic heel is another useful technique when the donor arterial wall is thick or there is a caliber mismatch between the donor artery and the vein bypass conduit (Fig. 112.4). Correction of significant deep femoral disease at the time of infrainguinal bypass is clinically important; should the bypass ever fail, adequate deep femoral artery perfusion may prevent the development of severe, recurrent limb ischemia.

Distal Anastomotic Site

Although inflow artery selection is generally straightforward, outflow site selection frequently requires greater judgment. The general principle of infrainguinal reconstruction is to bypass all hemodynamically significant disease and to insert the bypass

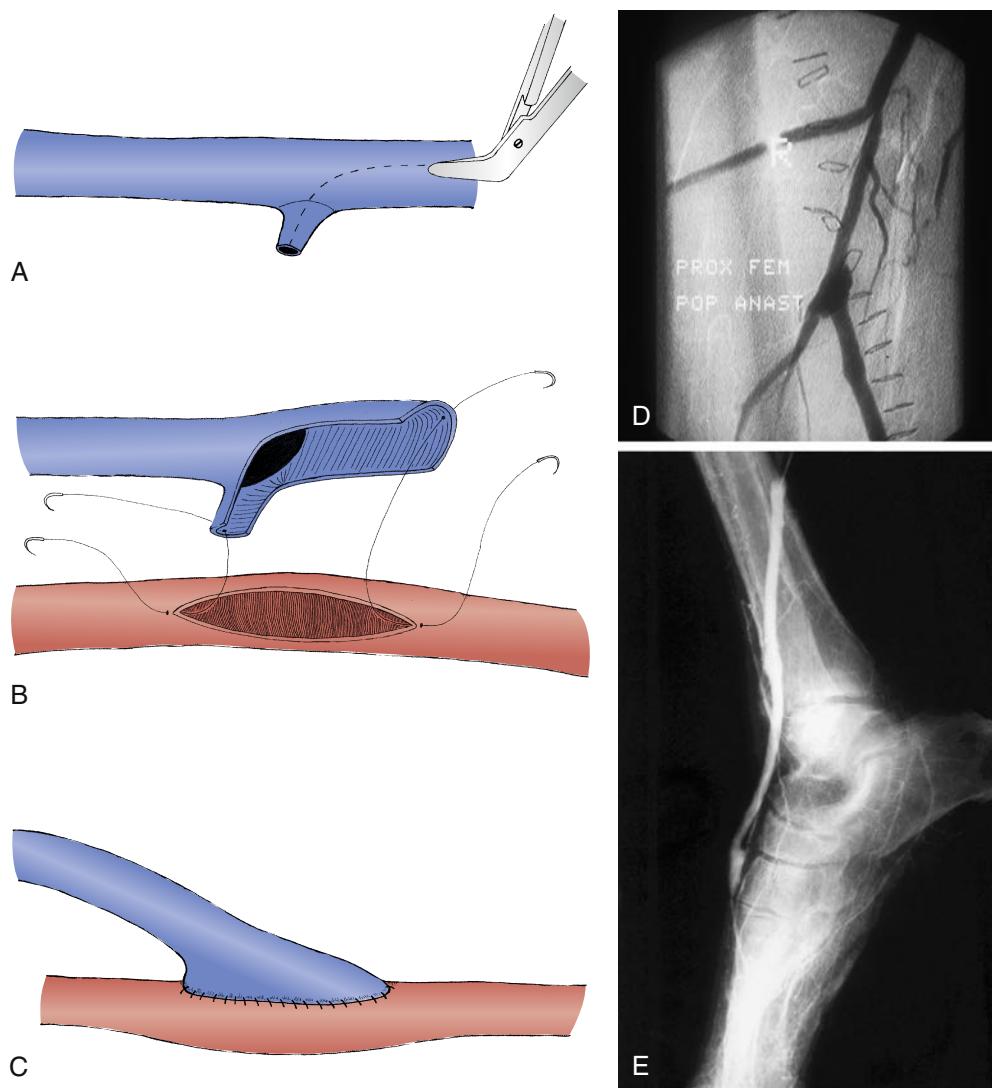


Figure 112.4 The venotomy through the reversed vein is extended through a suitable side branch (A) and anastomosed to the inflow artery (B and C) to avoid anastomotic stenosis at the graft heel.^{37,72} This technique can be used at either the proximal anastomosis (D) or the distal anastomosis (E) and is useful when the vein caliber is small or the arterial wall is thickened.

into the most proximal limb artery that has at least one continuous runoff artery to the foot. Thus, if the popliteal artery reconstitutes distal to an SFA occlusion and at least one tibial or peroneal artery is in continuity with the foot, the popliteal artery would be selected as the outflow site. It is possible, however, and sometimes desirable to bypass to an isolated or so-called blind popliteal segment.

Isolated Popliteal Target

An isolated popliteal artery is defined as a patent popliteal artery segment at least 5 cm long but with only geniculate collaterals and no major distal tibial or peroneal runoff artery in direct continuity with the foot. Such bypasses function surprisingly well and are especially useful in patients with limited vein availability.^{73–78} They may also be more useful in patients with claudication or rest pain than in those with frank tissue necrosis, for whom anything less than providing pulsatile flow directly to the foot may be insufficient for healing. In the presence of tissue loss, I prefer bypass to an artery in direct continuity with the foot. Five-year assisted primary or secondary patency rates of 50% to 74% have been reported for such blind-segment popliteal bypasses.⁷⁶ Successful bypasses to isolated tibial artery segments have also been reported.⁷⁴

Tibial, Peroneal, and Pedal Targets

Although most claudicants require only femoropopliteal bypass, a high proportion of patients with CLTI require tibial or pedal bypass. In general, the most proximal segment of tibial or peroneal artery that is continuous with the foot should be chosen as the outflow site. Thus, a patent anterior tibial or posterior tibial artery in direct continuity with the foot and pedal arch would be chosen over the peroneal artery as an outflow site if suitable vein length is available. There is still some controversy about whether one should choose the proximal or mid peroneal artery or a patent pedal artery for patients with tissue loss.⁷⁹ Most authors have found no adverse effects on graft patency or limb salvage for peroneal bypasses compared with tibial or pedal bypasses,^{80–82} but Pomposelli and others have made a strong case for pedal bypass,³⁶ particularly in diabetic patients with tissue loss.⁸³ They emphasize the importance of restoring a pedal pulse to maximize forefoot reperfusion. The pedal arteries are also more superficial and more easily exposed than the anatomically disadvantaged, deeply located peroneal artery. If the bypass must originate in the groin and the proximal or mid peroneal artery is of good quality on arteriography and has abundant collaterals with the foot (see Fig. 112.2), I generally perform a shorter bypass to the peroneal artery, especially if vein conduit length is a limiting factor. If the peroneal artery is diseased or does not appear to collateralize well with the foot, I preferentially bypass to the foot or ankle and splice vein if required to obtain sufficient length. I prefer dorsal pedal or paramalleolar posterior tibial–plantar artery insertion sites for short bypasses originating from the popliteal artery in diabetic patients with tissue loss.⁸⁴ Shortening the bypass in such patients allows one to optimize vein conduit quality, and the choice of an inframalleolar target artery maximizes forefoot perfusion.

OPERATIVE EXPOSURES

Standard Anterior Approach to the Common Femoral and Profunda Femoris Arteries

Thorough knowledge of anatomy and facility with multiple surgical exposures are critical to the success of infrainguinal bypass.⁸⁵ The standard approach to the CFA and the profunda femoris artery (PFA) is provided by a vertical incision overlying the CFA. This anterior approach allows complete exposure and mobilization of the CFA and its bifurcation; more proximal exposure can be obtained by dividing the recurrent portion of the inguinal ligament or the entire ligament (Peter Martin incision). Distal extension allows exposure of the PFA. Division of the lateral femoral circumflex vein offers access to the proximal PFA; careful progressive division of numerous crossing veins allows extensive exposure of the PFA. In selected patients, alternative exposures have been described.

Alternative Approaches to the Profunda Femoris Artery

If previous infection or scarring from multiple previous reconstructions makes standard exposure difficult and if there are no significant occlusive lesions in the CFA or proximal PFA, the mid or distal PFA can be approached laterally, anteromedially, or posteromedially (Fig. 112.5).^{74,86–89} The lateral PFA approach is the most useful for infrainguinal bypass. The incision is placed in the upper thigh lateral to the sartorius muscle. The sartorius and SFA are retracted medially. The raphe between the adductor longus and vastus medialis is incised to expose the PFA. This approach is useful when vein conduit length is limited or femoral triangle scarring is prohibitive (hostile groin). The surgeon must be certain that there are no hemodynamically significant lesions proximal to the PFA if this approach is used. With these caveats in mind, use of the PFA origin for distal bypass does not compromise long-term patency.^{88,89} Similarly, the SFA⁹⁰ and popliteal artery^{88–91} can be used as inflow sources in carefully selected patients without compromising graft patency.

Exposures of the Popliteal and Tibioperoneal Arteries

The standard exposures of the above-popliteal and below-knee arteries are through medial leg incisions, usually made by deepening the saphenectomy incision. Lateral approaches to these vessels are occasionally useful and are well described elsewhere.⁹¹ The posterior tibial and proximal to mid peroneal arteries are usually approached medially. The distal third of the peroneal artery is most expeditiously exposed by means of a lateral leg incision directly over the distal fibula. A short segment of fibula is carefully removed to expose the distal peroneal artery immediately beneath.

Posterior exposures of the popliteal, posterior tibial, and peroneal arteries are sometimes useful (Fig. 112.6).^{92,93} Diabetic patients frequently have relatively normal inflow to the popliteal

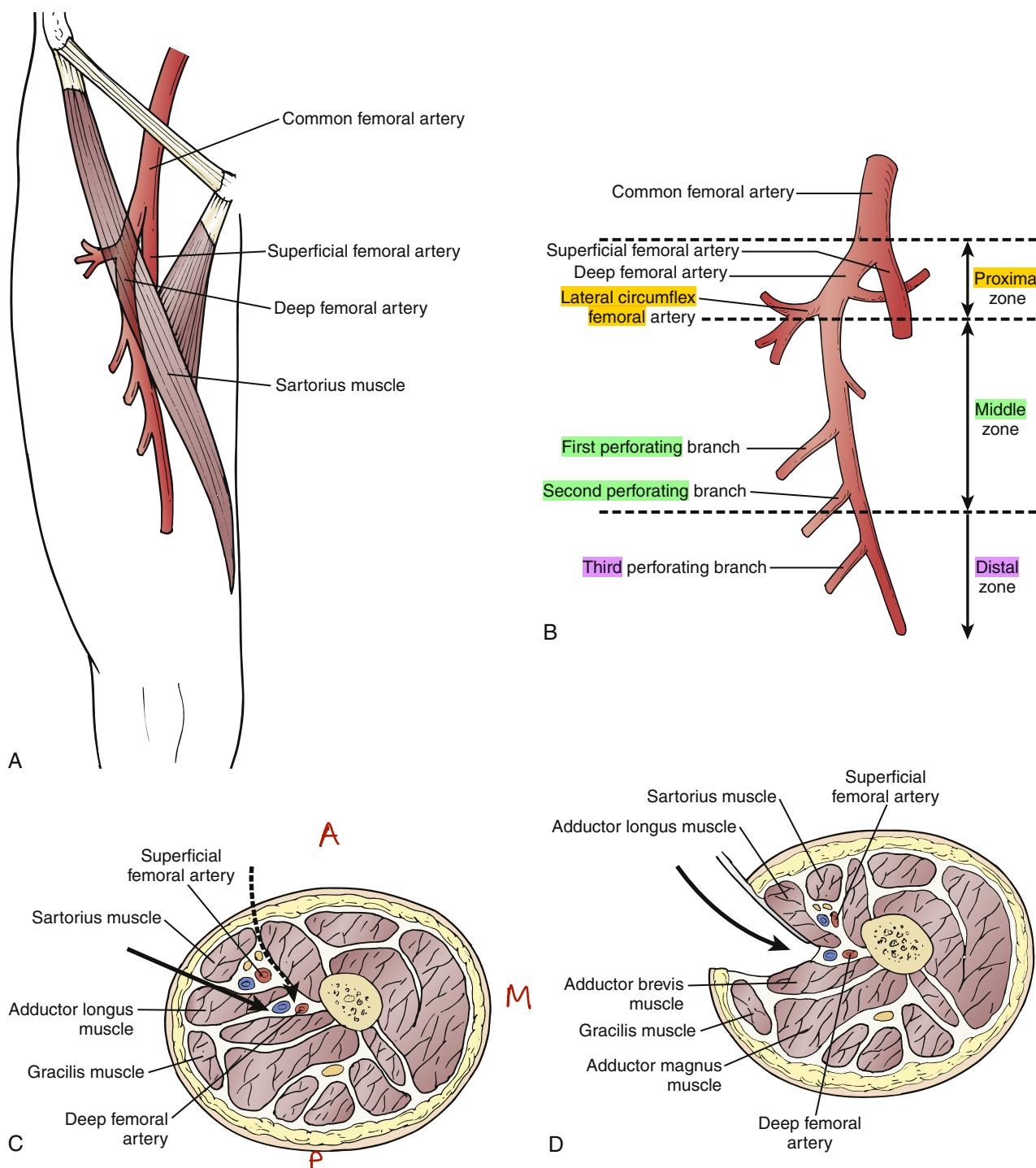


Figure 112.5 Alternative approaches to the distal deep femoral artery⁸⁸ are useful for reoperative femorodistal bypass and when it is desirable to shorten the bypass because of limited length of vein conduit.⁸⁹ (A) Location of the deep femoral artery. Note the surface landmarks used to identify its course. (B) The deep femoral artery can be divided into three zones: proximal, middle, and distal. (C) Transverse section of the thigh (viewed from above) shows the plane of dissection when the anteromedial approach (solid arrow) is used. Alternatively, the deep femoral artery can be approached through an even more anterior route (dashed arrow) by making an incision along the lateral border of the sartorius and retracting this muscle and the superficial femoral neurovascular bundle medially to reach the distal deep femoral artery. (D) Posterior approach to the distal deep femoral artery. (Note the fascial plane and structures separating the deep femoral artery from superficial femoral vascular structures and isolating it from the subsartorial canal.)

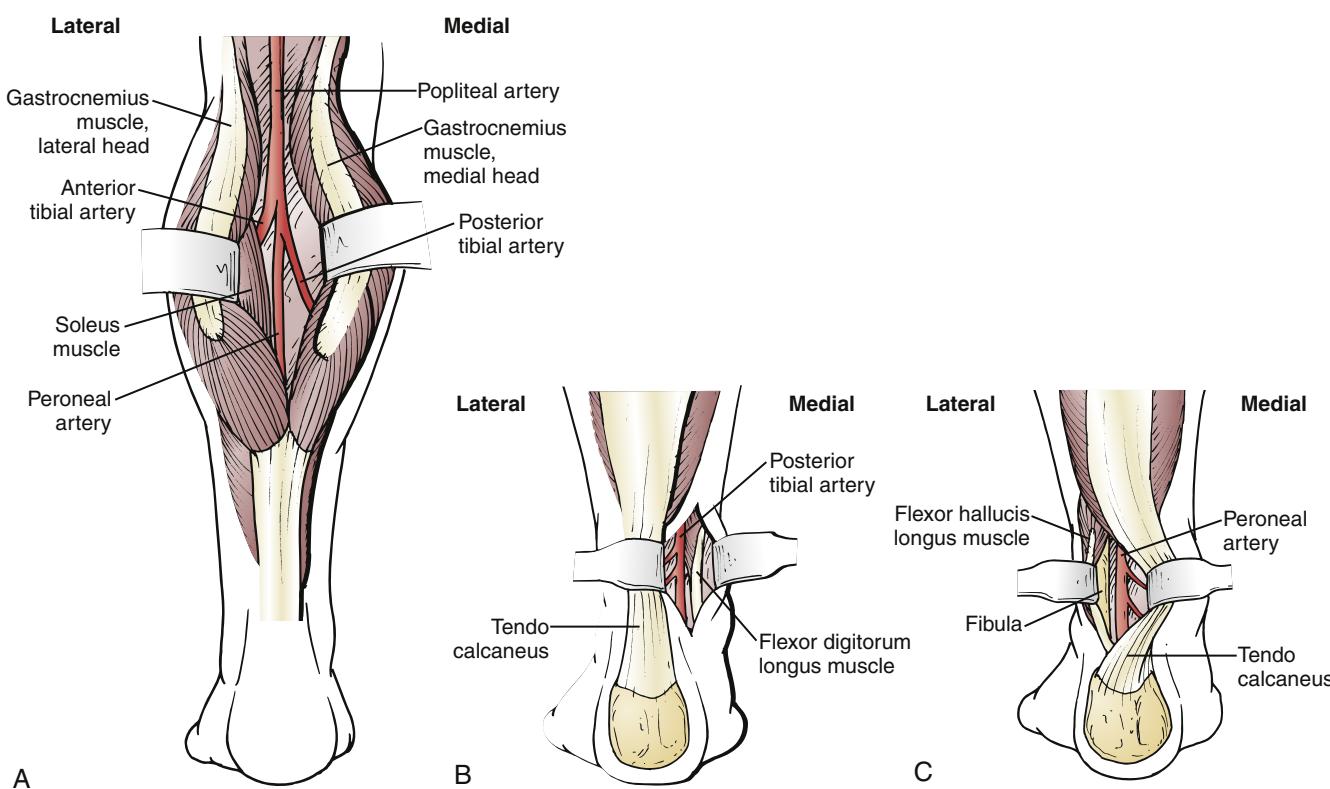


Figure 112.6 Posterior Exposures.⁹⁵ (A) Exposure of the popliteal and proximal crural arteries through a posterior approach. The two heads of the gastrocnemius muscle are separated, and the soleus muscle is lysed from its tibial origin. (B) Exposure of the posterior tibial artery through a posterior approach. The tendo calcaneus is retracted laterally. The flexor digitorum longus muscle is reflected medially in the lower portion of the calf because the artery lies posterior to the lateral border of this muscle near the level of the malleoli. (C) Exposure of the peroneal artery through a posterior approach. The tendo calcaneus is retracted medially and the flexor hallucis longus muscle is reflected laterally to expose the artery in the groove next to the fibula.

trifurcation. If the inflow site is the below-knee popliteal artery and the most appropriate target artery is the distal posterior tibial or distal peroneal artery, and if the small saphenous vein is of good quality on duplex imaging, one can perform the entire operation with the patient in a prone position through a posterior approach. These approaches have been well described by Ouriel⁹³ and should be considered not only in selected reoperative situations (e.g., failed bypass through a medial approach), but also if conduit length is limited and ipsilateral SSV is unavailable. Commitment to an all-autogenous bypass approach requires ingenuity and familiarity with numerous anatomic exposures and techniques to allow shortening of the bypass or to permit operation in a virgin field that is unscarred by previous operations. When such distal origin bypass grafts are used, a pneumatic tourniquet instead of vascular Silastic loops or clamps is occasionally useful to circumvent severe distal arterial calcification.⁹⁴ A thorough working knowledge of alternative exposures and the occasional use of the pneumatic tourniquet are of great benefit in performing reoperative bypass.

CHOICE OF CONDUIT

Autogenous conduit options for infrainguinal bypass include ipsilateral and contralateral GSV,⁹⁶ small saphenous vein,^{97,98}

femoral vein,⁹⁹ arm (basilic and cephalic) vein,^{100–105} endarterectomized segments of the SFA,¹⁰⁶ cryopreserved vein,^{107–109} and radial artery.^{110,111} Prosthetic options include Dacron, heparin-bonded Dacron, human umbilical vein, polytetrafluoroethylene (PTFE) with and without a distal cuff, and, most recently, expanded PTFE (ePTFE) covalently bonded with heparin. In my group's reported 10-year experience, we performed 93% of infrainguinal bypasses with all-autogenous conduits.¹¹²

Autogenous Grafts

The GSV is the preferred conduit as it outperforms all other conduit choices. If the ipsilateral GSV is absent, I do not hesitate to harvest the contralateral GSV and see no merit in saving this vein for possible use later.⁹⁶ Numerous reports suggest that the contralateral GSV is subsequently needed in no more than 20% to 25% of patients. I therefore advocate using it when necessary and saving a more difficult alternative vein reconstruction for a later time in those relatively few patients who require it. Exceptions occur whenever the contralateral limb is already ischemic, as manifested by severe claudication, rest pain, or ischemic ulceration. If the contralateral limb is asymptomatic and the ankle-brachial index exceeds 0.6, I have

experienced no significant wound healing complications from harvesting the GSV from the groin to the midcalf level. This approach usually allows the bypass to be performed with one segment of GSV and obviates the need to harvest arm vein and splice veins. Other groups prefer to harvest arm vein if the ipsilateral GSV is unavailable, preserving the contralateral GSV for later use.^{100,113}

Alternative veins are used when the GSV is unavailable or of insufficient length.¹¹⁴ Duplex mapping is useful to identify suitable vein sources. The small saphenous vein is suitable if the proposed bypass is relatively short. It is possible to perform a common femoral-to-above-knee popliteal bypass or a PFA-to-below-knee popliteal bypass with one complete segment of small saphenous vein harvested from the ankle to the knee. If a longer bypass with spliced vein is necessary, I prefer to use arm vein because it is less awkward to harvest. LoGerfo et al.¹¹⁵ and Holzenbein et al.¹⁰⁴ described novel techniques of harvesting the upper arm basilic, median cubital, and cephalic veins in continuity with valve lysis of the basilic segment and use of the cephalic segment in a reversed configuration to provide a relatively long, unspliced autogenous conduit. The femoropopliteal deep vein is occasionally useful for shorter bypasses but is large in caliber and more difficult to harvest; arm vein is therefore generally preferred. Treiman et al.¹¹¹ reported the use of the radial artery as a bypass conduit in selected patients requiring short infrageniculate bypasses, with good early results, but this technique has not been widely adopted as conduit length is often limited and the patients who need such bypasses most often have diabetes, renal failure, and unusable or diseased forearm arteries as well. Cryopreserved vein grafts are expensive and have not performed well in clinical practice^{107,108}; they may serve a niche role when revascularization is required after the removal of an infected bypass graft and autogenous vein is unavailable to create a new bypass through clean tissue planes.¹⁰⁸

Prosthetic Grafts

PTFE is the most commonly used prosthetic conduit for infrainguinal bypass, although reports suggest that in the above-knee position, it is not superior to Dacron.^{116–118} A prospective randomized trial from the United Kingdom reported by Devine et al.¹¹⁹ suggested that heparin-bonded Dacron was superior to PTFE for above-knee popliteal bypasses. The 3-year primary patency for heparin-bonded Dacron was 55% compared with 42% for PTFE ($P < 0.044$). Both of these patency rates are inferior to those of GSV, however, and the early apparent advantage of heparin-bonded Dacron over PTFE disappeared with longer follow-up.¹²⁰

Vein Cuffs

For bypasses that insert below the knee, the addition of a vein cuff confers a significant patency advantage (52% patency at 2 years for PTFE with vein cuff vs. 29% for PTFE with no cuff) and also improves limb salvage (84% vs. 62%; $P < 0.03$).¹²¹ My experience and that of others suggests that a distal vein cuff, patch or collar improves 2- to 3-year patency for infrageniculate bypass when PTFE is required.^{122–126} Nevertheless,

the results are still inferior to those of vein bypasses, even when alternative veins are used; these data emphasize the validity of the all-autogenous policy. If vein is truly limited, however, PTFE is an acceptable choice, and available data suggest that distal anastomotic modification with autogenous tissue is a worthwhile adjunct. The only prospective randomized clinical trial used a Miller cuff (Fig. 112.7).¹²¹ A distal Taylor patch (Fig. 112.8)^{122,124} and the St. Mary's boot (Fig. 112.9)¹²⁶ may yield equivalent results. Neville et al.^{128,129} reported an alternative PTFE adjunct consisting of anastomosis of a PTFE graft to an infrageniculate artery using a vein patch, analogous to the technique originally described by Linton. At least in their hands, this adjunct seems to work as well as a Miller cuff or Taylor patch. However, the only randomized prospective trial of such adjuncts used the Miller cuff, and this trial has not been repeated to my knowledge.

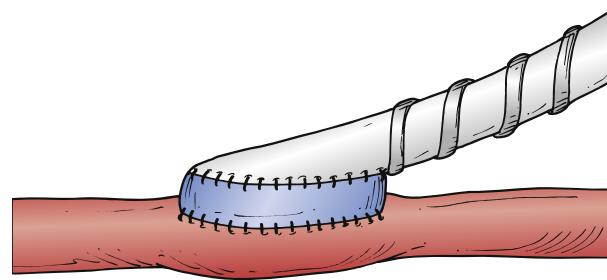


Figure 112.7 The Miller cuff technique^{123,127} improved the patency of below-knee popliteal and tibial polytetrafluoroethylene bypass grafts when used as a distal anastomotic adjunct in a controlled randomized clinical trial.¹²¹

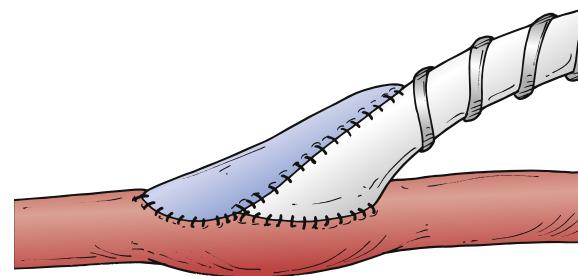


Figure 112.8 The Taylor patch technique can improve the patency of infrageniculate polytetrafluoroethylene bypass grafts.^{122,124}

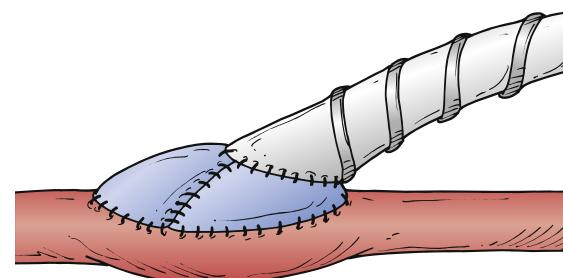


Figure 112.9 The St. Mary's boot or prosthetic venous collar technique¹²⁶ combines the attributes of the Taylor patch and the Miller cuff.

Human Umbilical Vein and Adjunctive Arteriovenous Fistula

Human umbilical vein is less commonly used than PTFE, primarily because it is thicker and more cumbersome to handle and due to concerns about subsequent aneurysmal degeneration.¹³⁰ Dardik et al.¹³¹ reported excellent results using human umbilical vein with an adjunctive distal arteriovenous fistula to promote increased graft flow velocity; there are no prospective trials comparing this technique with alternative prosthetic conduits, such as PTFE. A single prospective trial did not demonstrate any benefit of the addition of an arteriovenous fistula to femoral–infrapopliteal bypass with vein cuff.¹³²

Heparin-Bonded Polytetrafluoroethylene

The most recent addition to the inventory of prosthetic infrainguinal bypass conduits is ePTFE to which heparin has been covalently bonded. The commercially available product was originally called Carmeda BioActive Surface (CBAS).¹³³ Preclinical studies suggest that biologically active heparin has been successfully covalently bonded to ePTFE without causing systemic anticoagulative effects.¹³⁴ The drug is biologically active, at least in baboons and dogs, for up to 12 weeks.¹³⁵ In animal models of thromboresistance (short 3- and 4-mm grafts), CBAS appears to prevent early ePTFE graft thrombosis; this effect may persist up to 180 days, although not as strikingly. It also appears to reduce early platelet and fibrin deposition in animal models.

There is no proof, however, that these experimental findings will translate into improved prosthetic graft patency in humans. The five published reports of CBAS for peripheral infrainguinal bypass suffer from major flaws, including lack of randomization, lack of control groups, small numbers of patients, selection bias, large numbers of patients with relatively

prosthetic-friendly above-knee popliteal insertion sites, lack of intermediate follow-up (beyond 2 years), and flawed or unreliable life tables.^{133,136–139} In two of these five series, anastomotic adjuncts such as patches were used in addition to CBAS grafts, further confounding interpretation. In addition, aggressive combination antiplatelet therapy (oral and low-molecular-weight heparin) was used by nearly all the authors; this combination is not routinely used in North America.

If one assumes that there is no patient overlap between the two studies from the same center (an assumption that may well be false),^{136,139} the published human experience with CBAS infrainguinal grafts consists of 356 grafts with the following insertion site distribution: 142 (41%) above-knee popliteal, 115 (33.5%) below-knee popliteal, 75 (21.8%) femorocrural or tibial, and 24 indeterminate (one study does not specify target arteries).¹⁴⁰ The estimated number of patients available with documented follow-up in all five human clinical CBAS studies combined is as follows: 95 above-knee popliteal, 45 below-knee popliteal, and 25 femorocrural at 1 year; and 48 above-knee popliteal, 16 below-knee popliteal, and 9 femorocrural at 2 years. The data and follow-up length are thus insufficient to support assertions of improved patency conferred by covalently bonded heparin grafts. Long-term studies of this intriguing bioactive graft are needed to determine whether covalent heparin bonding confers any significant patency benefit. Heparin-induced thrombocytopenia has also been rarely reported with these grafts.

Graft Comparison

Table 112.1 summarizes the available level I data comparing conduit types with outcome.^{118–124,132,141–145} Vein is superior to all prosthetic materials, even in the above-knee position.^{145–147} The randomized clinical trials comparing human umbilical

TABLE 112.1 Patency of Above-Knee Popliteal Bypass and Below-Knee Popliteal or Infrapopliteal Bypass Grafts

Graft Type and Study	PATENCY (%)					P Value
	1-Year	2-Year	3-Year	4-Year	5-Year	
Above-Knee Popliteal Bypass: Dacron Versus Polytetrafluoroethylene						
Devine et al. ¹²⁰ (n = 209)						
Heparin-bonded Dacron	71		54	46		0.055 but not reproduced in subsequent studies
PTFE	62		44	35		
Post et al. ¹¹⁷ (n = 194)						NS
Dacron			64			
PTFE			61			
Green et al. ¹¹⁶ (n = 240)						NS
Dacron				43		
PTFE				45		
Robinson et al. ¹¹⁸ (n = 108)						NS
Dacron	70	56	47			
PTFE	72	52	52			

Continued

TABLE 112.1 Patency of Above-Knee Popliteal Bypass and Below-Knee Popliteal or Infrapopliteal Bypass Grafts—cont'd

Graft Type and Study	PATENCY (%)					P Value
	1-Year	2-Year	3-Year	4-Year	5-Year	
Above-Knee Popliteal Bypass: HUV Versus Polytetrafluoroethylene						
McCollum et al. ¹⁴⁴ (n = 191)						NS (0.27)
HUV	68	63	57			
PTFE	61	56	48			
Aalders et al. ¹⁴³ (n = 96)						NS
HUV	90	67 ^a				71.4 ^b
PTFE	80	63				38.7
Eickhoff et al. ¹⁴⁸ (n = 105)						0.001
✓ HUV (below knee)	74			42		
PTFE	53			22		
PTFE: ringed versus nonringed						
Gupta et al. ¹⁴⁹ (n = 122; above- and below-knee popliteal bypass)						NS
Ringed			74			
Nonringed			68			
Polytetrafluoroethylene: Vein Cuff Versus No Cuff						
Stonebridge et al. ¹²¹ (n = 261)						
<u>Above-knee popliteal</u>						NS
Cuff	80	72				
No cuff	84	70				
<u>Below-knee popliteal</u>						0.03
✓ Cuff	80	52				
No cuff	65	29				
Above-Knee Popliteal Bypass: Vein Versus Prosthetic (Polytetrafluoroethylene or Human Umbilical Vein)						
Klinkert et al. ¹⁴⁵ (n = 151)						0.035
✓ Vein				76		
PTFE				52		
Johnson et al. ¹⁴⁷ (n = 752)						0.01
✓ Vein		81		73		
HUV		70		53		
PTFE		69		39		
Tilanus et al. ¹⁵² (n = 49)						<0.001
✓ Vein				70		
PTFE				37		
Veith et al. ¹⁵³ (n = 845)						
<u>Above-knee popliteal</u> (n = 176)						>0.25
✓ Vein			61			
PTFE			38			
<u>Below-knee popliteal</u> (n = 153)						<0.05
✓ Vein			76			
PTFE			54			
<u>Infrapopliteal</u> (n = 204)						<0.001
✓ Vein			49			
PTFE			12			

HUV, human umbilical vein; NS, not significant; PTFE, polytetrafluoroethylene.

^aPatency determined at 18 months.

^bPatency determined at 6 years.

vein with PTFE have been inconclusive.^{143,144,148} The addition of rings to PTFE conferred no benefit in the single prospective randomized clinical trial conducted.¹⁴⁹ Thus, the most prudent recommendation is to use autogenous vein whenever possible for infrainguinal bypass. This dictum holds true not only for primary infrainguinal bypasses but also for reoperations, in which vein conduits outperform all other options.^{150,151} For long bypasses, ipsilateral GSV, contralateral GSV, and spliced vein are employed in decreasing order of preference. If only 5 to 15 cm of extra length is required and a more distal origin site is not feasible, eversion endarterectomy of a proximal segment of the SFA with anastomosis to the available vein conduit is a useful technique that avoids the harvesting and splicing of additional vein (Fig. 112.10).¹⁰⁶ For shorter bypasses, arm vein or small saphenous vein is effective, with the latter being especially useful when a posterior approach is applicable.

If vein is truly unavailable after a thorough search, PTFE, human umbilical vein, or Dacron are reasonable options for above-knee bypass. The initially favorable results with heparin-bonded Dacron were not confirmed during longer follow-up,^{119,120} so there appears to be no advantage to heparin-bonded Dacron conduit for above-knee bypass. A prospective randomized trial of human umbilical vein versus heparin-bonded Dacron showed no difference in patency in the above-knee popliteal position,¹⁵⁴ and published trials of PTFE versus Dacron have shown no clear difference.^{116–118,120} For infrageniculate insertion sites, PTFE with distal anastomotic modification (cuff, boot, or patch) is recommended if vein is unavailable. There is inadequate evidence to state a preference in terms of standard ePTFE versus heparin-bonded or carbon-coated PTFE. A prospective randomized trial of standard PTFE versus carbon-impregnated PTFE for infrageniculate bypass showed approximately 30% primary patency, with no difference between groups at 3 years.¹⁵⁵

BYPASS TECHNIQUE

Reversed, nonreversed, and *in situ* conduits appear to work equally well. The choice is primarily one of surgeon preference. Arm veins pose special challenges. Regardless of which type of conduit is used, meticulous technique and gentle vein handling are critical.

Reversed Vein Bypass

Harvest of the GSV begins with a groin incision two finger-breadths lateral to the pubic tubercle. Preoperative duplex vein mapping and drawing of a line with indelible ink directly over the vein conduit assist in following the course of the vein and avoiding the creation of skin flaps. The saphenofemoral junction at the fossa ovalis should be identified to ensure that the true GSV rather than an anterior or large posteromedial branch is being exposed. Once the main trunk is identified, the incision is extended distally, directly over the vein, with a no. 10 blade or Cooley scissors. I frequently leave short skin bridges, especially in the thigh and about the knee level, to avoid the creation of long skin flaps. If exposure or branch ligation is

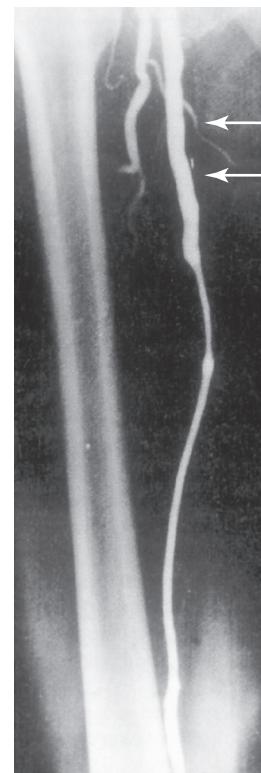


Figure 112.10 When vein length is limited, an eversion endarterectomy of a proximal superficial femoral artery segment (arrows) can be performed.¹⁰⁶ The everted arterial segment is anastomosed to the available vein graft to create an all-autogenous conduit of sufficient length for the required bypass to be performed.

difficult or if the course of the main vein is unclear, the skin directly over the vein is divided. The periadventitial tissue, not the vein wall itself, is grasped gently to avoid damage to the conduit. Side branches are meticulously ligated with 3-0 or 4-0 silk and divided. Leaving a short stump is preferable to placing a ligature too close to the main trunk and compromising the lumen. When first exposed, the vein should be soft and blue. Sclerotic segments are whitish and rubbery. Vein spasm can turn a blue vein white and should be treated with local papaverine or lidocaine irrigation.

Sufficient length of vein should be harvested for the proposed bypass to be performed. If adequate vein of good quality is not available, alternative inflow or outflow arteries should be considered to shorten the bypass; otherwise, alternative vein must be harvested from another site and spliced on a back table. Vein quality is extremely important, and segments less than 3 mm should be avoided. Once an adequate length of vein is identified, it is ligated proximally and distally and prepared on the back table by a senior surgeon while the rest of the team exposes the inflow and outflow arteries.

The vein is cannulated with a 3-mm olive or Marks tip needle and gently distended with chilled autologous blood (50–60 mL) to which 1000 units of heparin and 60 mg of papaverine have been added. With gentle irrigation, the vein should flow readily, distend smoothly, and be free of fibrotic segments that fail to distend with gentle pressure. Missed or small avulsed branches are repaired with longitudinally oriented 6-0 or 7-0 Prolene sutures on a BV-1 or BV-175 needle.

Overly forceful distention of the conduit should be avoided because it damages the endothelium. The entire length of the conduit is inspected to ensure that there are no sclerotic areas, no areas of persistent spasm, no strictures at branch ligature sites, and no bleeding branches. Once preparation is complete, the distal end of the vein is ligated with 3-0 silk, leaving the suture ends long; the prepared conduit is stored in chilled blood until the graft is ready to be tunneled. Proper intraoperative planning should result in minimal vein storage time. Many believe that autologous blood, rather than saline, better preserves graft endothelium.¹⁵⁶ Mills²⁰⁰⁰

Proper graft tunneling of reversed grafts is important. For primary leg bypasses with GSV, I prefer to tunnel the graft in a deep anatomic plane to avoid kinking and graft exposure should wound complications ensue. For above-knee popliteal bypasses, a subsartorial plane is frequently easier than a true anatomic tunnel. A large-caliber hollow-bore metal tunneler with a removable obturator is used. For below-knee popliteal and proximal to mid posterior tibial or peroneal bypasses, I generally prefer an anatomic tunnel between the two heads of the gastrocnemius for initial bypasses. It is often wise to tunnel reoperative bypasses subcutaneously to avoid scarring and render graft surveillance and revision easier. This approach is advantageous because the alternative vein conduits often used in these circumstances are at higher risk for the development of graft stenosis. Bypasses to the anterior tibial artery can be tunneled either through the interosseous membrane (anatomic) or in a lateral subcutaneous plane.

Arm Vein Harvest and Vein Splicing

If leg vein length is inadequate or unavailable and additional conduit is required, arm vein should be used. Arm veins, especially the basilic vein, are more fragile and demanding to harvest. Branches should be carefully identified and ligated a short distance away from their junctions with the main trunk to avoid troublesome bleeding from an injury at the crotch between the branch and the parent vein. Large branches are suture or doubly ligated. The initial distention of the vein is performed with heparinized saline and papaverine because defects in thinner walled arm veins are more difficult to visualize and repair if blood is used as the initial irrigant. Once major leaks have been controlled, the vein graft is prepared and stored in chilled blood as mentioned earlier. It is worth considering that arm veins frequently harbor abnormal segments containing intrinsic lesions such as webs, synechiae, and sclerotic valves. Angioscopy of such high-risk conduits may be a useful adjunct (see later under Angioscopy).

In Situ Vein Bypass

In situ bypass can be used successfully in many patients with intact ipsilateral GSVs. Proponents suggest that the vein–artery size match is frequently optimized by this technique.¹⁵⁷ This technique requires the use of a radial cutting blade (Mills valvulotome)⁵⁸ or fixed-diameter circumferential blades such as the Hall⁵⁹ and LeMaitre valvulotomes to accomplish valve

lysis.^{62,158} The proximal segment of GSV is initially mobilized in the groin as it would be for reversed vein bypass. The distal GSV is then mobilized in the region of the projected distal arterial anastomosis. The vein may be exposed by an open technique along its entire length, through skip incisions, or endoscopically. After systemic heparinization, the vein is transected below a Satinsky clamp placed at the saphenofemoral junction, and the stump is closed with running 5-0 Prolene suture. The most proximal valve is excised under direct vision with Potts scissors, and the vein is spatulated and sewn end to side to the selected arterial anastomotic site, usually the CFA. Arterial flow is allowed into the vein conduit; if the conduit is of large caliber, a circumferential valvulotome can be inserted from distal to proximal to lyse the valves. Many surgeons prefer to more carefully control valve lysis by progressive serial valvulotomy through large side branches, progressing from proximal to distal. The Mills valvulotome is introduced through side branches; the leaflets are usually just distal to branches and are oriented parallel to the skin. Under arterial pressure, the valve sinuses distend, and the valve leaflets are displaced toward the center of the lumen, where they can be safely engaged by the valvulotome and cut by sharp retraction on the valvulotome under direct visualization. The final valves are lysed from the distal end of the vein. The quality of the vein and the success of lysis are then assessed; flow should be highly pulsatile from the end of the conduit before the distal anastomosis is performed.

After completion of the anastomoses, the quality of pulsation and flow is assessed by palpation and handheld Doppler interrogation. The entire graft should be evaluated from proximal to distal; it can be manually compressed or occluded distal to the Doppler probe. The presence of continuous outflow despite distal graft compression indicates an arteriovenous fistula; these branches should be ligated. With either the reversed or the *in situ* technique, careful handling of the vein is important. The assurance of adequate valve lysis and the detection of major arteriovenous fistulae can be challenging; the type of completion study used depends on the type, source, and quality of the conduit and surgeon preference.

INTRAOPERATIVE COMPLETION STUDIES

Infrainguinal bypass can be complicated by insufficient or inadequate arterial exposure; inappropriate inflow or target artery selection (Fig. 112.11); intrinsic conduit defects; technical defects associated with clamp injury, local endarterectomy, anastomosis creation (Fig. 112.12), and valve lysis; graft tunneling errors (Fig. 112.13); and coagulation or platelet aggregation abnormalities. The surgeon should strive to avoid these complications but must be prepared to recognize and correct them should they arise. Ignorance is not bliss, and the best opportunity to correct a problem is at the initial operation. Failing to address a significant defect and hoping for the best compromises patient outcome and increases stress on the operating surgeon. “Take-backs” to the operating room for hemorrhage or graft thrombosis are inevitable, but their frequency can be

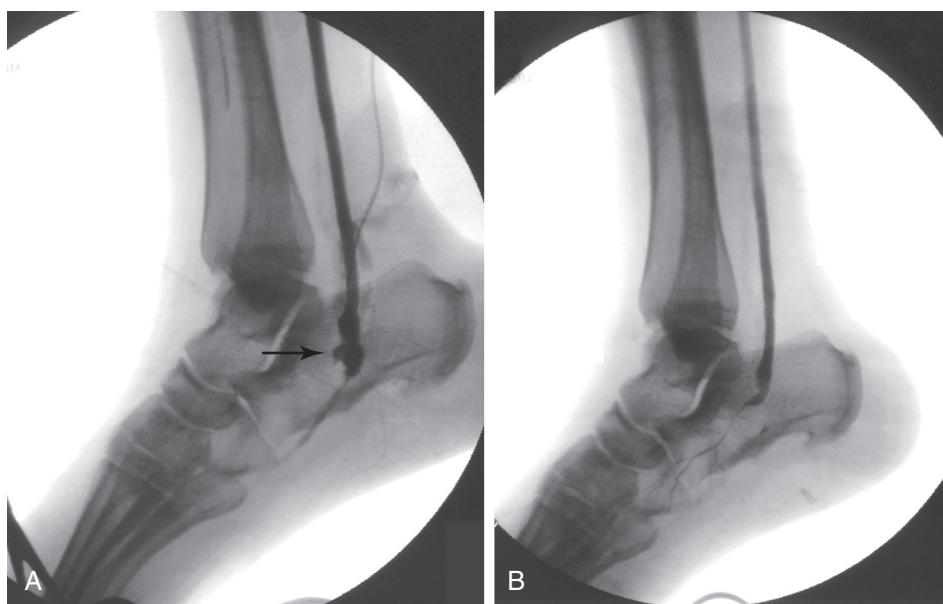


Figure 112.11 (A) Completion arteriography demonstrates poor runoff, with minimal branching of the target plantar artery (arrow). The initial exposure was inadequate, leading to incorrect selection of the target artery (lateral plantar). (B) The anastomosis was relocated to the medial plantar artery, and the graft remains patent 2 years postoperatively.



Figure 112.12 (A) Completion arteriography identifies a significant distal anastomotic defect (arrow), despite a good graft pulse and distal continuous wave Doppler signal. (B) The anastomosis was re-explored, the defect was corrected, and the graft is patent at 3 years.

markedly reduced by meticulous technique, prudent decision-making, and routine completion studies to ensure a technically optimal result.

There are four options for completion assessment that can be used alone or in combination: distal pulse palpation and Doppler flow assessment, with and without manual compression of the graft^{159,160}; completion arteriography^{161–163}; intraoperative duplex scanning, with and without papaverine administration^{164,165}; and angiscopy.^{166–178}

Doppler Flow Assessment

Doppler flow assessment should always be performed. Restoration of a palpable distal pulse or Doppler flow that clearly

diminishes with manual occlusion of the bypass graft documents graft patency. These techniques are sufficiently sensitive to detect only major conduit, technical, or outflow problems, however. Therefore other, more complex techniques should also be employed.

Arteriography

For reversed vein conduits, arteriography is the simplest and most effective completion study. With improved intraoperative imaging capabilities, it has become relatively easy to rapidly evaluate the conduit, tunnel, anastomoses, and outflow for significant graft-threatening lesions with minimal contrast material and little additional time (see Fig. 112.13). Renwick



Figure 112.13 (A) Routine completion arteriography identifies an unsuspected site of graft compression in the tunnel, despite a good distal graft pulse and continuous wave Doppler signal. (B) The site was explored, the compression was released, and the graft is patent at 2 years.

et al.¹⁶² identified defects requiring correction in 27% of infrainguinal bypasses using intraoperative angiography, despite a normal appearance by visual inspection and external pulse palpation. The 2-week primary patency was 100%, compared with 72% in a control group without completion arteriograms. Mills et al.¹⁶¹ prospectively evaluated 214 consecutive infrainguinal bypass grafts with routine completion angiography and identified significant lesions requiring revision in 8% of grafts, with a higher incidence in tibial than in popliteal reconstructions. The 30-day primary patencies were 99% for femoropopliteal bypasses and 93% for femorodistal grafts. Angiography may not be sufficiently sensitive to detect incomplete valve lysis during the performance of *in situ* or nonreversed grafts.^{173,175}

Duplex Ultrasound

Bandyk et al.,¹⁶⁴ Johnson et al.¹⁶⁵ and their colleagues have championed intraoperative duplex scanning after *in situ* bypasses and reported significant abnormalities requiring correction in 12% of cases. Lesions associated with focal peak systolic velocities exceeding 250 cm/s are repaired. In low-flow grafts without identifiable technical defects, if target artery relocation or graft extension is not possible, consideration is given to either the performance of an adjunctive arteriovenous fistula to augment graft flow velocity or the administration of postoperative anticoagulation. The short-term patency of infrainguinal bypasses with normal findings on intraoperative duplex scanning is superb. Intraoperative graft duplex scanning requires the availability of a machine and a technician, however, and most surgeons are less familiar with this technique and find it cumbersome to use. These issues have prevented its widespread application, although I have found it useful in difficult reoperative cases, particularly when alternative, spliced, or valve-lysed vein segments are used.¹⁷⁹

Angioscopy

Angioscopy has been employed to evaluate the conduit by many clinical investigators,^{166–178} who have used it to evaluate harvested arm vein¹⁶⁸ or as an adjunct to valve lysis to permit *in situ* bypass with minimal skin incisions.^{180–182} Marcaccio et al.¹⁷⁴ analyzed the use of intraoperative angioscopy in a series of 113 arm vein bypasses and identified significant intraluminal disease in 62.8% of cases; previous thrombosis with recanalization (54%) was the most commonly encountered lesion, followed by complex weblike lesions at valve sites or possibly associated with previous venipuncture. Angioscopy was used to correct 95.8% of vein abnormalities judged to be significant and allowed an “upgrade” of the conduit quality. The 1-month patency rate was 95.5% in grafts judged to be normal initially or after repair, compared with only 70% in conduits judged to be of inferior quality even after attempted repair. Wilson et al.¹⁶⁷ reported a similar yield of prognostically important information with intraoperative angioscopic evaluation of conduits. Angioscopy thus appears to be most useful for assessing arm vein conduits or ensuring the adequacy of valve lysis for *in situ* conduits. Wound and vein harvest incisional complications can compromise outcome and prolong hospital stay.^{183–187} Several groups have reported the adjunctive use of angioscopy both to assist in the performance of valve lysis and to allow *in situ* bypass to be performed with minimal skin incisions^{171,180–182,187–195}; whether these techniques improve outcome is uncertain.

Some objective assessment of the bypass, its anastomoses, and the outflow is an important component of infrainguinal bypass. I still recommend completion arteriography but recognize that duplex scanning and angioscopy are important adjuncts, especially in higher risk situations and with use of nonreversed or *in situ* conduits in which complete valve lysis

is critical. It seems even more important to perform routine completion studies in an era when the volume and experience with open bypass procedures has fallen at most centers owing to a paradigm shift toward endovascular therapy.

RESULTS

Outcomes must be reported according to the Society for Vascular Surgery reporting standards.^{5–7,196} Graft patency, limb salvage, and mortality are objective endpoints. Somewhat subjective but increasingly important endpoints are durability, functional outcome, and quality of life.

Objective Endpoints

The outcomes of infrainguinal bypass procedures have traditionally been reported solely in terms of graft patency, limb salvage, and patient survival rates. Several factors affect outcome when it is considered in these terms. Conduit type is the major determinant of long-term graft patency, with vein outperforming prostheses for all varieties of infrainguinal bypass. For vein conduits, vein quality^{197–199} and caliber^{199–201} are the most critical determinants of success. Vein grafts less than 3 to 3.5 mm in diameter are inferior whether they are used *in situ* or reversed.^{200,202,203} GSV is superior to alternative vein sources.^{114,202} Reduced graft patency has been attributed to high outflow resistance or poor runoff,^{199,204,205} although poor runoff is somewhat difficult to define, and autogenous vein grafts frequently remain patent in the presence of striking outflow disease (Fig. 112.14). Other factors, such as patient age and diabetes, do not appear to adversely affect graft patency, although diabetic patients exhibit prolonged wound healing times.²⁰⁵ Most investigators agree that the presence of end-stage renal failure is associated with reduced graft patency and increased limb loss and mortality.^{206–215} Anesthetic type has not been conclusively shown to influence graft patency or perioperative mortality.²¹⁶ It is also worth knowing that most of the randomized trials of different conduits and large bypass series are dated, and the patients we currently treat for CLTI and their expected outcomes may differ from those reported in the past. Bradbury and associates recently compared outcomes of surgical bypass from 2009 to 2014 with those from the original BASIL I Trial (2000–2004) and found that outcomes (limb salvage, amputation free survival, overall survival and major adverse limb events) were significantly worse in the contemporary cohort.²¹⁷

Graft Patency

Patency definitions

Patency may be primary, assisted primary (most applicable to vein grafts), or secondary. A graft with primary patency has been continuously patent without any actions being performed to maintain graft patency, except for treatment of more proximal or distal disease not involving the graft or its anastomoses. Dilations or minor revisions performed for stenoses or other structural defects before occlusion occurs do not constitute

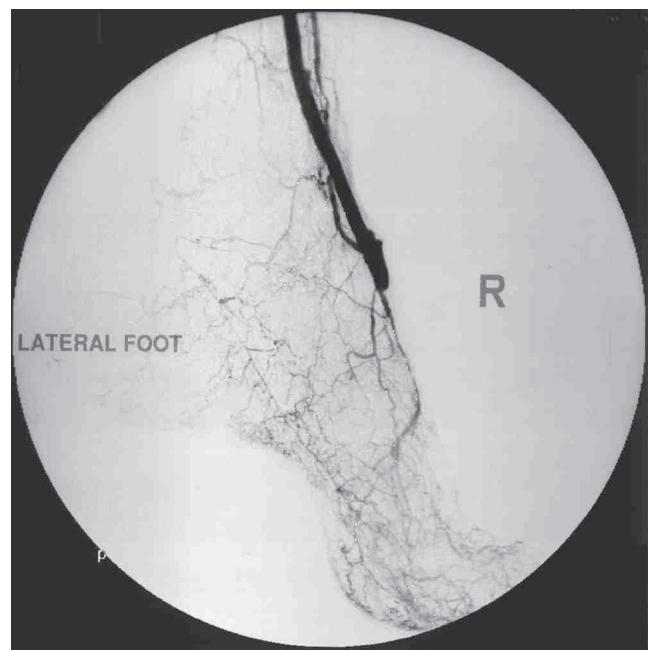


Figure 112.14 Distal view of completion arteriogram after popliteal artery-to-dorsal pedal artery reversed vein bypass in an 82-year-old diabetic man with chronic renal disease and a functioning renal transplant. Despite significant disease of the distal dorsal pedal artery, the patient's toe amputation healed and the graft has remained patent, with normal graft flow velocities, for more than 6 years.

exceptions because they are intended to prevent eventual graft failure.^{5–7,196} A graft with assisted primary patency has required an intervention (either percutaneous or open surgical) to maintain patency but never occluded. A graft with secondary patency thrombosed but was successfully thrombectomized. Primary patency thus reflects the durability of the initial reconstruction, assisted primary patency reflects the impact of graft surveillance and timely reintervention, and secondary patency reflects the persistence of the surgeon in restoring graft patency after failure. The most meaningful endpoints are thus primary and assisted primary patency.

Comparison of graft types

Randomized prospective trials demonstrate equivalence between *in situ* and reversed vein conduits (Table 112.2).^{218–225} The use of these techniques is thus dictated by operative considerations and surgeon preference and experience. Vein is superior to all prostheses, even in the above-knee popliteal position. Expected patency data, based on a review by Dalman²²⁶ and several meta-analyses,^{143,206,227–232} are summarized in Tables 112.3 to 112.6 and Figs. 112.15 and 112.16.

Subjective Endpoints

Durability

Choice of initial revascularization approach (endovascular vs. open) and conduit selection (autogenous vs. prosthetic) are likely to affect outcomes, especially in patients in whom durability of the intervention is an important consideration. Recently published data suggest that the durability of the

TABLE 112.2

Patency of Reversed Vein and *In Situ* Bypass Grafts = *some*

Series and Graft Type	PATENCY (%)		P Value
	RVG	<i>In situ</i>	
Watelet et al. ²²³ : AK/BK popliteal (<i>n</i> = 100 grafts) ^a	88	71	NS
Harris et al. ²²⁰ : AK/BK popliteal (<i>n</i> = 215 grafts) ^a	77	68	NS
Veterans Administration Cooperative Study Group, ²¹⁸ 1988 (<i>n</i> = 461 grafts) ^b			
BK popliteal	75	78	NS
Infrapopliteal	67	76	NS
Wengerter et al. ²²⁵ (<i>n</i> = 125 grafts) ^c			
Overall	67	69	NS
<3-mm veins	37	61	NS
Watelet et al. ²²⁴ (<i>n</i> = 91 grafts) ^d	70.2	64.8	NS

AK, above knee; BK, below knee; NS, not significant; RVG, reversed vein graft.

^aValues at 36 months.

^bValues at 24 months.

^cValues at 30 months.

^dTen-year results.

intervention may be important for subsets of patients. In particular, the Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial concluded that for patients who lived more than 2 years after randomization, a bypass-first revascularization strategy was associated with a significant increase in subsequent overall survival as well as a trend toward improved amputation-free survival. Recent studies of endovascular and open approaches to patients with CLTI suggest that for WIFL Clinical Stage 4 patients, endovascular therapy has a very high reintervention rate and high wound non-healing rate²³³ and at least one publication suggests that the limb salvage rate is higher in these patients with bypass.²³⁴ These data suggest that with proper stratification based on the underlying burden of disease, extent of ischemia, and depth of the wound as well as with an improved comorbidity index, one could select patients who would benefit more from bypass than from endovascular therapy as the initial revascularization approach.

The BASIL trial clearly demonstrated that patients who received prosthetic grafts for severe limb ischemia (constituting 25% of the surgical group) experienced reduced amputation-free survival compared with those who received vein grafts ($P = 0.003$).²³⁵ In addition, the BASIL authors observed that patients who underwent bypass surgery after an initial failed angioplasty experienced significantly worse amputation-free survival than did those who underwent bypass first as the initial

TABLE 112.3

Patency of Above-Knee Femoropopliteal Grafts

Graft Type	PRIMARY PATENCY (%)					
	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year
Reversed saphenous vein	99	91	84	82	73	69
Arm vein	99	—	82	65	60	60
Human umbilical vein	95	90	82	82	70	70
Polytetrafluoroethylene	—	89	79	74	66	60

^aAll series published since 1981.

TABLE 112.4

Patency of Below-Knee Femoropopliteal Grafts

Graft and Patency Type	PATENCY (%)					
	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year
Primary Patency						
Reversed saphenous vein	98	90	84	79	78	77
<i>In situ</i> vein bypass	95	87	80	76	73	68
Secondary Patency						
<i>In situ</i> vein bypass	97	96	96	89	86	81
Arm vein	97	—	83	83	73	70
Human umbilical vein	88	82	77	70	61	60
Polytetrafluoroethylene	96	80	68	61	44	40
Limb Salvage						
Reversed saphenous vein	100	92	90	88	86	75
<i>In situ</i> vein bypass	97	96	94	84	83	—

^aAll series published since 1981.

TABLE 112.5 Patency of Infrapopliteal Grafts

Graft and Patency Type	PATENCY (%) ^a					
	1-Month	6-Month	1-Year	2-Year	3-Year	4-Year
Primary Patency						
Reversed saphenous vein	92	81	77	70	66	62
<i>In situ</i> vein bypass	94	84	82	76	74	68
Secondary Patency						
Reversed saphenous vein	93	89	84	80	78	76
<i>In situ</i> vein bypass	95	90	89	87	84	81
Arm vein	94	—	73	62	58	—
Human umbilical vein	80	65	52	46	40	37
Polytetrafluoroethylene	89	58	46	32	—	21
Limb Salvage						
Reversed saphenous vein	95	88	85	83	82	82
<i>In situ</i> vein bypass	96	—	91	88	83	83
Polytetrafluoroethylene	—	76	68	60	56	48

^aAll series published since 1981.

TABLE 112.6 Patency of Ankle and Below-Ankle Grafts

Graft and Patency Type	PATENCY (%) ^a				
	1-Month	6-Month	1-Year	2-Year	3-Year
Primary Patency					
Reversed saphenous vein	95	85	81	—	—
Secondary Patency					
Reversed saphenous vein	96	90	85	81	76
<i>In situ</i> vein bypass	93	93	92	82	72
Foot salvage	99	94	93	87	84

^aAll series published since 1981.

therapy ($P = 0.006$), suggesting that there is a real potential adverse impact of the endovascular-first approach for all patients with severe limb ischemia. Others, including the Vascular Surgical Group of New England, have made similar observations. Nolan et al.²³⁶ reviewed 1153 patients who underwent lower extremity bypass from 2003 to 2008. Patients who had undergone a prior ipsilateral failed percutaneous intervention had significantly higher rates of graft occlusion and major limb amputation at 1 year by multivariate analysis. A detailed investigation of therapy for lower extremity occlusive disease in South Carolina documented a marked increase in the number of procedures required to obtain similar limb salvage rates coincident with the increase in endovascular therapy during a defined period.²³⁷ Taken together, such data strongly suggest that patients with severe limb ischemia and long-segment atherosclerotic disease who have usable vein, lack severe comorbidities, and have a life expectancy of at least 2 years are likely to be best served with an open surgical approach first with autologous vein.¹²

Functional Outcomes

Whereas graft patency and limb salvage are objective and important endpoints, numerous investigators have recognized that functional outcomes are equally important. Nicoloff et al.²³⁸ emphasized that an ideal outcome – defined by the expectations of a patent graft, healed wound, no need for reoperation, independent living status, and continued ambulation – was extremely difficult to achieve in patients with CLI. Only a small fraction of patients in their report (14.3%) met these basic criteria for success. Golledge et al.²³⁹ from South Australia, using similar criteria, showed that only 22% of patients had an ideal outcome. Abou-Zamzam et al.²⁴⁰ identified preoperative independence and ambulation as the best predictors of postoperative independence and continued ambulation. These data emphasize the severity of underlying comorbidities in CLI patients and the difficulties encountered in obtaining functional limb salvage.

Goshima et al.²⁴¹ from the University of Arizona analyzed a consecutive series of 318 patients undergoing infrainguinal

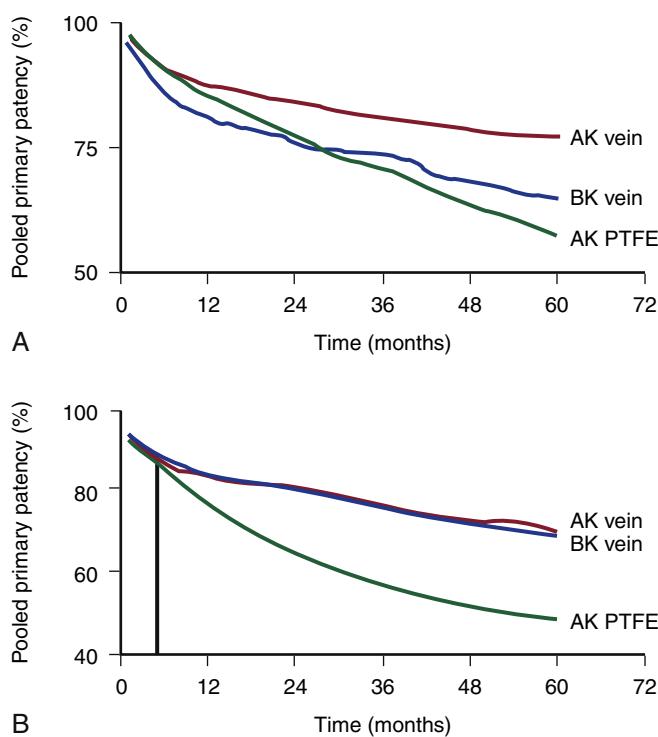


Figure 112.15 (A) Meta-analysis of primary patency in claudicants for above-knee femoropopliteal polytetrafluoroethylene (PTFE) bypass grafts (green line), above-knee femoropopliteal saphenous vein bypass grafts (red line), and below-knee saphenous vein bypass grafts (blue line). (B) Meta-analysis of primary patency in patients with critical ischemia for above-knee femoropopliteal PTFE bypass grafts (green line), above-knee femoropopliteal saphenous vein bypass grafts (red line), and below-knee saphenous vein bypass grafts (blue line). The vertical line indicates when above-knee saphenous vein grafts surpassed PTFE grafts.¹⁴¹ AK, above knee; BK, below knee.

bypass, 72% for CLI. Three nontraditional outcome measures were used to explore outcomes and to define the clinical realities of treating patients with CLI: index limb reoperation rate within 3 months of bypass, hospital readmission rate within 6 months, and wound healing time. Perioperative mortality was less than 1%, mean length of initial hospital stay was 9 days, 30-day graft patency was 97%, and 3-month limb salvage was 97%. Five-year limb salvage in a similar group of patients from the same center was 91%, and the costs of bypass combined with graft surveillance and revision for 5 years were equal to or less than those for patients undergoing major limb amputation.²⁴² However, 49% of patients required at least one reoperation within 3 months, and 50% required readmission to the hospital within 6 months. The cumulative length of stay for all readmissions was 11 days. More than half of CLI patients required more than 3 months of postoperative care to achieve wound healing. The presence of preoperative tissue loss increased the odds of reoperation by 3.1-fold (95% confidence interval, 1.9 to 6.8), whereas ischemic tissue loss, renal failure, and diabetes were independently associated by multivariate analysis with the need for readmission. Diabetes mellitus was the sole independent risk factor for prolonged wound healing (odds ratio, 3.4; 95% confidence interval, 2.3 to 6.2).

Outcome measurements have undergone a re-examination led by the initial effort of Conte et al.²⁴³ to develop objective performance goals. The Society for Vascular Surgery's objective

performance goal criteria were externally validated in 1039 lower extremity bypass operations for CLI in patients who were not on dialysis and in whom autologous vein grafts were placed.²⁴⁴ The objective performance goal criteria included patients at clinical high risk (>80 years of age and tissue loss) and anatomic high risk (infrapopliteal target and lack of single-segment saphenous vein) and showed that major adverse limb events and major adverse cardiovascular events were more common in the high-risk groups.

In sum, these data suggest that to better select patients for open bypass or endovascular therapy, reconsideration of the input (i.e., burden of disease or baseline of disease classification and a risk comorbidity index) as well as the output (i.e., objective performance goals and functional outcomes) will be necessary, as emphasized in the recent Global Guidelines.¹² Further studies using such functional or patient-related outcomes are needed to place the role of infrainguinal bypass in perspective,^{23,245–252} particularly to allow comparisons with less invasive techniques such as subintimal angioplasty or even primary amputation in selected high-risk patients with CLTI. Although it is generally agreed that nearly all patients with CLTI are best treated with revascularization, it is clear that both economic and functional outcome issues mandate the consideration of alternative therapies, at least for certain subsets of patients with CLTI, such as individuals confined to chronic care facilities, those who are minimally ambulatory, and patients with extensive tissue loss and infection who are receiving chronic renal replacement therapy.^{206,240,249,252–255} This issue is addressed in depth in Chapter 108 (Lower Extremity Arterial Disease: Decision Making and Medical Treatment).

Cost-Effectiveness and Risk Stratification

With respect to cost-effectiveness, the initial cost savings of endovascular therapy compared with open bypass for patients with severe or critical limb ischemia is lost after 1 year.^{256–258} Several authors have developed predictive indices to help select patients who have better (or worse) outcomes after open bypass surgery. These include studies performed by the group in Greenville, South Carolina (LEGS score), the Prevention of Infrainguinal Vein Graft Failure (PREVENT) III trial, the Finland National Vascular (FINNVASC) registry, and metrics developed from data derived from the BASIL trial.^{259–262} The Greenville group, in a series of 677 patients fairly evenly split between endovascular and open surgery, showed that impaired ambulatory status at the time of presentation, diabetes, end-stage renal disease, gangrene, and prior vascular intervention all increased the risk of failure. The presence of multiple comorbidities increased the risk of failure dramatically.

It is worth reviewing the FINNVASC, PREVENT III, and BASIL outcome prediction models. The FINNVASC score assigns one point each for diabetes mellitus, foot gangrene, CAD, and urgent operation, and the predictive model stratifies risk on a scale of 1 to 4 based on the sum of the points. The FINNVASC score has been externally validated. The PREVENT III prediction model assigns end-stage renal failure on dialysis 4 points, tissue loss 3 points, age older than 75 years 2 points, and CAD 1 point and stratifies risk into low (≤ 3 points), medium (4–7 points), and high (≥ 8 points). This prediction model has also been validated. The stratification system derived from BASIL used tissue loss, body mass index,

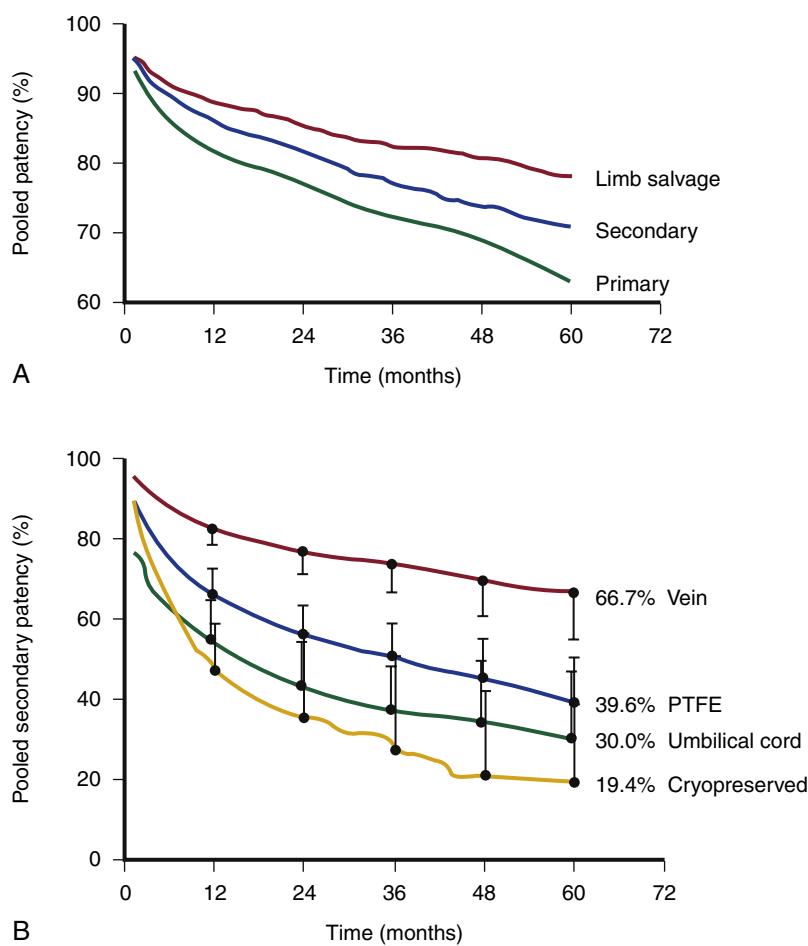


Figure 112.16 Patency of Infrageniculate Bypass Grafts. PTFE, polytetrafluoroethylene. (A) Random effects meta-analysis of popliteodistal bypass grafts for primary patency (green line), secondary patency (blue line), and foot preservation (red line).²³² (B) Meta-analysis survival curve of secondary patency for alternative autologous vein (red line), polytetrafluoroethylene (blue line), umbilical cord vein (green line), and cryopreserved vein (yellow line). Bars are half the amplitude of 95% confidence intervals.²³¹

serum creatinine concentration, Bollinger score, age, smoking, coronary disease, and ankle pressure and produced a complex model of mortality calculation that is likely too complex for standard clinical use and may not apply to all patients with CLTI because the study inclusion criteria differed from CLI as previously defined. Nonetheless, it seems that multiple comorbidities, especially those that are common to the major reports, need to be considered in offering a patient a bypass and trying to gauge the outcomes (Table 112.7).

Quality of Life

A substantial amount of new data, derived primarily from two large prospective trials (PREVENT III and BASIL),^{187,202,214,245,246,263–269} is beginning to put the role of successful bypass in the proper perspective. It also lends support to long-standing impressions about the effectiveness of leg bypass in relieving ischemic symptoms and improving quality of life in properly selected patients.^{236–238,269–274} Patients with CLTI have a markedly reduced quality of life compared with a normal control population,^{238,260} and their quality of life is markedly improved by successful bypass.^{260,263,264} It is also becoming evident, especially in CLTI patients with severe ischemia and higher grade wounds, that ongoing graft patency, at least

for the first 1 to 2 years, is critical to the maintenance of this quality of life improvement.^{268,269,275,276} Tissue loss at presentation and graft-related events or failure of percutaneous transluminal angioplasty (PTA) during the first 1 to 2 years after the index revascularization are associated with reduced quality of life and increased resource utilization. Thus, although the early BASIL results showed no difference in outcomes between bypass and PTA for CLI,²⁷⁵ the published intermediate follow-up analysis suggests that bypass is more effective than PTA in all but the most unfit patients. The bypass-first group had a better amputation-free survival (relative risk, 0.85) and a lower all-cause mortality than the angioplasty-first group (relative risk, 0.65; $P < 0.009$), probably because of the high failure rate of PTA and the more frequent need for reintervention to maintain patency.^{257,258} For patients with severe ischemia, particularly diabetics and those with tissue loss, ongoing vascular patency is important for maintaining quality of life and preventing amputation.^{241,248} These important findings may eventually lead to a gentle swing of the therapeutic pendulum away from endovascular therapy and back toward open bypass, at least for relatively fit CLI patients with GLASS III disease, available vein conduit, and estimated life expectancy of more than 2 years.^{276,277}

TABLE 112.7

Comparison of the Components and Output System of the FINNVASC, Prevention of Infringuinal Vein Graft Failure III, and Bypass Versus Angioplasty in Severe Ischemia of the Leg Scoring Systems

	FINNVASC	Prevent III	BASIL
Variables	One point for each: Diabetes mellitus Foot gangrene Coronary artery disease Urgent operation	Dialysis = 4 points Tissue loss = 3 points Age >75 years = 2 points Coronary artery disease = 1 point	Tissue loss Body mass index Creatinine concentration Bollinger score Age Smoking Coronary artery disease Ankle pressure
Output method	Risk stratified 1–4 on sum of points	≤3 points = low risk 4–7 points = medium risk ≥8 points = high risk	6-, 12-, and 24-month mortality rates calculated by model (http://basiltrial.com/survival_predictor.htm)
Externally validated	Yes (Arvela et al. ²⁶²)	Yes (Schanzer et al. ²¹⁴ ; Arvela et al. ²⁶²)	No

From Moxey PW, Brownrigg J, Kumar SS, et al. The BASIL prediction model in patients with peripheral arterial disease undergoing revascularization in a university hospital setting and comparison with the FINNVASC and modified PREVENT scores. *J Vasc Surg*. 2013;57:1–7.

POSTOPERATIVE MANAGEMENT

After bypass, patients should generally be maintained on their preoperative medical regimens for the control of angina, arrhythmia, congestive heart failure, and hypertension. Patients with a recent history of congestive heart failure are at high risk for prolonged hospital stay and readmission.^{214,239,241} Care should be taken to avoid volume overloading in these patients, and they may require supplemental diuresis. Perioperative beta blockade should be continued in the absence of contraindications; in moderate- and high-risk patients undergoing vascular surgery, beta blockade with targeted heart rate control reduces cardiac complications and improves mortality.^{18–20}

Antiplatelet Therapy

Most patients with PAD are already receiving antiplatelet therapy, usually aspirin (81 or 325 mg daily). Aspirin has well-recognized cardiac and cerebral protective effects and may also improve early graft patency.^{278–288} Clopidogrel may also be used,²⁸⁹ but it is more expensive and may have an increased risk of complications compared with aspirin alone. Most vascular surgeons consider antiplatelet therapy essential for patients undergoing infrainguinal bypass.

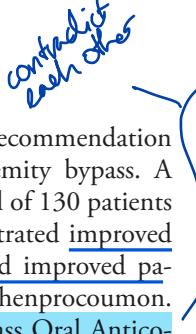
Anticoagulation

There are insufficient data on which to base a recommendation concerning anticoagulation after lower extremity bypass. A single long-term, randomized, prospective trial of 130 patients by Kretschmer et al.²⁹⁰ from Vienna demonstrated improved vein graft patency and limb salvage rates and improved patient survival in those randomized to receive phenprocoumon. An important clinical report, the Dutch Bypass Oral Anticoagulants or Aspirin (BOA) trial, summarized a study of 2690 lower extremity bypass patients randomized to anticoagulation

versus antiplatelet therapy (aspirin).^{291–293} Although overall differences were not significant, subgroup analysis suggested that oral anticoagulation improved vein graft patency compared with aspirin, whereas aspirin improved prosthetic graft patency compared with anticoagulation. If these data can be confirmed, it is likely to alter the typical practice in North America, where surgeons tend to treat vein graft patients with aspirin and to anticoagulate those with prosthetic grafts. The BOA trial, however, noted that anticoagulated patients had nearly double the major bleeding risk of patients receiving antiplatelet therapy, suggesting that anticoagulation should be used selectively in subgroups at greatest risk. A recent structured review suggests that anticoagulation may be beneficial in high-risk grafts, such as redo procedures or in the presence of poor arterial outflow.²⁹⁴

Such a selective approach has been recommended by the University of Florida group on the basis of a small randomized study of patients with high-risk vein grafts.²⁹⁵ High-risk grafts were defined on the basis of poor arterial runoff, suboptimal vein conduit, and reoperative cases. Patency (74%) and limb salvage (81%) rates at 3 years in the high-risk group randomized to warfarin and aspirin were significantly higher than in the aspirin-only group (51% and 31%, respectively), although again, bleeding was much more common in the group receiving warfarin.

Although this seems to be a logical approach, a Veterans Affairs cooperative trial reached a different conclusion based on 665 patients with infrainguinal bypasses who were randomized to aspirin and warfarin versus aspirin alone.²⁹⁶ Vein graft patency was not increased by the addition of warfarin to aspirin; in contrast, prosthetic graft patency was significantly improved by anticoagulation, but at the expense of double the risk of hemorrhagic events. These data all suggest a potential role for postoperative anticoagulation that requires larger trials with higher statistical power to permit an evidence-based recommendation. Until then, most surgeons will continue to routinely employ antiplatelet therapy (aspirin 81 to 325 mg



daily) and add anticoagulation in selected groups at highest risk (e.g., prosthetic infrageniculate grafts, poor outflow, reoperative cases, poor or alternative vein conduit).

Wound Care

All patients with CLTI are at risk for pressure ulcers not only in the affected limb but also in the contralateral limb and the sacrum. Unremitting nursing care is essential to prevent these complications. Considerable wound care is also required to achieve healing of ischemic foot lesions and forefoot amputations. Foot infection should have been controlled before revascularization. Basic science wound studies suggest that debridement and formal toe and forefoot amputations for areas of tissue ulceration or gangrene should be delayed 4 to 10 days after bypass to maximize tissue reperfusion and to allow the clear demarcation of marginal areas (see Chs. 118, Wound Care and 119, Podiatric and Vascular Teams).

COMPLICATIONS

The major early postoperative complications of infrainguinal bypass are wound problems, bleeding, graft occlusion, graft infection, and death (see Table 112.2). The results of the PREVENT III trial from 83 enrolling centers probably reflect realistic complication rates in clinical practice.²⁶⁵ The authors of this study reported the following early complication rates in a prospective trial of more than 1400 infrainguinal vein grafts in patients with CLI: death (2.7%), myocardial infarction (4.7%), major amputation (1.8%), graft occlusion (5.2%), major wound complications (4.8%), and graft hemorrhage (0.4%). Late complications include persistent lymphedema, graft infection, graft aneurysm, and graft stenosis.

Early Graft Occlusion

With experienced judgment and intraoperative attention to detail, early graft occlusion should be infrequent. Should a graft fail in the early postoperative period, the most important principle is to identify and correct the underlying cause.²⁹⁷ If no cause can be identified, the prognosis for long-term patency is poor. The outcome is much more favorable if the cause can be ascertained and addressed. The most common correctable culprits are anastomotic, local endarterectomy or clamp defects; valve defects; poor conduit quality; and inadequate outflow.

When the patient is returned to the operating room, one can usually begin by exploring the distal anastomosis first. If the graft hood is pulsatile, an arteriogram is obtained. If not, the hood is opened and gentle distal thrombectomy and graft thrombectomy are performed with balloon catheters of appropriate caliber. If the graft is a reversed vein, both proximal and distal anastomoses usually require exploration. An uninflated balloon catheter is passed from proximal to distal; a second catheter can be tied to the first one and drawn uninflated proximally. The tie is cut, the second catheter is inflated, and the graft is then thrombectomized from proximal to distal. Once the thrombus has been evacuated, heparinized saline is forcibly

irrigated through the graft to flush any residual thrombotic debris out the distal graftotomy. Both anastomoses can then be carefully inspected; if a distal anastomotic defect is identified, the graftotomy can be extended down the outflow artery and closed with a patch. If no defects are identified, the graft incisions are closed, and thorough arteriography of the entire graft and the outflow is performed. Significant conduit or anastomotic lesions should be corrected. If unsuspected or previously unappreciated outflow disease is identified, the graft should be extended beyond the lesion or to an alternative outflow artery if one is available. If a marginal vein conduit was used at the initial procedure and no focal defect is identified at re-exploration, one should consider replacing the conduit; this decision is difficult and may require the harvesting of additional vein or, if none is available, converting to a prosthetic conduit if outflow is sufficient.

Late Graft Occlusion

Late graft occlusion should be treated only if the patient's symptoms are severe enough to warrant intervention. When vein conduit is limited, I attempt thrombolysis, mechanical thrombectomy, or both and treat the underlying lesion responsible for graft failure. The results of this approach are generally poor, however. My preference for late graft occlusions is to perform a new bypass with autogenous vein, which provides superior results and durability.¹⁵¹ If vein is unavailable and thrombolysis is contraindicated or fails, a repeated bypass with PTFE and a vein patch or cuff is the best option, although in some patients native artery resurrection with complex endovascular techniques is useful. The optimal therapy for graft occlusion is to prevent its occurrence by identifying graft-threatening stenosis before the onset of graft occlusion through routine postoperative duplex graft surveillance.

GRAFT SURVEILLANCE

Vein graft surveillance is critical to the long-term success of infrainguinal bypass. It has been well documented for more than three decades that nearly one third of autogenous vein grafts develop lesions that threaten graft patency.²⁹⁸ Most such lesions, especially in the first 1 to 2 years after graft implantation, are intrinsic to the graft itself and result from intimal hyperplasia.^{299–301} Later, inflow and outflow lesions may develop and reduce graft flow, thus threatening ongoing graft patency. All these lesions can be readily identified, graded for severity, and monitored for progression by means of a program of ankle-brachial index determination and duplex graft surveillance.^{112,222,242,302–313} I obtain the first study within 4 weeks of surgery, either before hospital discharge or at the first postoperative visit.³⁰³ Serial studies are performed every 3 months for 1 year, every 6 months for 2 additional years, and annually thereafter. Grafts with focal lesions associated with a peak systolic velocity greater than 300 cm/s or a velocity ratio greater than 3.5 to 4.0 undergo prophylactic repair to prevent graft stenosis.^{311,312} Grafts that develop low-flow velocities over time (peak systolic velocity <45 cm/s throughout the graft) or

a drop in ankle–brachial index exceeding 0.15 in the absence of detectable graft lesions undergo arteriography to search for inflow, outflow, or missed graft lesions.

Abundant clinical data from multiple investigators and a single prospective randomized trial by Lundell et al.³¹⁴ suggest that vein graft surveillance improves long-term vein graft patency by approximately 15%. Although one trial questioned the benefit of vein graft surveillance,²⁶⁷ that surveillance protocol was flawed, the endpoints were inappropriate, and the follow-up was too short to detect a difference.³⁰⁸ Cost–benefit analyses both in Europe³¹³ and in the United States²⁴² confirm that vein graft surveillance is cost-effective. Graft occlusion is a morbid and costly event,^{242,268} and its prevention is worthwhile. Graft surveillance of prosthetic grafts has not been shown to be beneficial.^{315,316}

TREATMENT OF GRAFT AND ANASTOMOTIC STENOSES

Vein graft stenoses are solitary and focal in approximately 80% of cases. Multiple focal synchronous or metachronous lesions are identified in 15% to 20% of grafts; diffuse long-segment graft narrowing, presumably due to myointimal hyperplasia, is uncommon (3% to 5% of cases).³⁰⁰ If recurrent limb ischemia requires treatment in the latter circumstance, graft replacement is the treatment of choice.

There are multiple options for the treatment of focal graft lesions; selection of the optimal therapy depends primarily on the length of the lesion, the timing of its occurrence (early [<3 to 6 months] vs. late [>3 to 6 months]), and the patient's comorbidities. Focal lesions that develop after the 6th postoperative month respond fairly well to PTA,^{317,318} and data suggest that use of a cutting or scoring balloon is superior to standard balloon angioplasty.^{319,320} If a graft stenosis is treated by PTA, it should be closely observed by duplex ultrasound because the recurrence rate is generally higher than after open repair. Stent placement in infrainguinal vein grafts has also been reported for focal lesions.

If open repair is chosen, there are several options, depending primarily on the characteristics and location of the lesion. Circumferentially fibrotic midgraft lesions are best treated with excision and segmental interposition vein grafts. Less extensive lesions are amenable to vein patch angioplasty. There are no data demonstrating the superiority of patch versus interposition grafting,³⁰⁷ but circumferentially fibrotic, napkin ring-like lesions are better treated with replacement. Focal, less fibrotic lesions, particularly related to valves, can be treated with valve excision and vein patch through a longitudinal graftotomy that extends proximal and distal to the site of the lesion. Intraoperative completion angiography or duplex scan should be performed to document resolution of the lesion.

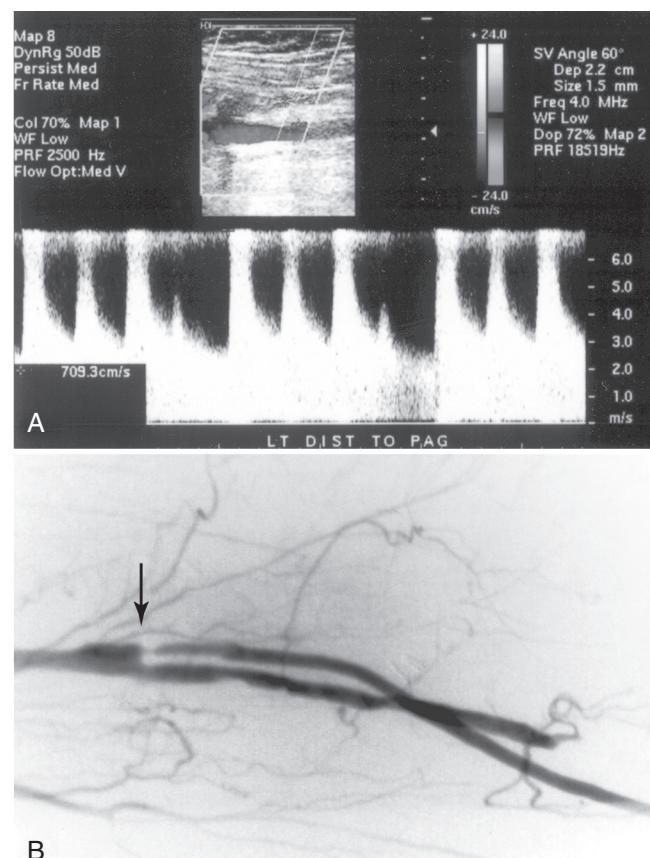
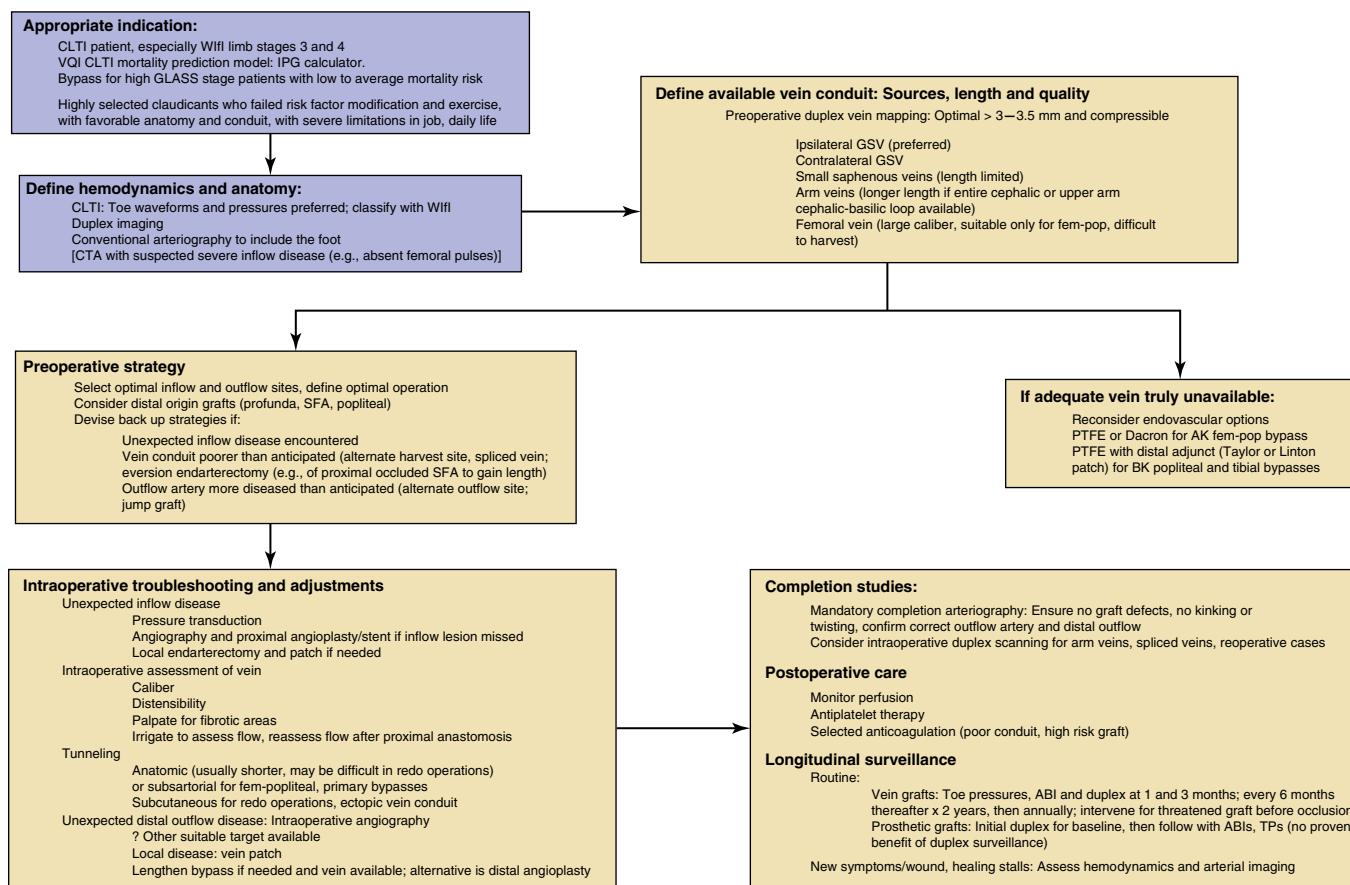


Figure 112.17 Duplex surveillance identified a critical vein graft stenosis in the proximal aspect of a femoropopliteal vein graft. (A) Marked spectral broadening and pronounced elevation of both the peak systolic and end-diastolic velocities are diagnostic of a high-grade vein graft stenosis. (B) A focal, severe proximal graft stenosis (arrow) was confirmed by arteriography and treated with a short interposition vein graft harvested from the upper extremity.

Focal juxta-anastomotic lesions often develop in the vein graft itself, immediately adjacent to the arterial anastomosis.³⁰⁰ These lesions can be treated by either patch angioplasty or short interposition grafts (Fig. 112.17). Another option that eliminates the need to harvest additional vein conduit is proximal anastomotic translocation.³²¹ This procedure involves resecting the lesion and oversewing the graft stump near its origin. If the vein graft below the stenosis is of good caliber, the graft can be transposed to an alternative inflow artery. For example, if the original anastomosis was to the CFA, and if the PFA is large and its origin is free of disease, the PFA can be exposed, and the graft can be mobilized below the proximal stenosis and swung over or transposed so as to reoriginate from the PFA. Distal juxta-anastomotic stenoses can usually be vein patched, but if the outflow artery has also developed progressive occlusive disease, a better option is a jump graft to a more distal target artery if one is available. These procedures have been described in detail elsewhere.³²¹

CHAPTER ALGORITHM

Algorithm for Infrainguinal Bypass for Atherosclerotic Occlusive Disease



ACKNOWLEDGMENT

The illustrations were drawn by Joseph L. Mills, Jr.

SELECTED KEY REFERENCES

Bradbury AW, Adam DJ, Bell J, et al. BASIL Trial Participants. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: a survival prediction model to facilitate clinical decision making. *J Vasc Surg*. 2010;51(suppl):S52–S68.

Although imperfect, the BASIL trial is the only published, prospective randomized trial of open bypass versus endovascular therapy for severe limb ischemia. Key points include significantly poorer outcomes for prosthetic compared with autogenous bypass conduits and trends toward improved overall survival and improved amputation-free survival in patients treated with bypass first who lived more than 2 years.

Conte MS, Bandyk DF, Clowes AW, et al. PREVENT III Investigators. Results of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. *J Vasc Surg*. 2006;43:742–751.

Landmark study of a novel molecular therapy for the prevention of vein graft failure in patients undergoing infrainguinal revascularization for critical limb ischemia. Despite a well-conceived trial design, an impeccably executed study, and high-quality surgical results at multiple centers, the proposed molecular therapy was found to result in no significant improvement in any of the primary endpoints.

Conte MS, Bradbury AW, Kohl P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg*. 2019;69:3S–12SS.

Important recent guidelines paper that resets definitions, classifications of limb threat and vascular anatomy, treatment and management algorithms and objective performance goals and measures for patients with lower extremity peripheral artery disease and CLTI.

Faries PL, Arora S, Pomposelli Jr FB, et al. The use of arm vein in lower-extremity revascularizations: results of 520 procedures performed in eight years. *J Vasc Surg*. 2000;31:50–59.

This Boston group has long championed an all-autogenous approach. Their study shows that autogenous arm vein can be used successfully in a wide variety of lower extremity revascularization procedures and achieves excellent patency and limb salvage rates, generally much higher than those reported for prosthetic or cryopreserved grafts.

Mills JL, Fujitani RM, Taylor SM. The characteristics and anatomic distribution of lesions that cause reversed vein graft failure: a five-year prospective study. *J Vasc Surg*. 1993;17:195–206.

Postoperative duplex surveillance was prospectively performed during a 66-month period in 227 patients after infrainguinal vein graft placement to determine the causes of graft failure. The authors found that a significant portion of these failures occurred during the intermediate postoperative period (3 to 18 months), usually as a result of focal intrinsic vein graft lesions that are readily detectable by duplex surveillance. They concluded that duplex vein graft surveillance is warranted by the 21% incidence of potentially remediable graft failure.

Mills JL, Conte MS, Armstrong DG, et al. on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Committee. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk Stratification based on Wound, Ischemia, and Foot Infection. *J Vasc Surg.* 2014;59:220–234.

Mills JL. The application of the Society for Vascular Surgery Wound, Ischemia, and foot Infection (WFIT) classification to stratify amputation risk. *J Vasc Surg.* 2017;65(3):591–593.

The SVS WFIT Classification defines baseline limb risk based on grades of Wound, Ischemia and foot Infection to create Clinical Stages of amputation risk (from 1 to 4). Even with revascularization, limb status based on WFIT Clinical Stage stratifies amputation risk. Future application and evolution of this rubric may be helpful in selecting the best revascularization approach in a given clinical scenario.

Stonebridge PA, Prescott RJ, Ruckley CV. Randomized trial comparing infrainguinal polytetrafluoroethylene bypass grafting with and without vein interposition cuff at the distal anastomosis. The Joint Vascular Research Group. *J Vasc Surg.* 1997;26:543–550.

This study was undertaken to determine whether an interposition vein cuff improved the short- and medium-term patency and limb salvage rates of femoral above-knee and below-knee popliteal artery polytetrafluoroethylene (PTFE) bypass procedures. The authors found that there was no improvement in patency rate with the use of a distal anastomosis interposition vein cuff in above-knee PTFE grafts, but there was a statistically significant

advantage when PTFE grafts were anastomosed to the popliteal artery below the knee. Vein cuffs or patches seem to be beneficial in those relatively uncommon patients requiring infrageniculate bypass in whom autogenous vein is not available.

Szilagyi DE, Elliot J, Hageman JH, et al. Biologic fate of autogenous vein implants as arterial substitutes: clinical, angiographic, and histopathologic observations in femoro-popliteal operations for atherosclerosis. *Ann Surg.* 1973;178:232–246.

Infrainguinal vein grafts implanted in 377 patients during a 10-year period were studied by serial arteriography to determine their natural history. This study set an early standard for long-term follow-up and demonstrated its importance in patients undergoing such procedures.

Watelet J, Soury P, Menard JF, et al. Femoropopliteal bypass: in situ or reversed vein grafts? Ten-year results of a randomized prospective study. *Ann Vasc Surg.* 1997;11:510–519.

Long-term studies with good follow-up provide the best information about treating patients with chronic diseases. For example, this study reported the results of 100 femoropopliteal bypass procedures performed in 91 patients during 5 years who were randomly divided into two statistically comparable groups: 50 in situ vein grafts and 50 reversed vein grafts. One conclusion: small veins do not work as well, even when they are used in situ.

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

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Infrainguinal Disease: Endovascular Therapy

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INTRODUCTION

The use of endovascular therapies for the treatment of infrainguinal vascular disease has become a key component of a multimodal approach to manage peripheral arterial disease. The decision to employ an **endovascular-first** interventional strategy **relies on several factors**, including clinical presentation, lesion anatomy, patient comorbidities and presence of autologous conduit. Most importantly, endovascular therapy should serve as a complement to other methods of treatment, including medical management and open surgical approaches. As such, it is paramount that the

vascular practitioner recognizes the advantages and limitations of the various endovascular strategies, ranging from diagnostic angiography to intervention with balloon angioplasty, stenting and even atherectomy. An “on-hand” knowledge of multiple endovascular techniques is especially important, as diagnostic angiography may serve to delineate disease that is amenable to intervention in the same setting. Indeed, the likelihood of success is predicated on the right tool at the right time, meaning both the right technique and the right indication. This chapter will serve as a review of the endovascular interventions, based on indication, currently available for infrainguinal disease.

INDICATIONS

Medical Management

Endovascular therapy often represents an attractive “minimally invasive” option, especially for patients with intermittent claudication with isolated, short segment lesions. However, it is best utilized as a component of an overarching strategy (rather than standalone therapy) to help manage chronic, progressive diagnosis. A key component in the management of these patients involves adherence to non-interventional strategies including smoking cessation, tight control of blood glucose levels in diabetic patients, use of appropriate antiplatelet and statin therapy, and enrollment in a supervised walking program. Adherence to medical optimization and enrollment in a supervised walking program is a key component at every stage of managing these patients, and certainly may be the most appropriate initial management before one even considers utilizing invasive measures. In the context of this chapter, it is important to consider medical optimization as an important adjunct to reduce surgical risk and improve anticipated outcomes following endovascular procedures.

Smoking Impact

Smoking cessation is a cornerstone in the management of patients with peripheral artery disease (PAD) and is recommended by American Heart Association (AHA), Society for Vascular Surgery (SVS) and Global Vascular Guidelines.^{1–3} Patients who present with IC and are actively smoking rarely progress to chronic limb-threatening ischemia (CLTI) and have improved cardiovascular survival if they can maintain smoking abstinence.⁴ Active smokers who undergo an open bypass have a threefold increased risk of graft failure.⁵ Those that quit smoking after their bypass experience a 50% risk reduction in all-cause mortality over the ensuing 5 years.⁶ However, a similar increase in risk of adverse limb events, including reintervention, conversion to surgical bypass and limb loss, following endovascular intervention in active smokers has not been appreciated.⁷

Statin Impact

Statin therapy, and in particular high-intensity statin therapy, has been shown to reduce rates of major adverse limb events and mortality in patients with peripheral artery disease.⁸ In the international First-Line Treatments in Patients with Critical Limb Ischemia (CRITISCH) registry, statin therapy demonstrated a significant survival benefit in patients with CLI, though amputation rates are similar to patients not on statin therapy.⁹ Patients undergoing endovascular revascularization have better outcomes when combined with statin therapy use. In a review of nearly 650 patients undergoing endovascular intervention, statin therapy was associated with an increased rate of primary patency, secondary patency, limb salvage and overall survival.¹⁰

ACE Inhibitor Impact

Overwhelming evidence has supported the use of angiotensin converting enzyme (ACE) inhibitor therapy in patients with

PAD to reduce cardiovascular mortality. Recent research in patients undergoing a heterogeneous mix of endovascular therapies for lower extremity disease demonstrated an improved overall survival and amputation-free survival among patients on ACE inhibitor therapy.^{11,12}

Antiplatelet Therapy Impact

Antiplatelet therapy has become a mainstay among patients with PAD, largely due to the high prevalence of comorbid coronary or cerebrovascular disease. However, evidence of benefit for using antiplatelet therapy for primary prevention of cardiovascular outcomes (including peripheral events) in asymptomatic patients with PAD are lacking.^{13,14} In contradistinction, multiple studies have demonstrated the significant cardiovascular risk reduction among symptomatic patients taking single antiplatelet therapy (either aspirin 75–325 mg or clopidogrel 75 mg monotherapy).^{15–17} Intermittent claudication is the predominant symptom for most patients within these trial populations. Despite these positive results, a meta-analysis by Berger et al., including asymptomatic and symptomatic patients, failed to demonstrate a significant difference in major adverse cardiovascular outcomes.¹⁸ Considering the potential positive impact of antiplatelet therapy for cardiovascular risk reduction in patients with atherosclerotic PAD, and the relatively low rates of bleeding complications, many practitioners have adopted the utilization of antiplatelet therapy in their medical management strategy for patients with PAD. Indeed, numerous societal guidelines, including the AHA 2016 Guideline Statement and SVS Practice Guideline Statement, provide Class 1A recommendations for the use of antiplatelet therapy for patients with symptomatic PAD.^{1,2} The use of newer antiplatelet therapies, such as ticagrelor, has become more prevalent with the improved results in patients taking this medication following PCI for MI though it does not demonstrate similar superior outcomes compared with Plavix monotherapy in patients with PAD.¹⁹ The use of antiplatelet therapy after percutaneous intervention is discussed in more detail later in this chapter.

Anticoagulation Therapy Impact

With the recent publication of the COMPASS trial, there has been a renewed interest in the use of long-term anticoagulation for patients with symptomatic PAD.²⁰ Within this trial, over 28,000 patients with cardiovascular disease in at least two beds or with at least two risk factors were randomized to low dose rivaroxaban, either alone (5 mg twice daily) or with aspirin (2.5 mg plus 100 mg aspirin daily) compared with aspirin alone (100 mg daily). With a median follow-up of 23 months, there were lower rates of a composite endpoint of cardiovascular outcomes (5% compared with 7%) and, importantly, fewer major adverse limb events including amputation (1% vs. 2%) among the patients with combination therapy of low dose rivaroxaban plus aspirin compared to aspirin alone. Nearly 7500 patients within this study had PAD and nearly 25% had a previous revascularization procedure.²¹ Subgroup analysis of

this population further supported an improved outcome on patients with low dose rivaroxaban plus aspirin. These results helped to inform the design of the VOYAGER trial, which focused specifically on the population of PAD patients undergoing revascularization. The results of this are discussed later in the chapter.

INTERMITTENT CLAUDICATION

To date, overwhelming evidence supports the role of medical management as the first-line therapy for patients with intermittent claudication (IC).² With appropriate medical management, few patients (1%–3%) with IC will progress to require amputation over the ensuing 5-year period.²² Surgical therapy, either open or endovascular, for patients with PAD with symptoms limited to IC is a reasonable strategy for those who fail medical management, including supervised walking therapy.^{23,24} If CT angiography is inadequate, the use of invasive angiography for patients who continue to have lifestyle-limiting claudication after best medical management can function as both an anatomic assessment and therapeutic intervention strategy.¹ “Failure” of medical management represents an individualized discussion between the patient and the vascular surgeon. In the real world, multiple reasons can contribute to failure of medical management, including patients who cannot modify their lifestyle, those that do not have access to supervised walking programs, and those who have personal reasons for a more aggressive approach to intervention (e.g., walking is a key part of their employment). It is incumbent on the vascular surgeon to recognize the available interventions, their likelihood of success and the associated risks to appropriately guide patients through the management of this disease. Importantly, current societal guidelines recommend against the treatment of IC solely for the purpose of preventing progression to CLTI.²

Endovascular therapies, including balloon angioplasty, stenting, or atherectomy, for IC have limited level 1 data regarding long-term durability, especially compared to supervised walking therapy.^{25–30} Much of the data for newer therapies are from industry-sponsored trials, which may have limited follow-up data, as they are often designed (understandably) for regulatory clearance. Further complicating the picture is the fact that many of these trials include a heterogeneous group of patients, including IC and CLI. Patients with IC actually comprise a large portion of the total included patients.^{31–35} Given the overall benign course of most patients with intermittent claudication, it is highly prudent for only interventions with durable benefits to be considered. The types of outcomes reported may make it difficult to interpret the actual value of endovascular intervention. Specifically, the use of “target vessel revascularization” (TVR) as an outcome measure may prioritize angiographic or anatomic evidence of success, rather than patient-reported outcomes or qualitative measures such as walking distance or amputation-free survival. For instance, a meta-analysis by Wilson examined six trials comparing PTA and stenting with medical therapy and found a significant

increase in ABI following endovascular therapy versus medical management.³⁶ However, at 6 months patients in the medical management group actually reported longer walking distances compared to those that had undergone endovascular therapy, a result maintained at 1 to 2 years in the majority of the trials. TVR undoubtedly imparts a cost to the patient and healthcare system and is important to consider; however, results reported herein will be centered around amputations, thrombosis or bleeding events, and patient-reported quality of life (QoL) scores whenever possible.

Femoropopliteal Segment

The femoropopliteal segment (FPS) is the most common affected infrainguinal area for patients with intermittent claudication. Lesions in this region that appear to compromise 50%–75% of the diameter of the lumen likely cause a hemodynamically significant reduction in flow. Lesions isolated to the common femoral artery are nearly universally better served with open femoral endarterectomy and patch angioplasty, allowing for preservation of the profunda.^{37,38} In patients with hostile groins, there are reports of endovascular approaches involving both angioplasty and stenting, with care taken not to cover the orifice of the profunda artery.^{39,40} To reduce the rates of dissection and vessel occlusion when treating CFA lesions, some have even reported the use of kissing stents, though these reports lack long-term follow-up and are limited in number.⁴¹

Endovascular therapy has become first-line therapy for managing stenosis or occlusions in the superficial femoral artery extending into the popliteal segment, especially those with short lesions measuring less than 4 cm.^{2,22,42} The sheer number of available treatment options, including plain balloon angioplasty (PBA), atherectomy, bare metal stent (BMS) placement, stent graft placement and, more recently, drug-incorporating therapies (drug-coated balloon [DCB] angioplasty and drug-eluting stent [DES] placement), offer the practitioner a wide gamut of tools to utilize an endovascular approach disease in these segments. The infrainguinal vessels are highly dynamic, with a combination of axial and radial forces exerted on the vessel during locomotion as well as the challenge pinching of the artery that can occur predominantly at the adductor hiatus.⁴³ Compression on these segments can increase three- to fivefold as the patient ages through an increase in the presence of calcific plaques as well as a change from atherosclerotic wall shear stress to atherosclerosis-inducing oscillatory shear stress.⁴⁴ Indeed, an improved recognition of these forces has been at the heart of device development, and has led to designs that resist both the mechanical as well as cellular response to intervention.

Balloon Angioplasty

During the early development of endovascular technology in the 1980s and 1990s, PBA was the primary tool for management of lesions in the FPS. PBA functions to disrupt atherosclerotic plaques by increasing the lumen diameter, with

balloon sizes chosen based on a combination of characteristics of the vessel both at the disease location and at a normal location, presumably distal to the diseased segment. Dissections are a common effect of this mechanical disruption, and are a key factor limiting the effectiveness and durability of PBA as a stand-alone therapy. Severe dissection can occur following PBA, and “bailout” stenting is frequently required, most typically in cases with residual stenosis or flow-limiting dissections. Further, the trauma induced by balloon inflation can lead to continued inflammation within the artery and activation of leukocyte adherence, smooth muscle cell migration into the intima, and macrophage recruitment into the ECM.⁴⁵ In combination, this response to balloon angioplasty results in “negative remodeling” and promotes restenosis in the treated segment.⁴⁶

Much of the recent data regarding long-term patency of primary balloon angioplasty in combination with maximal medical management are derived from comparisons with drug-coated balloon angioplasty. While the effectiveness of the latter strategy is discussed more fully elsewhere in this chapter, a review of these results helps to demonstrate the limited durability of primary balloon angioplasty in the FPS. In the European BIOLUX P-I trial, the uncoated balloon angioplasty arm had a 34.6% restenosis rate with target vessel revascularization required in 41.7% of treated vessels at 1 year.⁴⁷ Similarly, in a clinical trial comparing paclitaxel-coated balloon versus PBA, patients treated with PBA had a high rate of target vessel revascularization (33.3% at 6 months).⁴⁸ Interestingly, Rutherford class was only improved in 36% of patients after PBA at 6 months, though that rate stayed stable through 18–24-month follow-up.⁴⁸ In the IN.PACT SFA trial, patients with Rutherford stage 2–4 symptoms (with the majority Rutherford 2 and 3) were randomized to angioplasty with either DCB or PBA.⁴⁹ Primary patency for the PBA group was only 50.1% at 24 months and 29.2% required target vessel revascularization, though no patients had a major limb amputation in a treated limb during the study period.⁴⁹ These results are concordant with a large Cochrane Review that demonstrated no difference in limb amputation rates at 5 years for patients undergoing uncoated PBA compared with angioplasty with DCB, despite significant differences in TVR between DCB and PBA (favoring DCB).⁵⁰ PBA as a stand-alone therapy may have its greatest usefulness in patients with short lesions (<4 cm) who are willing to participate in aggressive post-interventional medical management and lifestyle changes, as well as routine follow-up with a vascular surgeon.

Balloon-Expandable Stents

Stenting in the FPS initially originated as a “bailout” technique after post-angioplasty dissection. Since that time, it has evolved to the preferred initial approach for medium-to-long segment occlusions in the superficial femoral and popliteal arteries. This advent has been made possible by a large number of trials demonstrating the superiority of stenting to PBA among these patients. The vast majority of peripheral stenting occurs with self-expanding stents rather than balloon-expandable due

to their ability to recoil after undergoing mechanical forces exerted by the SFA during ambulation. Early reports from trials examining balloon-expandable stents (primarily Palmaz) in patients with claudication showed higher rates of patency at 6 months, but no differences in primary patency at 12 or 24 months when compared with PBA alone.^{51–55} In many reports, patients had improved hemodynamic outcomes at long-term follow-up with PBA alone compared to adjunct use of balloon-expandable stents.⁵⁶ Given these poor long-term results, the use of balloon-expandable stents in the FPS should be limited.

Self-Expanding Stents

Self-expanding (SE) stents with nitinol (a nickel–titanium alloy) are among the most commonly used in the FPS today. Early experimentation with nitinol actually began with Dotter and colleagues in the 1980s, when they reported on a spun coil that would expand to a set diameter upon warming in heated saline.⁵⁷ These stents are loaded onto a scaffolding or catheter while in their contracted state, and then expand to a predetermined diameter once exposed to body temperature. They continue to exert a radial force and are highly resistant to compression.⁵⁸ The safety and efficacy of nitinol-based self-expanding stents compared with angioplasty alone were reported first in the RESILIENT trial.⁵⁹ This multicenter trial enrolled patients with Rutherford class 1–3 claudication symptoms in Europe and the United States, recruiting a total of 206 patients in 24 centers. The average lesion length in the stent group was 6.2 cm. This study demonstrated higher rates of TVR in patients with angioplasty alone at 6 months (47.4% vs. 2.5%) and 1 year (54.9% vs. 16.5%). The trial was not powered to study amputation rates (which should presumably be low amongst a claudication-only population) so reported a combined outcome of major adverse clinical events (MACE) instead, defined as 30-day death, stroke, myocardial infarction, emergent surgical revascularization, significant embolization in the target limb, thrombosis of the target vessel and worsening of at least one Rutherford classification.⁵⁹ The rates of MACE were low and similar in both groups, as were improvements in QoL measures and improvements in walking distance.

The safety and efficacy trials associated with each device's FDA approval process also provide important insights into the performance of self-expanding stents in the FPS. The DURABILITY II Trial (United States Study for Evaluating Endovascular Treatments of Lesions in the Superficial Femoral Artery and Proximal Popliteal by using the Protégé Everflex Nitinol Stent System II) published results from multicenter, international recruitment of primarily claudicants (95.1% Rutherford class 2 or 3) with an average lesion length of nearly 11 cm.³⁴ The trial reported high rates of primary patency at 1 year (77.2%), which were highest among patients with lesion lengths less than 8 cm (86.2%). There were no amputations during the study period and the rates of clinically driven target limb revascularization was 13.9%, comparable to reports with other stents. Importantly, at 1 year, 83.5% of patients reported an improvement in their Rutherford classification of at least 1 point, with 55.9% being totally asymptomatic. The

high proportion of patients reporting mild claudication or no claudication symptoms at one year after self-expanding stent placement were echoed in the Complete SE trial, in which 83% of patients reported Rutherford class 1 or 2 symptoms on follow-up.⁶⁰ Long-term follow-up from patients treated with a helical woven nitinol stent (Supera Peripheral Stent System, Abbott Laboratories, Inc, Webster, TX), showed low rates of reintervention at 36 months (18%) and high rates of primary patency at 72 months (63.1%).^{61,62} The rates of amputation were low and highly concentrated in the first 6 months after stent implantation, likely secondary to the nearly 42% of enrolled patients with tissue loss present on enrollment.⁶²

Patients with very long (defined as >15 cm) lesions have lower overall patency but appear to benefit from SE stent placement based on data demonstrating 1-year patency rates significantly higher in the stented group (49% vs. 34%).⁶³ Even among this long segment group, there were no amputations in patients who underwent stenting for claudication symptoms.⁶³ These results are further bolstered from the DURABILITY 200 trial utilizing 200 mm Protégé Everflex stents (ev3 Endovascular Inc, Plymouth, MN) in a large group of claudicants with average lesion length of 242 mm.⁶⁴ In this group, primary patency at 12 months was nearly 65%. It is important to note that the rates of stent fracture were higher at 6% when compared to reports from other studies with shorter length SE stents. The use of covered stent grafts has also been explored for longer lesions. In the VIBRANT (Viabahn vs. Bare Nitinol Stent in the Treatment of Long Lesion Superficial Femoral Artery Occlusive Disease) trial, nearly 150 patients, with lesions averaging nearly 20 cm, underwent stent graft placement versus bare metal nitinol stenting.⁶⁵ The primary patency rates appear to be equivalent between the two groups, but patients in the stent graft group had a significantly lower primary-assisted patency rates (69.8% vs. 88.8%).⁶⁵ Even more concerning, stent graft failure appears to affect collateral vessels more, particularly if covered at time of stent placement, and has an association with higher limb ischemia rates with device failure than BMS.⁶⁶

The use of self-expanding stents in the FPS should be considered the first-line endovascular intervention for patients with claudication, who have failed medical therapy, and have lesions of mid-to-long length (>4 cm). There are two key takeaways from the multiple trials in this population – the need for active follow-up and surveillance of implanted stents. Reported patency rates at 1 year of 65%–75% are comparable to the 5-year patency rates of femoral to below-knee popliteal bypass with autogenous vein. Therefore, it is reasonable to consider endovascular therapy first, but only in patients in whom distal targets for bypass are not compromised or in whom there is no suitable autogenous conduit. Further, the fact that TVR rates are significantly higher than amputation rates in patients with implanted stents suggests the value for consistent and routine follow-up for these patients. As with any intervention, efforts at repeat angioplasty or revascularization should be both anatomically and clinically driven to avoid the risks of exposure to unnecessary procedures and potential embolization to a future outflow target. This is an especially

important consideration in patients with claudication, in whom there is a very low risk of limb loss at baseline.

Drug-Eluting Stents and Drug-Coated Balloons

The use of targeted drug delivery to treat the cellular response to inflammation caused by endovascular intervention has become an increasingly popular option. Both DESs and DCBs aim to reduce inflammation and neointimal hyperplasia, largely through inhibiting SMC migration, to reduce in-stent restenosis or late vascular injury. The benefits of mitigating the cellular response to endovascular injury were first reported in patients undergoing coronary artery revascularization, with improved patency rates compared with bare metal stenting.⁶⁷ Drug-eluting coronary stents have been used off-label for the treatment of infrapopliteal (IP) lesions, and will be discussed later in this chapter. However, DES for FPS required creation and validation of new stents. The SIROCCO (sirolimus-eluting versus bare nitinol stent for obstructive superficial femoral artery disease) examined the use of the SMART stent (Cordis, Miami, FL) for treatment of atherosclerotic disease isolated to the superficial femoral artery. The majority of these patients (>90%) had moderate to severe claudication (Rutherford class 2 or 3).⁶⁸ Despite the low rate of TVR (13%) and restenosis (22.9%) at 2 years, the study failed to demonstrate a difference compared to BMS. The authors concluded that a key component to this “negative” finding was the better than expected performance of patients being treated with bare metal stenting.

The Zilver PTX trial helped to bring more widespread use of DES (paclitaxel-coated) in the FPS. It was designed to compare patients undergoing femoral PBA versus stenting with the Zilver PTX (Cook Medical, Bloomington, IN) DES.⁶⁹ As with the SIROCCO trial, greater than 90% of patients enrolled in the trial had Rutherford class 2–3 symptoms. Patients who underwent primary stenting with the Zilver PTX DES experienced significantly higher rates of primary patency at 12 months (83.1% vs. 32.8%).⁶⁹ The drastically improved patency rate was maintained at 5 years (72.4% vs. 53%) with lower rates of TVR among patients with primary DES placement (15.1% vs. 28.4%).³¹ Interestingly, a subset of the patients was also randomized to provisional DES placement at their index procedure if deemed to have unsuccessful PBA. These patients too reported higher patency rates than the PTA group at 1 year (89.9% vs. 73%).⁶⁹ The study also reported results from more clinically based outcome measures, including ABI values, Rutherford scores, and walking impairment scores. Patients from both intervention arms experienced a significant benefit in all measures. However, “clinical benefit,” an outcome measure defined as freedom from persistent or worsening claudication, rest pain, ulceration or tissue loss after the initial study, occurred in nearly 90% of patients in the DES category compared with 75% in the PBA group.⁶⁹ This clinical benefit improvement also appeared better maintained at 5 years in the DES group compared with the PBA group (81.8% vs. 63.8%).³¹ These results from the Zilver PTX trial have provided the strongest evidence in support of increased use of DES in the claudicant population. However, as discussed further in the chapter, more

DES < sirolimus
DES < paclitaxel

DCB = paclitaxel

recent concerns over potential increased mortality rates in the group of patients treated with paclitaxel-coated therapies has marred their widespread acceptance.

In contrast to the different agents available for DES for coronary artery disease, DCB therapy for lower extremity interventions is based solely on the use of balloons and stents coated with paclitaxel. Patients with claudication (Rutherford class 1–3) make up the vast majority of the patients enrolled in these studies, with enrollment percentages as high as 95% of some study cohorts.^{48,70–73} These trials have compared DCB with either standard PBA alone^{48,70,71,74} or combined with BMS.⁷² The trials examining DCB use compared with PBA all demonstrate lower rates of loss of patency and targeted revascularization in the DCB cohorts compared to those undergoing PBA, with sustained results varying from 12 to 24 months. The THUNDER trial released follow-up 5-year data which additionally demonstrated sustained angiographic improvement.⁷⁵ The true clinical benefit is more difficult to interpret as rates of amputation were exceedingly low for each group. The PACI-FIER trial reported a lower major adverse outcome, a combined endpoint of death, amputation, and TLR, in the DCB group, but this was largely driven by reduction in TLR rather than any difference in major amputation.⁷⁰ The IN.PACT SFA trial demonstrated no major amputations among the PBA group and only one amputation among the DCB group over a 5-year period.⁷³ Similarly, the 5-year data from THUNDER demonstrated only one amputation in claudicating patients in the PBA group compared with two in the DCB group.⁷⁵ These data highlight an important consideration: limb loss rate for claudicating patients is extremely low and does not appear to be impacted by DCB use.

Controversies in DES and DCB Therapy

The enthusiasm for targeted drug delivery has been dramatically tempered by the release of a systematic review of RCTs for paclitaxel-containing DCB and DES that demonstrated an increased all-cause mortality at 2 years for patients treated with paclitaxel-containing devices (PCDs)⁷⁶ (Table 113.1). The reaction was significant and resulted in many vascular surgeons halting the use of paclitaxel-containing devices in their practices. The findings also prompted a renewed interest in long-term post-market surveillance results for patients who already had treatment with this therapy. These results have been more mixed. Long-term follow-up with the Zilver PTX stent demonstrated no difference in mortality through 5 years.⁷⁷ In the largest dataset to be evaluated thus far, over 70,000 medicare patients treated with drug-coated devices were followed for a median of 2.7 years with no difference in mortality (PMID 33993204). However, an analysis of de-identified patient data supplied by the US Food and Drug Administration for trials resulting in the approval of PCDs (DESs and DCBs) further confirmed a nearly 40% relative risk increase in all-cause death over 5 years when these devices were used in the FPS.⁷⁸ The mechanisms for this persistent association with increased death and PCD has not been established. As such, an important component when considering the use of PCBs in any patient should be a frank conversation

paclitaxel DES ↑ risk than
" DCB

TABLE 113.1

Sensitivity and Subgroup Analyses of All-Cause Patient Death

	Risk Ratio (95% CI)
All-cause death at 2 years	
Fixed effects model	1.84 (1.27–2.68)
Random effects model	1.68 (1.15–2.47)
All-cause death at 4–5 years	
Fixed effects model	1.94 (1.28–2.96)
Random effects model	1.93 (1.27–2.93)
Subgroups (random effects)	
Paclitaxel DES only	1.87 (1.11–3.15)
Paclitaxel DCB only	1.44 (1.04–2.00)
Multicenter studies only	1.48 (1.11–1.97)
Dose subgroups (beyond 1 year)	
3.5 µg/mm ² paclitaxel balloon	2.31 (1.15–4.63)
3.0 µg/mm ² paclitaxel stent	2.10 (1.15–3.83)
3.0 µg/mm ² paclitaxel balloon	1.65 (0.95–2.87)
2.0 µg/mm ² paclitaxel balloon	1.27 (0.70–2.32)
Trial sequential analysis (TSA; random effects at 2 years)	
TSA diversity adjusted ($\alpha=5\%$, $\beta=20\%$)	1.70 (1.19–2.43)
TSA diversity adjusted ($\alpha=5\%$, $\beta=10\%$)	1.70 (1.24–2.33)
TSA diversity adjusted ($\alpha=5\%$, $\beta=10\%$)	1.70 (1.08–2.69)

with the patient regarding the mortality risk known to date balanced with the patency benefits. To help vascular specialists account for the evolving data on this topic, the Society for Vascular Surgery (SVS) established the SVS Paclitaxel Safety Task Force in 2019. In part, this task force has helped focus efforts utilizing the Vascular Quality Initiative through the SVS Patient Safety Organization to provide bi-annual updated data on the risks, benefits, and patient factors affecting this technology.

Behind-the-Knee Popliteal Artery

As the above-knee popliteal artery traverses the popliteal fossa, the mechanical forces and motion of the artery become exaggerated. Additionally, the size of the artery reduces by a few millimeters. Therefore, placing stents in this area has not been recommended as there is an increased risk for stent fracturing from the motion, which can lead to restenosis and occlusion. In patients with CLI and significant comorbidities, placing a stent in this area may be applicable for limb salvage. As new technology develops, behind-the-knee stenting for isolated popliteal disease may become an option for select patients, primarily those with comorbidities that preclude open repair.

Infrapopliteal Segments

The contribution that isolated IP segmental stenosis or occlusion may have on calf claudication symptoms is unclear. As

such, intervention on these segments solely for the purpose of relieving claudication symptoms is generally not indicated.² Data are overall lacking regarding the utility and durability of isolated interventions in this distribution for patients with claudication. Most of the data regarding use of angioplasty, stenting, or targeted drug delivery with either DCB or DES in the tibial vessels has been collected in patients with CLI, for whom the risks for limb salvage are inherently different than patients with isolated claudication. A study of patients with IP disease and Rutherford class 2–3 symptoms who underwent tibial angioplasty did show high rates of technical success and acceptable primary assisted patency at one year (81.9%).⁷⁹ Baseline ABI was 0.61 and immediate postoperative clinical status appeared improved; however, repeat ABI or treadmill walking distance was not performed routinely at the one-year follow-up so the durability of the clinical status improvement is unknown.⁷⁹ Taken together, it is unknown if claudication symptoms are durably relieved by treating isolated IP disease. However, the risk of dissections, thrombosis, and potential compromise of a later outflow target are tangible.

Atherectomy

Directional (DA), rotational (RA) and laser atherectomy are endovascular techniques meant to disrupt and debulk the plaque to improve lumen diameter. They may also provide a mechanism to debulk the inciting lesion as a way to improve the durability of angioplasty and/or stenting. These devices typically involve a rotating cutting blade that essentially shaves the plaque (directional atherectomy), or a bit that spins coaxially to bore the plaque (rotational atherectomy) to reduce plaque burden. Distal embolization is reported to occur in 1%–2% of all lower extremity interventions, and is reported as high as 20% for atherectomy.⁸⁰ The incidence of embolization has not been documented routinely, but can be as high as 20%.⁸¹ To prevent distal embolization, there is often an aspiration portion of the catheter to allow for capture and removal of the disrupted plaque. This distal embolization has been one of the primary pitfalls of use of these devices in the FPS. Atherectomy of the FPS or tibioperoneal segments, performed for intermittent claudication, is associated with high rates of reintervention and amputation.⁸² In the DEFINITIVE LE trial examining atherectomy use in diabetic and non-diabetic patients with claudication or CLI, patency rates were similar to second-generation nitinol stent.⁸³ Despite limited long-term benefit, the use of atherectomy (either directional, orbital or laser) continues to rise, especially in the outpatient and office setting. Perhaps one phrase from the previous edition of this chapter of Rutherford's best encapsulates the concern for this increased utilization despite limited demonstrative benefit: "reimbursement drives practice."

CHRONIC LIMB-THREATENING ISCHEMIA

Patients presenting with CLTI (Rutherford class 4–6) represent a patient population in whom aggressive and timely

not just to alleviate sx

intervention is necessary to preserve limb and functionality. As such, these are often the patients in whom the primary consideration is not whether to intervene at all (as is the case with claudicants) but rather which type of surgical management strategy would be best. Indeed, it is in this arena that many of the evaluations comparing open surgical management with endovascular approaches have been conducted. The Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial was completed in 2005 to help evaluate a comparison of open versus endovascular management of CLTI.⁸⁴ It enrolled 452 patients to receive either open surgery first (228 patients) or angioplasty first (224 patients) upon presentation for CLTI for infrainguinal disease. Highlighting the severity of this disease process, at 5 years only 55% of patients were alive without an amputation and 37% of patients were dead (either with or without an amputation). While the data are older now (recruitment was from 1999 to 2004) and endovascular techniques have changed significantly, the thoughtful approach outlined by the authors for considering open versus endovascular-first approaches in these patients warrants review. Of the 237 patients that underwent an angioplasty-first strategy, 21 (8.8%) required open surgery during the same hospitalization and 43 (20%) were deemed immediate technical failures.

From 6 months to 2 years, the rates of amputation-free survival and all-cause mortality did not differ significantly between the two groups. At 2 years, however, the surgical arm started to show statistically significantly better outcomes in both domains. The authors comment that both morbidity and surgical costs were higher for patients undergoing surgical therapy rather than endovascular for the first year. This included patients who underwent an angioplasty first only to require a surgical revascularization afterwards. As such, the benefits of surgery in terms of durability are best realized after 2 years. The authors recommend that angioplasty be considered first for patients expected to live only 1–2 years.⁸⁴ The balance between life expectancy of the patient and morbidity of the procedure has long remained a cornerstone in determining the best approach for patients presenting with CLTI. The newest Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia further define the high-risk surgical candidate as one with an anticipated perioperative mortality greater than 5% and anticipated 2-year survival less than 50%.³

There are several reasons to interpret BASIL cautiously since its publication in 2005. As discussed with claudicants, the use of advanced endovascular approaches, including the use of drug-coated or -eluting devices, has increased dramatically. The only method of endovascular intervention in BASIL was balloon angioplasty and there are some data to suggest DCBs and DESs in the IP distribution may improve patency. On the other hand, one-quarter of patients in BASIL underwent bypass with a prosthetic graft, a departure from the current recommendations for bypasses to below-knee targets (AHA and SVS recommendations). This is especially true in patients with below-knee or IP targets, which comprised two-thirds of the BASIL surgical population. To evaluate this new landscape for treating CLTI, the Best Endovascular Versus the Best Surgical Therapy in Patients with Critical Limb Ischemia (BEST-CLI)

TABLE 113.2

Primary and Secondary Endpoints for Upcoming Randomized Control Trials for Management of Patients with PAD

Endpoints	BASIL, 2/3	BEST-CLI
Primary	AFS	MALE-Free Survival
Secondary	Freedom from all-cause mortality In-hospital and 30-day morbidity and mortality MALE MACE Relief of ischemic pain Psychological morbidity Re- and cross-over intervention rates Healing of tissue loss (ulcers, gangrene) Extent and healing of minor amputations Hemodynamic changes; absolute ankle and toe pressures, ABPI, TBPI HRQL (VascuQoL and EQ-5D) Health economic analysis	Freedom from all-cause mortality RAFS Freedom from MALE+POD AFS Freedom from myocardial infarction Freedom from stroke Freedom from re-interventions (major and minor) in index leg Number of re-interventions (major and minor) per limb salvaged Freedom from hemodynamic failure Freedom from clinical failure Freedom from CLTI HRQL (VascuQoL and EQ-5D) Health economic analysis

ABPI, Ankle-brachial pressure index; AFS, amputation-free survival; BASIL, bypass versus angioplasty in severe ischemia of the leg; BEST-CLI, best endovascular versus the best surgical therapy in patients with critical limb ischemia; EQ-5D, EuroQol five dimensions questionnaire; HRQL, health-related quality of life; MALE, major adverse limb event; POD, perioperative death; RAFS, re-intervention and amputation-free survival; TBPI, toe-brachial pressure index; VascuQoL, vascular quality of life.

trial was developed among 100 centers in Europe and the United States to randomize patients with critical limb ischemia to surgical versus endovascular intervention⁸⁵ (Table 113.2). The major advantage of this study is that procedural specifics, including device selection and targets, within each major category are left to the discretion of the practitioner, allowing for a more real-world experience. Enrollment has been slower than anticipated, likely secondary to patient preferences and practitioner biases.⁸⁶ However, the study finally completed its enrollment in early 2020 and is now actively following enrolled patients.⁸⁷ The results of BEST-CLI, in conjunction with the expected results of BASIL-2 comparing vein bypass versus best endovascular in 2022 and BASIL-3 comparing PBA versus

stenting in 2023, should help to identify patients best served by either open or endovascular strategies.^{88,89} Currently, the choice to pursue endovascular therapy in the CLTI population is based on the estimated perioperative risks and the severity of any associated wounds.

Femoropopliteal Segments

Patients with CLTI often have multilevel disease involving both the FPS and below-knee segments. As such, the strategy for approaching these lesions can be varied and complex. The data regarding intervention in the FPS for CLTI are limited. As mentioned previously, the majority of patients enrolled in trials for endovascular devices reported claudication, rather than CLTI, at the time of enrollment. From retrospective and small case series studies, there seem to be some overarching principles. Patients undergoing femoral intervention for CLTI rather than claudication appear to have worse outcomes, even after successful intervention.⁹⁰ Further, SFA disease that results in occlusion of the femoral artery rather than stenosis appears to have lower patency when treated with endovascular means.

Trials examining the role of isolated SFA intervention for the treatment of CLTI are minimal. Limited short-term data have demonstrated similar primary patency rates and limb salvage rates in SFA PBA versus bypass; however, these reports are limited by low occurrence rates over the study period.⁹¹ Data regarding the utility of PBA are extrapolated from the endovascular arm of patients within the BASIL trial as the majority of patients in this arm had isolated SFA intervention.⁹² In patients with CLTI, there is a higher rate of technical failure with PBA compared with patients being treated for IC, often driven by inability to cross the SFA lesion or inability to successfully reenter the true lumen after crossing in a subintimal plane.⁹³ Within the PBA-first strategy in BASIL, early reintervention (within 8 weeks) may be common but may actually benefit early amputation-free survival and overall survival though the impact on long-term survival is unclear.⁹² However, practitioners offering SFA angioplasty first for patients presenting with CLTI should recognize that failed PBA, even if followed by successful bypass, is associated with worse overall outcomes.⁹²

Despite the limitation of PBA, it is unclear if the addition of stent placement improves outcomes.⁹⁴ In fact, an evaluation of CLTI patients (two-thirds of whom had tissue loss) showed a higher rate of restenosis following stenting than PBA.⁹⁴ This is in contradiction to more recent literature supporting improved patency and walking outcome with nitinol stenting compared with PBA alone in patients with SFA disease and IC symptoms.⁹⁵ A knowledge of the entire “toolkit” available (including limitations) is necessary to ensure the best possible outcomes for patients in whom endovascular strategies are attempted for CLTI. An additional consideration is the high prevalence of multi-level disease, which raises concerns for outflow adequacy and increases the likelihood of multi-level intervention.

Drug-Coated Balloons

In the DEBATE-SFA trial examining the role of drug-coated balloon use in the femoral artery, 79.2% of patients in the DCB

+ stenting arm and 68.6% in the PBA + stenting arm reported Rutherford class 4–6 symptoms, with the majority of these being class 5.⁹⁶ At the 12-month follow-up, no patients had undergone amputation in either arm and only 83% in the DCB arm had restenosis of the treated segment. The DEBELLUM (Drug Eluting Balloon Evaluation for Lower Limb Multilevel Treatment) trial similarly randomized mostly CLTI patients to DCB vs. PBD.⁹⁷ Over three-quarters of the lesions treated were in the femoral artery. The authors found lower rates of targeted revascularization at 6 months in the DCB group but equivalent amputation rates between the two cohorts. However, the fact that the actual amputation rates were so different (4% for DCB vs. 12% for PBA) but still not statistically significant may suggest an insufficient power to truly evaluate this clinical outcome measure. Overall, it appears that measures of restenosis and targeted revascularization at 6 months and one year are lower in patients undergoing DCB compared with PBA, but clinical measures such as amputation and mortality are equivalent.⁹⁸ In part, these results may be due to the overall poor cardiovascular health of these patients, which should temper excitement about initial technical success in the absence of data regarding long-term outcomes. DCB treatment of FPS may be best suited to improve outcomes in patients who are at high risk for perioperative events and who are relegated to endovascular-only approaches because of this. It is important to note that the controversy surrounding the use of DCB and DES and mortality risks may not be as pronounced in patients being treated with CLTI, perhaps given their overall reduced survival compared to IC patients.⁹⁹

Infrapopliteal Disease

As stated previously, the endovascular toolbox has increased significantly since the first evaluation comparing angioplasty to surgery in BASIL. One of the areas that has experienced the greatest amount of growth has been DES and DCB therapy, particularly IP interventions in patients with CLTI. The peroneal and tibial vessels were particularly attractive targets since their size approximated coronary arteries and therefore drug-based interventions developed for PCI could be used in these segments as well. Even before the widespread evaluation of drug-based endovascular therapies, PBA alone has been used as a viable strategy to treat IP disease. In comparison with propensity-matched patients undergoing surgical bypass, patients with PBA have shown similar 5-year survival (47.5% vs. 43.3%), amputation-free survival (37.7% vs. 37.3%) and limb salvage (75.3% vs. 76.0%).¹⁰⁰ The equivalence in clinical outcomes, such as amputation, occurs despite much lower primary and secondary patency rates with tibial angioplasty compared to surgical bypass.¹⁰¹ Indeed, tibial PBA is an attractive option in patients too ill to tolerate distal bypass and in whom the primary objective is to heal a distal wound. In a report of CLTI patients with wounds, isolated tibial PBA was found to achieve wound healing in nearly 70% of patients though the wound healing time can be significant (average 11.5 months).¹⁰²

Stenting

The use of self-expanding nitinol based in the IP segment has been examined. The EXPAND trial examined the use of the

self-expanding Astron Pulsar (Biotronik AG, Bülach, Switzerland) versus PBA in a population of whom 60% had CLTI.¹⁰³ It demonstrated similar improvement in Rutherford classification among the two cohorts as well as similar rates of major amputation at 12 months (PBA: 8.7%; stent: 6.7%). In 2018, the Cochrane Library reviewed 7 studies that examined PBA versus stent using patients with CLTI and IP disease.¹⁰⁴ They demonstrated higher early technical success and patency with stenting compared with PBA, but these differences are lost by just 6 months and there are no differences in amputation rates or limb salvage.¹⁰⁴ As with many meta-analyses, heterogeneity in patient care, including the use of antiplatelet therapy, hampers the ability to draw firm conclusions about the best strategy for IP disease. However, in the absence of clear benefit, a tempered approach using balloon angioplasty primarily seems reasonable.

Drug-eluting stents

As compared with nitinol-based self-expanding stents, the use of DES in the IP arteries has had promising results. The majority of these trials have been examined using sirolimus-based DESs rather than paclitaxel as is used in the FPS. In the CLTI cohort of the YUKON-BTK trial, in which patients with sirolimus-eluting stents were compared with bare-metal stenting, the rate of major amputation was significantly lower in the DES group (5.3% vs. 22.6%).¹⁰⁵ The PARADISE trial investigated the safety and efficacy of two different DESs (83% everolimus-based and 17% paclitaxel-based) in 106 patients with CLTI and severe below-the-knee disease.¹⁰⁶ It reported an impressive 3-year amputation rate of only 6% with an amputation-free survival of 68%.¹⁰⁶ The authors compare this to a historical expectation of nearly 40%–50% amputation rate in the same population. This impressive reduction in amputation rates seen in the YUKON-BTK and PARADISE trials has not been recapitulated in other trials examining IP DES use. The ACHILLES trial compared PBA versus implantation of DES in the IP system of patients with CLTI and found no difference in amputation rates at one year despite higher patency rates.¹⁰⁷ Further, the DESTINY trial looked at use of everolimus-coated Xience V stent (Abbott Vascular, Redwood City, CA) compared with BMS and found reduced TLR but no impact on amputation rates at 12 months.¹⁰⁸ Of note, there were only three amputations recorded in the entire cohort of 140 patients so it is difficult to make strong conclusions about amputations in the two intervention arms. Ultimately, the improved patency rates with DES point towards a possible improvement in more clinical-based outcomes, but the often limited life-expectancy may mean the clinical benefit is not realized. It should be noted that stents for tibial vessels are only short segment and are coronary based. Most tibial disease is long segment and multifocal in patients with CLI, and to date there are no long segment stents available.

Drug-coated balloons

The IN.PACT DEEP trial has recently reported 5-year outcomes for patients undergoing DCB (paclitaxel-based) versus PBA in the below-knee arteries for CLTI (over 80% Rutherford class 5 and 6).¹⁰⁹ Impressively, the rate of amputation

was similarly low in both groups (DCB: 15.4%; PBA: 10.6%). Given the results were published amidst the controversy with using paclitaxel-based therapies, the authors explored the potential impact on all-cause mortality and found no difference between the two groups either.¹⁰⁹ Again, the similar amputation rate does not seem to reflect the early patency benefits seen in patients with IP disease treated in the DEBATE trial, which also used the Amphirion DCB (Medtronic, Inc, Minneapolis, MN, USA).⁹⁶ The patients in DEBATE had both diabetes and severe PAD (>95% Rutherford class 5 or 6), which should predispose them to predictably high amputation rates. However, only one patient in the trial had a major amputation at 1 year, making any comparisons unfeasible. The BIOLUX II registry reported a combined clinical and angiographic outcome with all-cause mortality, target extremity major amputations, target lesion thrombosis and TVR and found similar rates at 30 days, 6 months and 1 year for patients treated with DCB and PBA.¹¹⁰ In all of these trials, the aggressive follow-up and medical management of patients with severe PAD may have lowered expected amputation outcomes compared with historical expectations. Perhaps most encouraging, these laudable results show that DCB or PBA can be used as part of an aggressive treatment strategy for IP lesions in CLTI. Like DES, today there are technical limitations of DCBs for tibial disease, as there are no commercially available balloons in the 2- to 3-mm diameter range, which is the size of most tibial vessels.

Special Considerations

Hybrid Procedures

The use of a hybrid approach, utilizing both open revascularization and endovascular techniques during the same setting, has become an attractive option to leverage the strengths of each approach. For example, the use of a femoral endarterectomy combined with either retrograde iliac stenting or antegrade femoral stenting obviates difficulties with access for the endovascular technique while limiting the incision location to a single site in the groin. The use of iliac stenting, combined with either femoral endarterectomy, femoral-to-femoral artery bypass, or femoral-distal bypass has become a commonly reported strategy.¹¹¹ Autologous vein is the preferred conduit for below-knee artery bypasses. Femoropopliteal stenting can be used to move the proximal anastomosis more distally in patients in whom there is limited vein length. This strategy has yielded promising results, with high primary and secondary patency rates, even with the use of pedal targets.^{112,113} Schanzer et al. reported a 70% primary assisted patency and 70% limb salvage rate at 5 years in patients with CLTI utilizing the approach of femoral stenting followed by popliteal-to-distal artery bypass.¹¹⁴ Loss of patency often occurs secondary to progression of outflow disease from the bypass graft rather than in-stent stenosis at the femoral stent. Graft occlusion may even be amenable to another hybrid operation, using graft thrombectomy and outflow vessel PBA.¹¹⁵

Safari

Subintimal Arterial Flossing with Antegrade-Retrograde Intervention (SAFARI) for the treatment of occlusive disease that cannot be crossed with traditional antegrade techniques has

become an increasingly attractive option in patients who lack surgical options. In this technique, distal retrograde access is obtained usually from a pedal artery in addition to antegrade access to allow for easier re-entry into the true lumen when the subintimal plane is entered. Access of the dorsalis pedis or posterior tibial artery at the level of the ankle is typically employed to allow for retrograde recanalization and is particularly assisted when there is at least 1 cm of patent outflow vessel above the ankle.¹¹⁶ Reports of 3- and 6-month follow-up demonstrate patency rates of around 60% with limb salvage rates at 5 months approximating 80%.¹¹⁷ These results have been recapitulated in small retrospective studies, even some with reports of limb salvage rates as high as 88% at 1 year.¹¹⁸ Retrograde revascularization is a viable strategy, especially in patients with complex tibial disease, and is another tool in the limb salvage armamentarium.

MEDICAL MANAGEMENT FOLLOWING ENDOVASCULAR INTERVENTION

Antiplatelet or Antithrombotic Therapy After Endovascular Intervention

Multiple societal guidelines support antiplatelet therapy for all symptomatic patients with PAD. Though not explicitly stated, it would follow that this same guideline should extend to all patients after endovascular management. Subgroup analysis of patients undergoing endovascular revascularization in the Antithrombotic Trialists' Collaboration (ATC) demonstrated a nonsignificant improvement in major adverse cardiovascular events but was not designed to analyze limb-specific outcomes among this subgroup. A large Cochrane meta-analysis further investigated the role of high-dose aspirin following endovascular revascularization and found an improved 6-month patency for patients on aspirin compared with placebo.¹¹⁹ There is evidence to suggest a mechanistic benefit from dual antiplatelet therapy compared to aspirin monotherapy in the peri-interventional period through a reduction in peri-interventional platelet activation in the group with DAPT.¹²⁰ Analysis of practice patterns within the Vascular Quality Initiative (VQI) from 2003 to 2016 regarding dual antiplatelet therapy (DAPT) after endovascular therapy demonstrated nearly 70% of patients are discharged on dual antiplatelet therapy following endovascular intervention.¹²¹ This highly prevalent strategy of dual antiplatelet therapy after lower extremity endovascular revascularization is likely best suited for certain indications only, particularly chronic limb-threatening ischemia versus intermittent claudication, to improve benefit while reducing bleeding risks.¹²¹ Interestingly, a Cochrane review in 2012 demonstrated lower rates of restenosis and occlusion using LMWH (compared with aspirin alone) following endovascular revascularization for PAD, but only in patients whose indication was critical limb ischemia rather than intermittent claudication. The data informing these findings, however, are from low quality studies and therefore reduce the generalizability of

the recommendation for patients to receive anticoagulation in addition or in place of antiplatelet therapy following endovascular intervention.

The VOYAGER-PAD trial is a pivotal trial exploring the effects of low-dose rivaroxaban for patients with PAD who have undergone peripheral revascularization. Its design and conduct were informed by the similarly designed COMPASS trial, which focused on the use of low-dose rivaroxaban in PAD patients regardless of treatment status.¹²² Within this trial, over 6500 patients were randomized to receive either low-dose rivaroxaban (2.5 mg twice daily) plus aspirin (100 mg daily) versus aspirin alone. Eligible patients received their revascularization procedure within 10 days prior to randomization. Of an important note, clopidogrel could be administered at the clinician's discretion for up to 6 months after intervention. The majority (65%) of these patients were treated with an endovascular approach. The primary outcome was a composite cardiovascular endpoint that included acute limb ischemia, major amputation for vascular cause, myocardial infarction, ischemic stroke or death from cardiovascular cause. Patients on low-dose rivaroxaban were less likely to experience the primary outcome (17.3% vs. 19.9% aspirin alone; $P = 0.009$) as well as need for unplanned revascularization for recurrent ischemia (HR 0.88, CI 0.79–0.99; $P = 0.03$) over the subsequent 3 years after randomization. This benefit should be balanced with the 40% increased risk of ISTH major bleeding, though rates of fatal bleeding and intracranial hemorrhage were the same between groups. There was not a significant difference in outcomes based on type of intervention. Interestingly, the use of dual antiplatelet therapy in addition to low-dose rivaroxaban did not show any benefit compared to single antiplatelet therapy, but did have a higher incidence of bleeding. These data suggest that careful patient selection is necessary, and future efforts to identify which patients will experience benefit from combined antithrombotic and antiplatelet therapy are warranted.

Cilostazol Use After Endovascular Intervention

Three months of cilostazol has been shown to improve pain-free walking distance in patients with intermittent claudication with a relatively mild side effect profile.¹²³ There may be a benefit to cilostazol use in the post-intervention setting as

well for patients who have had endovascular lower extremity revascularization. A large Cochrane review demonstrated lower rates of restenosis and fewer re-occlusions in patients on cilostazol therapy after endovascular revascularization compared to those not taking it.¹¹⁹ Therefore, it is a reasonable strategy to consider initiating cilostazol after endovascular intervention, especially in patients with limited walking distance as the indication for their intervention.

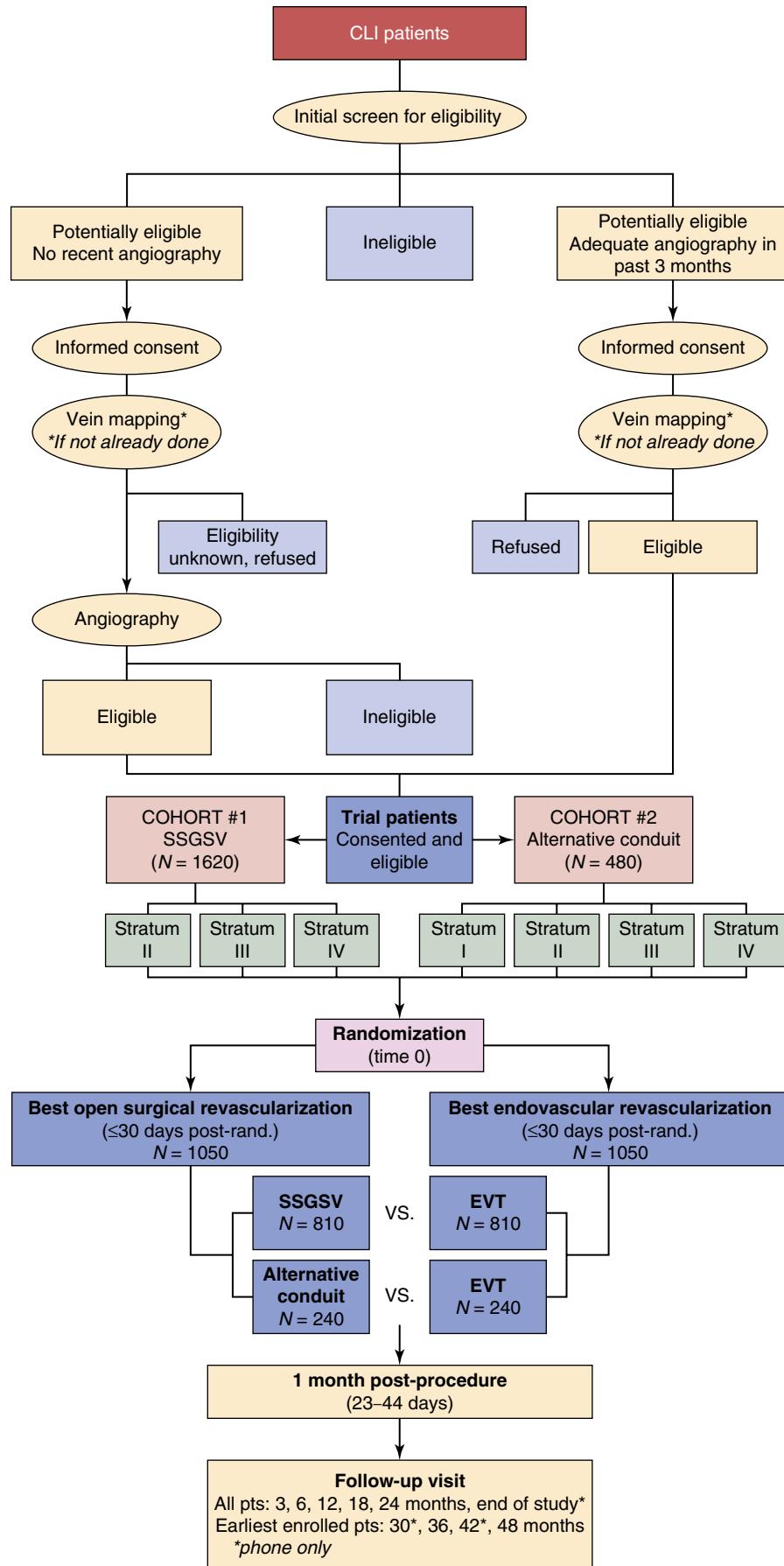
SURVEILLANCE AFTER ENDOVASCULAR INTERVENTION

Any patient with PAD should have routine follow-up scheduled for evaluation of disease progression, including reduction in walking distances, rest pain or wound development, and adherence to best medical practice. Following endovascular intervention, routine duplex sonography and physiologic testing can help to identify early in-stent restenosis and indicators of intervention failure. Troutman et al. reported a strategy of initial surveillance at 1 week, then 3 months for one year then every 6 months thereafter and were able to identify several factors that predicted stent failure, including peak systolic velocity greater than 300 cm/s, uniform peak systolic velocity less than 50 cm/s throughout the stent and ratio of adjacent velocities greater than 3.¹²⁴ The findings of low graft velocity and high velocity ratios have borne out to be the most significant indicators of graft stenosis.¹²⁵ Importantly, the absence of these findings is strongly predictive of stent patency. Further, a reduction in ankle-brachial index of more than 0.1 is often the first sign of intervention failure, even before symptoms re-develop.

CONCLUSIONS

Endovascular therapy for infrainguinal occlusive disease has and continues to evolve with improvement in technology and studies which evaluate the comparative effectiveness of each therapy, whether medical, endovascular and open surgical. There are many tools to treat infrainguinal occlusive disease, which allow the surgeon to tailor the approach based on each patient's needs, the physician skill sets, and available therapy.

CHAPTER ALGORITHM



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

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Lower Extremity Amputations: Epidemiology, Procedure Selection, and Rehabilitation Outcomes

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INTRODUCTION

Major lower extremity amputations continue to be part of all vascular practices despite the general approach of aggressive limb salvage. Although often viewed as a failure of treatment, a major amputation should be considered a reconstructive and definitive treatment option. The convergence of several important factors, including the increased life expectancy of the general population as well as the epidemics of diabetes and peripheral artery disease (PAD), suggest that amputations will remain an important issue facing patients and surgeons for the foreseeable future. The goal

of amputation is to remove all infected, gangrenous, or ischemic tissue and provide the patient with the longest functional limb. Avoidance of repeated amputations and uncomplicated healing of operative sites is crucial for the patient's optimal recovery and best functional rehabilitation or palliation.

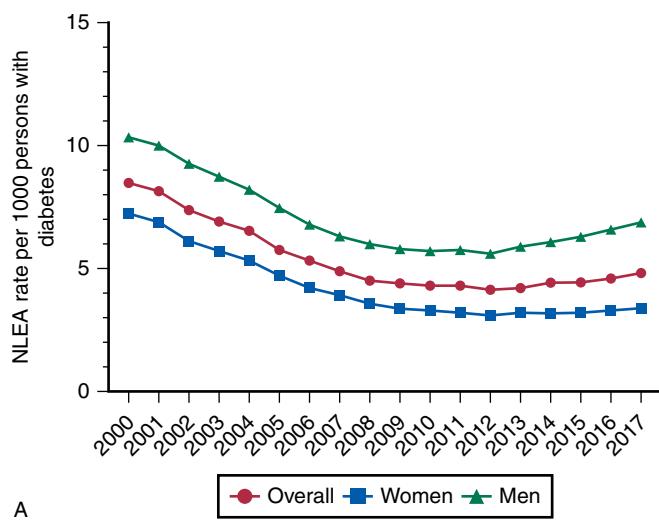
EPIDEMIOLOGY

In the United States, approximately 60,000 major amputations (amputations above the ankle) are performed annually.¹⁻³ Diabetes and PAD remain the major risk factors for lower

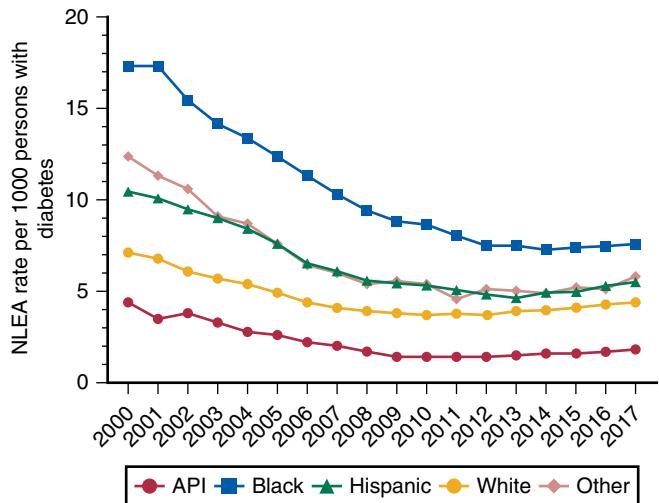
extremity amputation worldwide.⁴ Patients with diabetes have an eight-fold greater risk of amputation than those without diabetes.³ Studies show that 25% to 90% of all amputations are associated with diabetes.^{2,4} This association is due to the presence of neuropathy and infection, as well as the increased prevalence of PAD in patients with diabetes.

Despite the rising incidence of diabetes, current published data support an overall decrease in major amputation rates.^{5–7} A review of all Medicare claims from the Centers for Medicare and Medicaid Services between 1996 and 2006 showed a 29% decline in amputations.⁵ A report from the National Hospital Discharge Survey data on nontraumatic lower extremity major amputations (NLEA) and National Health Interview Survey data on diabetes prevalence showed the age-adjusted NLEA discharge rate per 1000 persons decreased from 11.2 in 1996 to 3.9 in 2008, while rates among persons without diabetes

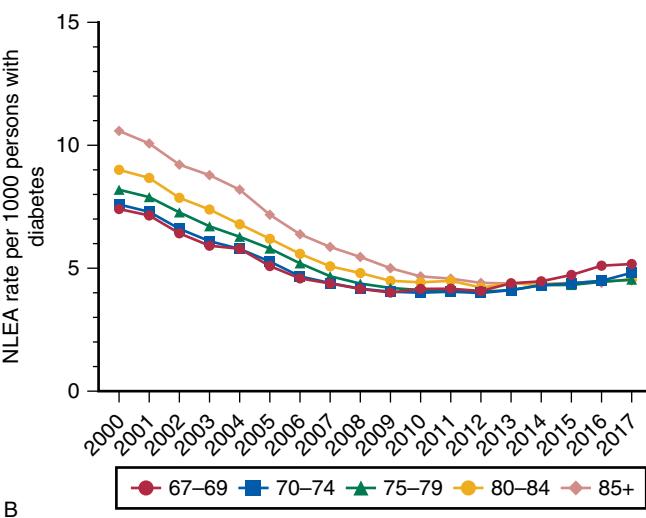
were unchanged.³ These trends were validated in a Scottish national cohort study from 2004 to 2008 where major amputations rates decreased by 40.7% from 1.87 per 1000 in 2004 to 1.11 per 1000 in 2008.⁷ This decrease in amputation rates initially plateaued around 2009 with nontraumatic lower extremity amputation occurring in 4.4 patients per 1000 people with DM, a decrease of nearly 50% compared to 2000.^{8,9} Since 2009, however, there has even been a slight increase in the rates of NLEA reported on a state and national level among diabetic Medicare patients up to 4.8 per 1000 patients.⁹ The most recent study, however, includes foot and toe amputations in their overall calculation of NLEA; looking at subgroups of patients undergoing isolated below-knee and above-knee amputations, these rates actually continue to be stable and even slightly improved when compared to rates in reported in 2009 (Fig. 114.1).



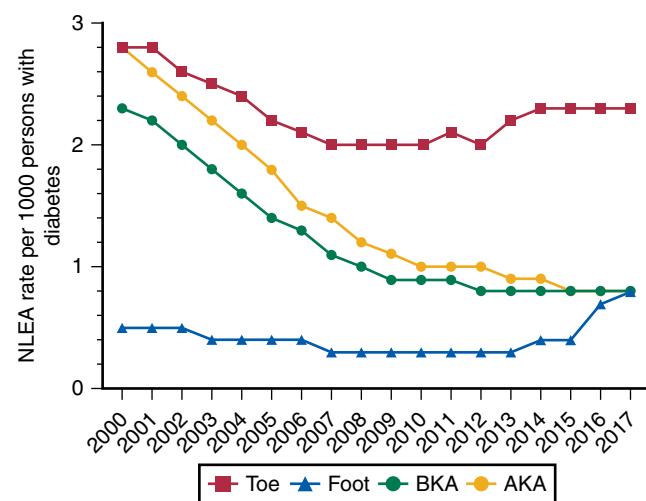
A



C



B



D

Figure 114.1 Trends in nontraumatic lower extremity amputations (NLEA) among US medicare beneficiaries with diabetes between 2000 and 2017 by sex (A), age group (B), race/ethnicity (C) and NLEA level (D). (Reprinted with permission from Harding, J, Andes, L, Rolka, D, et al. National and State level trends in nontraumatic lower extremity amputation among US Medicare beneficiaries with diabetes, 2000–2017. *Diabetes Care*. 2020;dc200586; <https://doi.org/10.2337/dc20-0586>.)

Variation in Amputation Rates

There is significant regional variation in the performance of amputation around the world, suggesting that factors other than medical issues may affect amputation rates.^{4–8,10,11} A United Kingdom study cited significant regional variation in amputation rates and stressed the need for consensus guidelines.¹⁰ The Global Lower Extremity Amputation Study Group reported that Navajo men undergo the highest amputation rate (first major amputation) at 44 per 100,000 population per year; the lowest rate was 2.8 per 100,000 per year in Madrid, Spain.⁴ Physician experience plays a key role in the selection of amputation as a treatment. In the treatment of critical limb ischemia, surgeon caseload and hospital volume have been shown to affect amputation rates, with low volumes being associated with higher amputation rates.¹²

A study of a Medicare claims database demonstrated that the supply of vascular specialists influences the rate of amputation. A 0.30 increase in the number of vascular surgeons per 10,000 Medicare beneficiaries was associated with a 1.6% reduction in amputations.¹³ The distribution of vascular surgeons and interventional radiologists in the United States is strongly correlated not only with regional medical needs but also with local climate, education, crime, and transportation. This observation suggests that policies to increase the supply of vascular specialists in underserved areas may reduce regional disparities in amputation rates.¹² Patient and healthcare provider education has also been demonstrated to reduce amputation rates.¹⁴ Earlier identification of patients at risk leads to timelier referral, and intervention.

Effects of Ethnicity, Economic, and Social Factors

A complex interaction exists between race, ethnicity and amputation rates. In certain groups, such as the Native American Navajo population, amputation rates appear to be related to the high incidence of diabetes.⁴ However, Blacks are more likely than Whites to undergo amputation as opposed to revascularization even when controlling for the presence of diabetes.^{15,16} These differences have been attributed to variations in access to healthcare, treatment of comorbidities, and possible physician and patient factors. Insurance status also has an effect on amputation rates. Patients without insurance coverage have higher rates of amputation than those with access to health insurance.¹⁷ Data from the National Inpatient Sample documented that 34% of the 691,833 patients presenting with lower extremity ischemia from 1998 to 2002 underwent amputation. The primary amputation rates were significantly higher among patients who were non-White, low income, and without commercial insurance.¹⁶ Similar results showed that Black patients were 1.7 times more likely to have both primary and repeat amputations compared to other patients.¹⁸ These findings have also been affected by the recent changes in access to healthcare put forward by the Affordable Care Act (ACA). The Healthcare Cost and Utilization Project State Inpatient Database concluded that admissions

for amputations across six states had increased since the enactment of the ACA, indicating enhanced access to medical care in those states.¹⁹ When Massachusetts adopted their expanded insurance coverage in 2006, there was an apparent decrease in preexisting disparities between Whites and non-Whites presenting with PAD.²⁰ Another promising example of improved outcomes with better access is demonstrated in Arkansas, where patients with private insurance had a lower rate of amputation compared to those without.²¹ Whether this can be replicated on a national scale remains to be seen, although more states are noted to have similar trends as recently reported for Alabama and Massachusetts.⁹

Effect of Revascularization Rates

The interplay between revascularization and amputation is complicated. Over a 10-year period the Mayo Clinic reported a 50% reduction in amputation rates that corresponded to increased rates of lower extremity revascularization by both surgical and endovascular (EV) techniques.²² A Finnish study also demonstrated that an increased revascularization rate correlated with a decrease in major amputation among elderly patients.²³ A U.S. study of two national (Nationwide Inpatient Sample and National Hospital Discharge Survey) and four state databases demonstrated that both the number of lower extremity revascularizations and the number of major amputations have declined; this has been accompanied by a substantial increase in lower extremity EV interventions. From 1998 to 2003 the volume of major amputations decreased 16% regionally (New York, California, New Jersey, and Florida) and 25% nationally.^{1,5} However, minor amputations increased 4% regionally and 3% nationally. It has been speculated that the improved limb salvage rates are partially explained by the increase in total revascularization procedures (driven by EV interventions due to the perceived decreased morbidity). Earlier EV interventions in less critical lesions and expanding EV procedures to the patient who is too high-risk for open surgery may contribute to the lower rates of major amputations. Additionally, failed EV procedures may not directly translate into amputations, since not all of these procedures are performed on people with extensive tissue loss or even advanced CLTI. Other possible factors contributing to lower rates of amputation include greater awareness of PAD, clear guidelines for the medical management of PAD risk factors, atherosclerosis, and improved wound care.

High-risk patients treated with EV interventions have superior rates of limb salvage and maintenance of ambulation compared to patients undergoing primary amputation. However, these patients have no better functional benefit than those treated with primary amputation after 1 year.²⁴ When autologous vein is available, the long-term results of the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial indicate that the outcomes of a bypass surgery–first approach is superior to a balloon angioplasty–first strategy in terms of amputation-free survival.²⁵ The ongoing debate over which patients benefit from EV interventions first over surgery first is the surmountable task undertaken by the Best Endovascular

versus Best Surgical Therapy in patients with Critical Limb Ischemia (BEST- CLI) trial investigators, the results of which are greatly anticipated.

The ideal balance of EV and open surgical reconstructions has yet to be determined for lower extremity ischemia. Nationwide Inpatient Sample data suggest that lower extremity revascularizations have reached a plateau of approximately 140,000; similarly, major amputation may have settled near 60,000 annually.^{1,2} The Trans-Atlantic Inter-Society Consensus (TASC) II Working Group documented that the incidence of major amputations varies from 12 to 50 per 100,000 population per year.²⁶ The total number of revascularizations, in particular endovascular procedures, may be underestimated because same-day EV procedures (not hospitalized), as well as procedures performed in outpatient-based laboratories (OBL) are not being captured in the Nationwide Inpatient Sample database.² This has multiple effects, primarily limiting the capture of these procedures in national databases, as well as limiting the ability to track their outcomes. This trend potentially skews our overall numbers when it comes to procedures performed, immediate technical results, effect of patient ambulation as well as longevity of procedures performed. With an increasingly aging population and their physiologic limitations, our ability to perform traditional open revascularization is limited yet endovascular approaches seem feasible even in the most frail patients and may greatly confound the rates of amputation after revascularization attempts.

INDICATIONS FOR AMPUTATION

Indications for amputation have traditionally been divided into acute ischemia, chronic ischemia, foot infection, severe traumatic injury, and lower extremity skeletal or soft tissue malignancies. Trauma and malignancy are beyond the scope of this chapter and are not discussed. In the presence of acute ischemia, major amputation is undertaken for irreversible ischemia, for severe ischemia with no revascularization options, or following unsuccessful attempts at revascularization. Amputation for chronic ischemia may be performed owing to failure of revascularization, lack of suitable conduit or target arteries, severe patient comorbidities, poor functional status, or extensive gangrene or infection such that foot salvage is not possible. Pedal sepsis without ischemia constitutes another major subgroup of patients undergoing amputation; this presentation is extremely common in patients with diabetes and associated neuropathy. The underlying indications for amputation frequently overlap, making it difficult to evaluate outcomes based on the indications as reported in literature.

Malone reported the indications for amputation as follows: complications of diabetes (60%–80%), infection without diabetes (15%–25%), ischemia without infection (5%–10%), chronic osteomyelitis (3%–5%), trauma (2%–5%), and miscellaneous (5%–10%).²⁷ These classifications have a certain degree of overlap and mask the interaction between ischemia and diabetes. This simplistic breakdown does not provide clear

insight into the true influence of ischemia or the full potential of revascularization to reduce amputation rates. In addition, because no revascularization is universally successful, amputation may ultimately follow revascularization.

Impact of Diabetes

The presence of diabetes, either alone or in combination with PAD, contributes to the majority of major nontraumatic lower extremity amputations. The overall incidence of diabetes in patients undergoing amputation is reported as approximately 60% (ranges from 25%–90%).^{2–4,9} This information is based on hospital discharge diagnoses and thus may not be all encompassing and completely accurate; however, it is perhaps the most inclusive data we have. Although many general classifications overemphasize the role of diabetes and underestimate the role of concomitant ischemia, it is clear that diabetes alone confers a higher risk (as high as an eight-fold increase) of amputation.³

Impact of Tissue Loss and Anatomy

Attempts have been made to categorize the indications for major amputation to explain why amputations continue to be performed despite aggressive revascularization programs.²⁸ When identifying the indications for amputation, it must be recognized that with chronic ischemia, limb loss may ultimately occur despite revascularization. In addition, the index presentation may be someone with an acutely or chronically ischemic limb that is beyond any hope of salvage. The influence of gangrene and pedal sepsis must also be considered because they have a significant impact on the options for limb salvage. Lastly, patient comorbidities and ambulatory status influence the decision for amputation.

The TASC II Working Group reported that the rate of primary amputation in chronic critical leg ischemia is approximately 25%. Non-reconstructable vascular disease is the most common indication for secondary amputations, which accounts for nearly 60% of patients.²³ In an article further assessing the indications for amputation, a series of 131 consecutive major lower extremity amputations were reviewed and the indications for amputation were classified (Table 114.1).²⁷ In this academic vascular setting, more than 50% of patients who underwent amputation did so following a prior attempt at limb salvage via revascularization or had no anatomically feasible revascularization options. This group of patients had exhausted the armamentarium of the vascular surgeon. Seventeen percent of patients were not considered candidates for aggressive attempts at limb salvage owing to preexisting medical issues including nonambulatory status (8%), or having excessive surgical risk (9%). In addition, 32% of patients had nonsalvageable limbs at presentation due to extensive pedal gangrene, pedal sepsis, or a nonviable foot that mandated primary amputation.

Similar findings were reported in another series of 172 major amputations.²⁹ The indication for amputation was critical ischemia in 87%, and complications of diabetic neuropathy without

TABLE 114.1

Indications for Major Amputation by Vascular Surgeons

Indication for Major Amputation	Percentage of Cases (n = 131)
Critical limb ischemia with failed revascularization	39
Extensive pedal gangrene	15
Unreconstructable arterial anatomy	11
Overwhelming pedal sepsis	9
Excessive surgical risk	9
Nonviable, acutely ischemic foot	8
Nonambulatory status	8

From Abou-Zamzam AM, Jr, Teruya TH, Killeen JD, Ballard JL. Major lower extremity amputation in an academic vascular center. *Ann Vasc Surg.* 2003;17:86–90.

significant ischemia in 13%. Forty-six patients (30%) had prior bypass failures or amputations despite patent reconstructions, and 10 (6%) had no revascularization options; therefore, 36% had exhausted the resources of revascularization. Eighty-five patients (55%) underwent primary amputation because of severe comorbidities, poor functional status, extensive necrosis, or a combination of these factors. Together the previous studies highlight the central role of both ischemia and tissue loss in the determination of the need for major amputation.

The Society for Vascular Surgery's Wound, Ischemia and foot Infection (WFII) classification system helps define the factors influencing limb salvage.³⁰ This system includes the grading of key elements of the wound (W), degree of ischemia (I), and severity of foot infection (fI). The composite WFII stage then gives greater detail regarding the risk of amputation and benefit of revascularization. Early validation studies demonstrated that worsening WFII stages are associated with major amputation in patients undergoing revascularization for chronic limb-threatening ischemia (CLTI).³¹ However, among patients with diabetic foot ulcers, while the WFII score predicted wound healing, it was not predictive of amputation in patients without peripheral arterial disease.³²

Impact of Delay in Presentation

The significant role that delay in patient presentation plays in limb salvage cannot be overstated. The mean time to vascular surgery consultation was 73 days for pedal tissue loss and 27 days for ischemic rest pain in the report by Nehler and colleagues.²⁹ This delay likely accounts for the large percentage of primary amputations in their series and underscores the need for patient and referring physician education. In a report by Bailey and coworkers, only 24% of patients with critical limb ischemia were perceived as needing “urgent” vascular consultation, with a mean 8-week duration of symptoms before vascular evaluation.³³ This suggests that delayed patient presentation involves patient factors, referring physician issues, as well as issues with access to specialist care.

PRIMARY AMPUTATION VERSUS REVASCULARIZATION

The most important decision in treating CLTI is the initial determination of whether to attempt limb salvage or proceed with primary major amputation. Despite widespread discussion of great triumphs in revascularization, there is a growing awareness that primary amputation may be the best approach in specific patient subsets. As stated earlier, more than 140,000 lower extremity revascularizations are performed annually in the United States. In recent years, open revascularizations have been partially replaced by EV procedures, yet nearly 60,000 major amputations are still being performed each year.^{1,2} This implies that the ratio of amputation to revascularization may be close to 1:2 nationally. Many specialty centers may have a much lower ratio, owing to the filtering effect of referring physicians. Many patients perceived as not being candidates for revascularization are treated locally with amputation and are never referred to these high-volume centers specializing in revascularization.

The ratio of major primary amputation to revascularization differs among facilities and may vary because of surgeon experience and practice protocols. One prospective study demonstrated that 43% of the 224 patients presenting with limb-threatening ischemia were treated by primary amputation, and 57% were treated with revascularization.³⁴ Diabetes mellitus, end-stage renal disease, tissue loss, and poor functional status were all predictors of treatment with amputation as opposed to revascularization.

Groups Benefiting from Primary Amputation

A reasoned approach to patients presenting with CLTI is necessary. A thoughtful strategy considering the patient's comorbidities, the status of the foot, and the complexity of the required revascularization has been outlined by Nehler and colleagues.³⁵ In a good-risk patient with minimal pedal tissue loss, an aggressive attempt at revascularization should be undertaken with appropriate EV or open bypass techniques including the consideration of alternative vein conduits. However, when the patient's overall health status is poor or the foot lesions are extensive, primary amputation must be considered. Additionally, patients presenting with poor baseline functional status, extreme frailty or overall poor physiologic state should be considered for primary amputation. An aggressive use of revascularization, particularly EV interventions, likely has resulted in limb salvage attempts in higher-risk patients which may have contributed to the reduction of overall major amputations.^{1,2} Despite this, secondary amputations are not an uncommon occurrence. In a study of 358 patients (412 limbs), patients with limb loss despite patent EV interventions were compared with the rest of the EV-treated group and with those who underwent amputations with patent bypasses (APBs). Amputations occurring despite a patent, revascularized segment constituted 38% of limb loss in open and 80% in EV-treated patients ($P = 0.001$).³⁶ Most amputations in the EV group were performed within 3 months and the indications were extensive tissue loss

or limb dysfunction after radical debridement of infection or gangrene (37%), recurrent infection (42%), and failure to reverse ischemia (21%).³⁴

The perceived improved outcomes following revascularization compared with amputation have driven the belief that revascularization is always the better option. However, an examination of the data demonstrates that functional outcomes following amputation may not be markedly different from those following revascularization for specific patient subgroups. Taylor and associates analyzed 553 patients who underwent 627 primary major limb amputations.³⁷ In patients younger than 60 years, functional outcomes following BKA were similar to those of patients undergoing successful revascularization. Such information lends credence to the observation that primary amputation should be considered not a failure of therapy but a valuable, and often rehabilitative treatment option.^{28,33,35}

The advances in percutaneous revascularization have raised the question of how best to treat the patient considered “unfit” for open revascularization. Taylor and colleagues reported an analysis of 314 patients treated for critical limb ischemia who were unsuitable for open revascularization owing to medical, functional, or mental comorbidities.²³ Patients were treated with either percutaneous transluminal angioplasty (PTA) or major amputation. The 131 patients treated with PTA had higher rates of maintenance of ambulation and independent living compared with the 183 patients treated with amputation. However, the PTA group had a higher mortality rate, and the advantages in ambulation and independent living lasted only 12 months and 3 months, respectively. In the “unfit” patient, EV treatment may indeed be no better than primary amputation.

In patients with extensive foot lesions, severe comorbidities, or unfavorable anatomy, primary amputation is often the best treatment option.^{28,33,35} In addition to unfit physiology and anatomy, the patient frailty (overall functional status measured by a variety of methods) should be immediately considered prior to deciding on a course of treatment. Because of delayed referral, many patients ultimately undergoing amputation present to the vascular surgeon with extensive pedal necrosis, making limb salvage unlikely, regardless of arterial targets for revascularization. End-stage renal disease presents a particularly difficult challenge, and the presence of advanced heel gangrene in this group of patients may also best be treated with primary amputation.^{38,39}

PERIOPERATIVE EVALUATION

Although surgeons have traditionally focused on the preoperative evaluation and near-term (usually 30-day) results of amputations, a lengthier view of the perioperative period can be helpful. For the patient, the overall experience is important and clearly lasts longer than the 30-day postoperative period. A more global view of the patient during the first year may help to identify key issues at different points in the patient’s treatment and recovery. A team approach to the patient is useful during all stages of the perioperative period because the results in any series of amputations are directly related to the skill and enthusiasm of the people involved in the program.⁴⁰ Members of the team include

the patient, family, surgeon, physiatrist, therapist, rehabilitation medicine specialist, prosthetist, nurse, social worker, psychologist, peer support group, and case manager. The common goal should be maximum recovery and rehabilitation after limb loss. The team should be flexible because different team members share the leadership and service responsibilities throughout the 12- to 18-month time frame that typically defines the perioperative period following a major amputation.

Perioperative Stages

The postoperative continuum does not separate easily into “stages.” However, for practical purposes, five stages in the treatment of the amputation patient have been described.⁴¹

Stage 1: The *preoperative stage*, starting with the challenging decision to amputate. This stage includes an assessment of the vascular status, as well as the candidacy of the patient for revascularization. The preoperative evaluation of a patient undergoing major amputation should strive to reduce perioperative complications and mortality, and should be rational and expeditious. Evaluation should include the duration and severity of limb ischemia, extent of tissue loss, presence of wound infection, and anatomic considerations of revascularization. An analysis of the patient’s systemic comorbidities is essential and should be performed systematically. The surgeon typically is the team leader during this stage.

Stage 2: The *acute hospital postoperative stage* begins immediately after the surgery and spans the hospital length of stay. This stage ranges from 3–10 days, and during this time the patient transitions to the appropriate rehabilitation facility. The surgeon is still involved and ensures appropriate postoperative care is delivered, as well as leads the treatment for any local and systemic complications.

Stage 3: The *immediate post-acute hospital stage* begins with hospital discharge and extends 4 to 8 weeks after surgery. This is the time of recovery from surgery, a time of wound healing, and a time of early rehabilitation. During this phase the surgeon is minimally involved, however must ensure wound healing is appropriate as it is essential to rehabilitation.

Stage 4: The *intermediate recovery period* is the time of transition from a postoperative strategy to a functional one, during which the patient is fitted with the first formal prosthetic device. It is during this stage that the most rapid changes in limb volume occur, due to the beginning of ambulation and prosthetic use. This stage begins with the completed healing of the wound and usually extends 4 to 6 months from the healing date.

Stage 5: The *transition to stable stage* is defined as a period of relative limb stabilization, although the limb will continue to change to some degree for a period of 12 to 18 months after initial healing. The newer prosthesis will still require occasional adjustments, and visits to the prosthetist will remain relatively frequent until after the first year of prosthetic use. In this phase the patient should move toward social reintegration and higher functional training. The patient should become more empowered and independent from his or her healthcare practitioner during this period.

*Cx total - 34%
Cx local - 10%. MR ← BIC - 8%.
AR - 16%.*

Reducing Perioperative Risk

The quoted overall mortality for major amputations is approximately 8%. Most reports double the mortality when comparing AKAs to BKAs.⁴² A study of 2911 patients enrolled in the ACS National Surgical Quality Improvement Program (NSQIP) demonstrated a 30-day mortality of 7% for BKAs. Multivariate analysis identified renal insufficiency, cardiac issues, preoperative sepsis, COPD, steroid use, and increased patient age as predictors of mortality.⁴³ The same study identified preoperative sepsis, regular alcohol use, steroid use, cardiac issues, renal disease, and contaminated/infected wounds to be independent predictors of developing postoperative complications. The overall perioperative complication rate was 34.4%. Local stump complications occurred in nearly 10% of patients. Of note, the incidence of cardiopulmonary, venous thromboembolic, and cerebrovascular events ranged from 0.5% to 2.1%. The low observed incidence is probably due to the current widespread use of beta blockers, statin therapy, and antithrombotic medications in the vascular patient.^{44,45} A similar study of 8696 veterans who underwent major amputations showed that patients undergoing AKA were older (69.0 vs. 66.5) and suffered a higher mortality (16.5% vs. 9.7%) when compared to BKA patients, whereas both groups had a similar rate of postoperative complications.¹⁰ This study found that increased age, increased patient complexity, and admission with acute thromboembolism were predictive of death.¹⁰

Perioperative treatment with antiplatelet agents, statin medications, and beta blockade has been extensively studied in the general vascular surgery population, but many of these important studies included few patients undergoing major amputation.^{42,43} Although the data suggest a limited role for initiating beta blockade in naive patients, there does continue to be support for use of antiplatelet and statin medications in the patient population presenting for amputation.^{43,46} With regard to the need for preoperative "cardiac clearance," the guidelines by the American College of Cardiology and the American Heart Association denote that the purpose of preoperative cardiac evaluation is not to give medical clearance but rather to evaluate the patient's current medical status and cardiac risks over the entire perioperative period.⁴³ These guidelines recommend that no test be performed unless it is likely to influence the patient's treatment.^{4,12}

The management of associated hypertension, diabetes, and renal failure should be optimized. Antiplatelet and statin medications can be safely continued throughout the hospitalization. The timing of hemodialysis in relation to operation is important in managing fluids and electrolytes in the perioperative period. An aggressive approach to normalize glucose levels is essential to ensure proper wound healing. VTE prophylaxis with either subcutaneous unfractionated heparin or low-molecular-weight heparin appears to be safe and effective.⁴⁷ The importance of thrombo-prophylaxis is reflected in the fact that up to 17% of all amputation-related deaths are caused by pulmonary emboli.⁴¹ Noteworthy is the propensity of these patients to suffer falls, thus fall precautions should be instituted during the early postoperative period.

Managing Infection

Special consideration should be given to patients presenting with extensive pedal infection necessitating amputation. Aggressive control of infection, with surgical extirpation of the source and adjunctive intravenous antibiotics, is the mainstay of treatment. The two-stage approach of guillotine amputation followed by formal amputation at a later time has a lower complication rate than single-stage amputation.⁴⁸ Guillotine amputation is a rapid procedure, but an additional operation to treat the amputation stump is necessary. Another option in patients who are moribund is a physiologic cryoamputation, which can be performed safely at the bedside.^{49,50} The materials needed to perform cryoamputation are dry ice, a large plastic bag, an umbilical tape or elastic tape for use as a tourniquet, towels, blankets, adhesive tape, a Styrofoam container large enough to accommodate the limb, and a heating pad. Preparation includes crushing enough ice to cover the limb, and cutting out a hole on the side of the Styrofoam box large enough to allow passage of the limb into the box yet snug enough to prevent the "frost line" from ascending. After parenteral analgesics are administered, an umbilical tape is tied around the affected extremity just proximal to the diseased area and a large plastic bag is placed over the affected leg. A heating pad covered with a protective towel is placed around the extremity adjacent to the frost line. The leg is then placed in the Styrofoam container and covered circumferentially with dry ice. The dry ice bag is wrapped with blankets and secured with adhesive tape. The contralateral leg should be covered with numerous blankets to avoid collateral injury. The frost line and the frozen limb should be checked periodically by the staff, and dry ice added as needed. This bedside procedure alleviates any time pressures for amputation, controls infection, and allows optimal treatment of associated conditions. If necessary, a cryoamputation can be maintained for several weeks. When the patient's physiologic status improves, they may be taken to the operating room for a one-stage amputation.

Planning Rehabilitation

Whenever possible, an evaluation of rehabilitation and prosthetic candidacy should be performed prior to proceeding with amputation. Centers with dedicated multidisciplinary teams have much more successful rehabilitation outcomes.⁵¹ Addressing key elements of infection, glycemic control, vascular disease, and local wound issues in a coordinated manner with a multidisciplinary team has even been shown to reduce major amputations.⁵² Understanding the various stages of the perioperative period and adjusting the areas of focus throughout the recovery period may optimize the outcomes. Tempering the patient's expectations, the timing of prosthetic use, and reinforcing the ultimate functional goals is best undertaken by the team members throughout the perioperative period.

SELECTING AMPUTATION LEVEL

The goals of amputation are: (1) to eliminate all infected, necrotic, and painful tissue; (2) to achieve uncomplicated wound healing; and (3) to have an appropriate remnant stump that

BIC → 10–40%. ↑ energy use

AIC → 50–70%.

can accommodate a functional prosthesis. The length of the preserved limb has important implications for rehabilitation. Prosthetic use following major amputation puts an increased energy demand on the patient. Unilateral below-knee amputees require a 10% to 40% increase in energy expenditure for ambulation, and above-knee amputees require 50% to 70% more energy to ambulate.²⁶ This differential may explain why the successful rehabilitation rate is much lower following AKA than BKA. Prosthetic use is reportedly 50% to 100% following BKA but only 10% to 30% following AKA.^{28,49,53,54} Interestingly, the true rate of ambulation is significantly lower than that of prosthetic use and shows a steady attrition in the 5 years following amputation.^{28,51,52} Partial foot or toe amputations are minor procedures that preserve the majority of the extremity and allow ambulation without the need for bulky prostheses. Most minor amputations, including toe and ray amputations, lead to minimal increases in energy expenditure and require simple orthotic inserts.

Failure of an amputation to heal is multifactorial. Much emphasis has been placed on assessing blood flow at the level of the amputation to predict wound healing. However, failure may be caused not just by ischemia but also by infection, hematoma, or trauma related to falls. This explains why no single test can predict with 100% accuracy the ability of an amputation to heal or, conversely, its inability to heal. Most tests are better at predicting wound healing than failure to heal. Thus using any single criterion may lead to unnecessarily proximal amputation. The importance of optimizing level selection is underlined by the need to revise BKAs to AKAs in 15% to 25% of patients.^{2,27,28,55} This revision rate is frequently accompanied by a perioperative mortality rate of greater than 5%.²⁶ Such events also lead to increased patient anxiety, depression or fear of repeated, more proximal amputations. A recent Portuguese survey study looked at the individual contributions of anxiety and depression on outcomes of amputations; the authors note that while depression alone is not associated with mortality or reamputation, anxiety is negatively associated with healing and recommend early psychosocial interventions.⁵⁶

Objective Testing and Clinical Judgment

The drive to maximize limb length in amputees and to minimize the need for revisions has led to a search for the optimal modality for selecting an amputation level. Physical findings (pulses, skin quality, extent of foot ischemia or infection, skin temperature), noninvasive hemodynamic tests (segmental arterial pressures, Doppler waveforms, toe pressures), invasive anatomic tests (angiographic scoring systems), and physiologic tests (skin blood flow, skin perfusion pressure, muscle perfusion, transcutaneous oxygen measurements) have all been extensively investigated.

Physical Findings

Physical examination is the essential first step in determining the level of amputation. The extent of gangrene and infection dictates the maximal attainable residual limb length. In this evaluation the presence of dependent rubor should be

considered analogous to gangrene because this tissue is ischemic. The presence of pulses should be accurately assessed. The presence of a palpable pulse immediately proximal to a proposed amputation level predicts successful healing in nearly 100% of patients undergoing either major or minor amputation.^{57,58} However, the absence of a pulse does not necessarily lead to failure of wound healing; therefore, sole reliance on the presence of a pulse leads to unnecessarily proximal amputations. Using “clinical judgment,” which incorporates physical findings and consideration of the patient’s overall status, yields wound healing rates of 80% in BKAs and 90% in AKAs. Wagner and colleagues found that objective data may supplement clinical judgment but not replace it; more distal amputations were achieved with clinical judgment than with sole reliance on objective examinations.⁵⁹ Experience is important in the determination of amputation level; therefore, this should not be relegated to junior surgeons or trainees.

Skin Temperature Measurements

The subjective interpretation of skin temperature as a guide for amputation is not reliable. However, several investigators have demonstrated that objective, direct skin temperature measurement may predict amputation healing with an accuracy of 80% to 90%.^{56,60} In a study comparing several noninvasive techniques, direct skin temperature measurement at the level of amputation with a threshold of 90°F demonstrated the best accuracy.⁵⁶ Special attention must be paid to room temperature, and comparison with a normal contralateral extremity can be helpful.

32.2°C

Ankle and Toe Pressure Measurements

The use of noninvasive hemodynamic tests has been extensively evaluated. Frequently used tests include segmental arterial pressures, Doppler waveforms, and toe pressures. Absolute ankle pressures greater than 60 mm Hg can predict the healing of BKAs with an accuracy of 50% to 90%. Calf pressures and thigh pressures have shown similar reliability.² However, Doppler-derived pressures at the thigh, popliteal, calf, and ankle levels are less reliable than clinical judgment in predicting the healing of BKAs.⁵⁶ This inaccuracy may be due in part to the high prevalence of diabetes in this population, making measured pressures less reliable because of arterial medial calcinosis.

The ankle-brachial index (ABI) should always be obtained, regardless of the presence of a palpable pulse. Marston and colleagues reported on the role of ABI in predicting the need for amputation in a cohort of high-risk patients with critical limb ischemia treated with meticulous wound care but without revascularization. In patients with an ABI less than 0.5, 28% and 34% of limbs required amputation at 6 and 12 months, respectively, versus 10% and 15% in those with an ABI greater than 0.5 ($P = 0.01$).⁶¹

The use of toe pressures has also been widely advocated as being predictive of forefoot healing. Vitti and associates demonstrated universal failure of minor amputations in diabetic patients with toe pressures less than 38 mm Hg.⁶² However, there was no similar threshold in patients without diabetes, limiting the generalization of this parameter.

Arteriography

Invasive testing with arteriography has been investigated as a means of determining amputation level, but the correlation between arteriographic findings and healing potential has been poor. Dwarts and coworkers found that angiographic scores did not correlate with amputation healing.⁵⁸ In fact, in their report, angiographic patency tended to be greater in limbs with failed or delayed healing than in limbs with successful healing.

Radioisotope Scans, Scintigraphy, and Skin Perfusion Pressure

Physiologic tests attempt to predict wound healing based on tissue perfusion or oxygen delivery at the proposed level of amputation. One technique of measuring skin blood flow involves injecting an *intradermal isotope* (xenon 133 or iodine 125) and then calculating blood flow by measuring the isotope washout rate using nuclear medicine scanning devices.^{26,63} Malone and associates initially reported excellent results with xenon 133 clearance, with an accuracy of 92% to 97%.⁶⁴ However, in a follow-up report, this same group found that the overlap in values between patients with healed and failed amputations made this test too unreliable.⁶⁵

(2) Sarikaya and coworkers used technetium (^{99m}Tc) ^{99m}sestamibi scintigraphy to predict the healing of extremity amputation based on deep tissue perfusion.⁶⁵ Perfusion to the ischemic limb was evaluated preoperatively based on the ^{99m}Tc ^{99m}sestamibi uptake pattern. Nonviable tissue in the extremity was suggested by a clear-cut edge of perfused muscle. The most distal level of amputation was determined above the nonviable tissue. In their cohort of 25 patients the proposed level of amputation, initially based on physical examination and Doppler study, was revised to a lower level after ^{99m}Tc ^{99m}sestamibi scintigraphy results in 65% of cases. The group reported 100% healing rate in the scintigraphy-directed amputations.

(3) **Skin perfusion pressure (SPP)** is another physiologic test to determine amputation level. This test involves a scintigraphy technique in which *intra-cutaneous iodine 123* is injected at different amputation levels. External pressure is applied, and by measuring the washout of isotope, the skin perfusion pressure is determined. A level less than 20 mm Hg was predictive of wound failure in 89% of amputations, and a reading greater than 20 mm Hg predicted healing in 99%.⁵⁵ Skin perfusion pressure can also be measured by laser Doppler velocimetry, thus avoiding the need for injection of isotopes and markedly simplifying the technical aspects of the test.

(4) **Skin fluorescence** uses a Wood or ultraviolet light following the intravenous injection of fluorescein dye. A qualitative determination of regional blood flow is used to determine the level of amputation. Success rates in predicting healing have ranged from 86% to 100%.²⁷ Owing to the wide availability of these tools and no requirement for radioisotope, this technique is more accessible than scintigraphy techniques. However, the fluorescein technique may be more affected by the presence of inflammation and cellulitis than are scintigraphy techniques.

Transcutaneous Oxygen Measurements

Transcutaneous oxygen measurement is a completely noninvasive method that may be used to select an amputation level. A small sensor is placed on the skin in the area of interest. By heating the sensor and skin to 44°C, local skin hyperemia results in decreased flow resistance and arterialization of capillary blood. The partial pressure of oxygen measured transcutaneously (tcPo₂) approximates the true arterial oxygen pressure in the area of interest.⁶⁶ The sensors can be placed anywhere on the body, and readings are given in millimeters of mercury (mm Hg). Absolute readings can be recorded, or readings in areas of interest can be indexed to a reference site (often the chest). The probes are small andatraumatic, and multiple sites can be tested simultaneously, depending on the machine. Readings in the supine position are more predictive than measurements in the dependent position or during supplemental oxygen breathing.⁶⁷ The values recorded are reliable and show an acceptable day-to-day variability in repeat measurements.⁶⁸ Transcutaneous oxygen levels have an accuracy of 87% to 100% in predicting wound healing.^{54,60,69} Malone and coworkers reported no amputation failures in patients with tcPo₂ greater than 20 mm Hg and universal failure when tcPo₂ was less than 20 mm Hg.⁶³ Unfortunately, other investigators have not confirmed any consistent absolute tcPo₂ threshold.^{54,56} Some authors have reported a useful tcPo₂ threshold of 30 mm Hg, whereas others have reported 16 mm Hg as a cutoff value. In general, tcPo₂ readings greater than 40 mm Hg are consistently associated with healing and readings less than 20 mm Hg are associated with failure.^{63,66} The lack of a consistent minimal level is likely due to the fact that nutrient blood flow may be present even in the setting of tcPo₂ readings of 0 mm Hg. The tcPo₂ may be artificially low in the setting of infection, inflammation, or edema, and repeat measurements are advised once such processes have resolved. Incidentally, in addition to modest utility in predicting wound healing, tcPo₂ has accuracy in predicting outcome following revascularization. Increases in tcPo₂ of greater than 30 mm Hg following revascularization are predictive of a successful clinical outcome.⁶⁶

In direct comparisons with segmental pressures and skin blood flow, tcPo₂ has been the most accurate predictor of wound healing.⁶³ This applies not only to major amputation but also to forefoot amputation.^{66,70} Transcutaneous oxygen measurements are also more accurate than fluorescein dye injections.⁶³ In addition, tcPo₂ has several advantages over other tests in terms of ease of measurement, noninvasiveness, reproducibility, and simple instrumentation that can be readily introduced into any vascular laboratory.

Yamada and colleagues studied 211 patients with 403 ischemic limbs using skin perfusion pressure, toe pressure, ankle pressure, and tcPo₂.⁷¹ The correlations between these methods demonstrate that the combination of skin perfusion pressure and toe pressure can accurately predict wound healing. However, the combination of skin perfusion pressure and tcPo₂ did not result in a more accurate prediction. A meaningful approach to the accurate determination of amputation level should therefore include a combination of physical findings, clinical judgment, and objective testing.^{54–56,60,63}

TABLE 114.2 Prediction of Wound Healing by Noninvasive Vascular Studies

Study	Threshold (mm Hg)	WOUND HEALING (%)		Sensitivity (%)	Specificity (%)
		Below Threshold	Above Threshold		
SPP	40	10	69	72	88
tcPo ₂	30	14	63	60	87
TSP	30	12	67	63	90
ABP	80	11	45	74	70

ABP, ankle blood pressure; SPP, skin perfusion pressure; TSP, toe systolic pressure; tcPo₂, transcutaneous oxygen pressure.

From Yamada T, Ohta T, Ishibashi H, et al. Clinical reliability and utility of skin perfusion pressure measurement in ischemic limbs—comparison with other noninvasive diagnostic methods. *J Vasc Surg*. 2008;47:318.

Technique Selection

Whether skin temperature, skin blood flow or perfusion, or transcutaneous oxygen measurements are used depends on local experience and availability. Measurement of tcPo₂ is easily incorporated into a noninvasive vascular laboratory, requires minimal equipment and training, and is reliable and reproducible. For these reasons, our preferred objective test is tcPo₂, with a threshold value of 30 mm Hg. However, strict utilization of a single objective method, rather than taking all available clinical data into account, leads to unnecessarily proximal amputations and denies patients the best opportunity for successful rehabilitation. The various methods of predicting wound healing and their accuracies are shown in Table 114.2.⁶⁸

REHABILITATION CONSIDERATIONS

In the United States there are approximately 1.6 million people living with limb loss. Vascular disease accounts for the majority (82%) of limb loss hospital discharges. It is projected that the number of people living with the loss of a limb will more than double by the year 2050 to 3.6 million.^{41,72} Rehabilitation is crucial to maximize the functional outcome of these patients. The significant physical and psychological changes following major amputation make rehabilitation a complex process. Integrated rehabilitation requires an interdisciplinary team that incorporates members from surgery, internal and family medicine, psychiatry, physical therapy, occupational therapy, prosthetics, social services, nursing, nutrition, and recreational therapy.

As mentioned earlier in this chapter, greater energy expenditure is required for ambulation in patients with higher levels of amputation. Energy expenditure and ambulatory rates at various amputation levels are shown in Table 114.3.⁷³ Many studies have shown that BKA patients have a significantly greater chance to achieve ambulation than AKA patients. In general, the goal is the preservation of maximal limb length at which a healed stump wound can be achieved. Preoperative evaluation and amputation level selection should always include postoperative rehabilitation considerations. Preoperative ambulatory ability, comorbidities, age, and mental status affect rehabilitation potential. Patients with limited preoperative ambulatory function, age older than 70 years, dementia,

TABLE 114.3

Energy Expenditure and Ambulation Rate at Various Amputation Levels

Amputation Level	Energy Expenditure Above Normal (%)	Ambulation Rate (%)
Below-knee amputation		80
Long stump	10	
Short stump	40	
Knee disarticulation	71.5	31 (prosthetic fitting rate)
Above-knee amputation	63	38–50
Hip disarticulation	82	0–10 (vascular patients)

From Tang PCY, Ravji K, Key JJ, et al. Let them walk! Current prosthesis options for leg and foot amputees. *J Am Coll Surg*. 2008;206:548.

end-stage renal disease, and advanced coronary artery disease perform poorly following amputation.³⁵

A comprehensive treatment plan should be developed at the beginning of rehabilitation and updated frequently based on the patient's condition. A dedicated team approach clearly improves the ultimate outcome for amputees.^{39,67} One report documented that successful rehabilitation following major amputation increased from 69% before the institution of a co-ordinated team approach to 100% after the development of such a team.⁴⁹ Medical assessment and treatment should be targeted to optimize the patient's overall condition. Addressing comorbidities increases the patient's ability to participate in the rehabilitation process. Pain management is essential to ensure that amputees can actively participate in intensive rehabilitation and prosthetic training. Assessment and modification of health risk factors can improve long-term functional outcome. All patients should be encouraged to exercise daily to improve their performance of activities of daily living.

Amputation Wound Dressings

An important aspect of rehabilitation is the uncomplicated healing of the remnant limb. The role that early wound dressings play in ultimate wound healing and rehabilitation deserves special mention. Currently, no consensus exists on the most effective



Figure 114.2 Above-Knee Prostheses. (A) Standard mechanical knee with swing control. (B) “Intelligent” transfemoral microprocessor-controlled prosthesis (without socket). (C) Patient with “intelligent” above-knee prosthesis seated on an examination table.

postoperative management strategy for individuals who undergo major amputation. Due to the longer residual limb and functional knee, there are more dressing options for BKA than AKA. Most practitioners elect a soft dressing following a standard AKA. Typical postoperative dressings and management strategies following BKA include soft gauze dressings with an elastic wrap; thigh-level rigid plaster dressings without an immediate prosthesis; thigh-level rigid plaster dressings with an immediate postoperative prosthesis (IPOP); short, removable rigid plaster dressings; and a prefabricated pneumatic postoperative prosthesis (prefabricated pneumatic IPOP).^{74–79} A soft gauze dressing with a mild compression wrap is the most widely used dressing following BKA. Patients remain non-weight-bearing on the stump until the fitting of a prosthesis 4 to 6 weeks after surgery. There are concerns that this type of dressing may delay effective physical therapy and rehabilitation.

Data from controlled trials have found that for soft dressing strategies the uncomplicated healing rates, postoperative pain, prosthetic use, and mortality are not significantly different when compared with other types of dressings.^{71,80,81} However, other studies have shown that thigh-level rigid dressings lead to significantly shorter rehabilitation times compared to soft dressings when measured as time to initial gait training.^{82–85} The technique known as IPOP placement, proposed by Berlemont in the 1950s, has been documented to improve both primary healing and rehabilitation rates.⁸² An IPOP, which is applied at the initial operation, combines a rigid postoperative dressing with a temporary prosthesis and has been advocated for the early rehabilitation of nonischemic amputees. Concerns from surgeons include lack of familiarity with the prosthesis, fear of placing a

hard cast on a potentially compromised remnant limb, and the inability to inspect the wound frequently. To allay these fears, a report from Schon et al. found that significantly fewer patients with a prefabricated pneumatic IPOP had postoperative complications (16%) when compared with patients receiving soft gauze dressings (65%).⁸⁰ Other investigators have suggested that placement of an IPOP may actually reduce the need for surgical revision of the amputation stump.⁷⁴

Prosthesis Selection and Training

Prosthetic training plays an important role in rehabilitation. An appropriate durable prosthesis should be prescribed based on the individual's situation. Advanced prosthetic technology provides amputees with more choices. New functional designs and ultralight materials help amputees to live independently. Various lower extremity prostheses are commercially available for patients following AKA and BKA (Figs. 114.2 and 114.3).⁷⁰ The advantages and disadvantages of different types of prostheses and the indications for their use depend on the individual patient and should be fully explored by the experienced prosthetist.^{70,86} For example, microprocessor-controlled above-knee prostheses are now typical of the high-technology products (see Fig. 114.2B). These “intelligent” prostheses can change the orifice size based on different walking speeds, to allow the appropriate shin swing time. The shin includes numerous sensors to accumulate biomechanical data, such as vertical loading amplitude and sagittal knee movement, to determine the direction and angular acceleration of the artificial knee joint. A software analysis system can optimize prosthetic characteristics through a process of data sampling and calculations



Figure 114.3 Below-Knee Prostheses. (A) Standard prosthesis with solid ankle and cushioned heel foot. (B) Dynamic, energy-conserving athletic prosthesis. (C) Below-knee prosthesis for patients with wound difficulties.

up to 60 times in a 1.2-second gait cycle.^{70,83} A patient wearing one of these prostheses can easily step up and sit on an examination table (see Fig. 114.2C).

Different types of prostheses are available to meet the needs of amputees with different amputation levels, physical conditioning, and exercise demands.⁷⁰ In general, persons of smaller stature with a slow to moderate cadence are better suited to smaller, simpler, and lighter hydraulic swing-control prostheses. Taller, more active ambulators benefit from larger, more powerful hydraulic swing-control prostheses.⁸⁷ Below-knee prostheses are generally much more lightweight than above-knee prostheses. The below-knee prostheses vary and include standard passive ankle designs, energy-conserving ankles, and open-type sockets that can accommodate slowly healing stumps (see Fig. 114.3).

Reasonable goals must be set for each patient. Many patients may not walk independently, but many wear prostheses, and the large majority return to their home environments. Although all patients may be offered the eventual fitting of a prosthesis, only a fraction will actively walk with their prostheses. In a large series of major amputations, 42% used a prosthetic limb, and 92% of patients were able to return to community living, but only 29% of patients were able to walk outside the home with a prosthesis.²⁸

Functional Outcome

The assessment of functional performance following major amputation is a complex issue that influences decision making at the outset. The most important factors that influence functional outcome are age, preoperative functional status, comorbidities,

mental status, amputation level, stump healing status, unilateral versus bilateral amputation, and postoperative rehabilitation. Integrative and vocational rehabilitation combined with newly designed prostheses allow high-level amputation patients to achieve independent lifestyles. Interdisciplinary management should be used in the care of all amputees. Preoperative and postoperative optimization of a patient's medical condition, intensive rehabilitation, wound care, pain management, and proper prosthesis fitting all significantly improve the patient's ultimate functional outcome. A key concept in defining functional outcomes is that success should be defined in relation to an individual's mobility prior to the development of their limb impairment. This patient-centered measure should be the ultimate measure of a successful outcome.⁸⁸

Impact of Amputation Level and Comorbidities

Among amputees with healed stumps, 80% of those with BKAs can achieve ambulation, compared with only 38% to 50% of patients with AKAs.⁸⁹ Taylor and coworkers documented that patients older than 70 years had a three-fold greater chance of not wearing a prosthesis, a 3.1-fold greater chance of death, a 2.3-fold greater chance of being nonambulatory, and a 4-fold greater chance of losing functional independence at 1 year compared with patients younger than 50 years.³⁷ Patients aged 70 years or older and those with limited preoperative ambulatory ability, dementia, end-stage renal disease, and advanced coronary artery disease all had a significantly higher chance of experiencing death, nonambulatory status, loss of functional

independence, and never using a prosthesis. Patients receiving an AKA who were not ambulatory preoperatively had a 10-fold greater chance of not wearing a prosthesis and twice the chance of death at 1 year. Amputees with dementia were 2.4 times less likely to wear a prosthesis. Patients with advanced comorbidities, including coronary artery disease, end-stage renal disease, and severe chronic obstructive pulmonary disease also had a greater chance of not ambulating following amputation.³⁵

Most recently the Northern Netherlands Epidemiology of Dysvascular Amputation (NEDA) study group investigated risks factors for 30-day and 1-year mortality after major amputation.⁹⁰ The observed 30-day mortality was 14%, and 1-year mortality was 34%. Advanced age carried a higher rate of mortality with patients aged 75–84 having a three-fold increase, and patients aged >85 being 4 times more likely to die in the first year. Other risk factors associated with higher 1-year mortality included transfemoral amputation (OR 2.2), hemodialysis (OR 5.7), heart failure (OR 2.3), myocardial infarction (OR 1.7), immunosuppression (OR 2.8), and guillotine amputation (OR 5.1).⁸⁷

Through-knee amputation is not commonly performed because of poor soft tissue coverage and a higher risk of wound complications. However, in the patients with adequate residual skin and subcutaneous tissue, through-knee amputation is an option. Through-knee amputees are able to achieve higher normal and maximal walking speeds with lower relative energy expenditure than above-knee amputees. In elderly patients or those with significant comorbidities preventing them from postoperative ambulation, through-knee amputation allows earlier weight-bearing with a lower risk of wound complications compared with BKA.⁷⁰

Minor amputations, such as digital, ray, transmetatarsal, and midfoot amputations, are considered limb salvage procedures. Patients with digital or ray amputations may walk with little additional energy expenditure. Partial foot amputations require less ambulation energy than more proximal amputations. Pinzur and associates demonstrated that energy demands after midfoot, Syme, below-knee, through-knee, and AKAs are directly related to the level of amputation.⁹¹

Impact of Age

Patients younger than 60 years with well-controlled comorbidities who were ambulating preoperatively can anticipate an ambulatory rate of 70%, a survival rate of 80%, and an independent living rate of 90% at 1 year following major amputation.³⁵ A Canadian study showed that although older patients had more comorbidities at admission, they benefited as much as younger people from an intensive rehabilitation program with a comparable length of stay.⁹² However, younger amputees continued to improve after 3 months, whereas older patients tended to plateau. In selected patients who developed stump wound complications but had good perceived healing potential, a “redo” BKA yielded better functional outcomes than conversion to an AKA.⁹³

Fate of the Contralateral Limb After Amputation

Following a major amputation, many patients worry about the fate of their remaining limb. Patients surviving several years after the first amputation have a significant chance of needing a contralateral amputation. Fifteen percent to 35% of amputees with diabetes lose their remaining leg within 5 years.⁹⁴ The presence of renal failure is a particularly poor prognostic indicator of second limb amputation.²⁷ These facts underscore the need for diligence in protecting and surveying the remaining limb. Continued efforts focused on patient education and preventive foot care are essential. Periodic evaluation and management of PAD in the contralateral limb after unilateral amputation is important for the long-term functional outcome of these patients.

Depression After Amputation

As in other areas of vascular surgery, the successful completion of the operation is only the beginning of the patient’s recovery. Although the surgeon may initially focus on the surgical wounds, other considerations are unique to the recovery of an amputee. Although depression is common following major amputation, especially in younger amputees, depression may itself be associated with a higher risk of major amputation.^{95,96} The loss of a limb has been compared with the loss of a spouse. Although the feeling of bereavement abates over the first year, many amputees experience a continued sense of loss extending beyond 1 year.⁹⁷ In the recovery period, positive outcomes should continually be stressed, and clinical screening with appropriate medical therapy for depression should be considered. Amputees with significant depression may become malnourished owing to loss of appetite; malnutrition may delay healing, contribute to the development of pressure ulcers, and seriously affect the patient’s overall recovery. A prospective study recently performed on patients undergoing amputation demonstrated a 40% incidence of depressive symptoms at baseline, with substantial improvement in these symptoms by 6 weeks.⁹⁸ Identifying risk factors early on, and supporting patients accordingly has been shown to be associated with improved quality of life in amputees.⁹⁹ Incorporating psychiatric evaluations and therapy early on is essential for patient satisfaction, improving mental and psychological wellbeing.

Importantly, successful rehabilitation can decrease the severity and incidence of depression following amputation.¹⁰⁰ Social discomfort, the appearance of the prosthesis, and individual coping skills should be addressed in the recovery process.^{101–103} The psychological impact of the loss of independence may be minimized by aggressive, focused rehabilitation that openly addresses the concerns of the amputee. Dealing with these issues requires the participation of psychologists, nurses, and geriatric and rehabilitation specialists and is an integral part to the successful management of these patients.

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

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See notes

Lower Extremity Amputations: Operative Techniques and Results

ANTHONY L. RIOS and JOHN F. EIDT

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Limb amputation, practiced throughout the centuries, is one of the most effective surgical procedures.¹ With benefits ranging from pain relief to preservation of life, amputation offers a clear path to cure the patient. Despite the importance of a well-executed amputation, the task is often relegated to the least-experienced surgeon on the team. Incorporating deliberation with surgical technique can bring about an outcome that is both pain-free and functional. A small amount of additional time and effort spent in the operating room can potentially save the patient from a life of severe chronic pain and offers the best opportunity for functionality and independence.

Historically, amputation was challenging due to the critical triad of hemorrhage, infection, and pain. In France, Ambroise Pare, a French barber surgeon, introduced vessel ligatures, thus making the application of hot oil obsolete. Tourniquets were used by Morell, another French barber surgeon, in the battle of Besancon in 1674. Prior to the introduction of antisepsis by Joseph Lister in 1867, it is estimated that more than half of all amputees died from infection.¹

GENERAL PRINCIPLES

The surgeon must ensure adequate blood supply, sufficient viable soft tissue for coverage, and intact bony architecture (Box 115.1). Other priorities include minimizing surgical trauma by avoiding crushing-type surgical instruments. Although surgical hemostasis is essential to successful amputation, there is a lack of consensus regarding the optimal methods. Beveled skin incisions should generally be avoided, skin should not be separated from underlying tissue, and skin flaps should not be under tension.

In general, a longer stump is preferred due to improved prosthetic fitting and biomechanics, but not at the cost of leaving poorly perfused or infected tissue. Excessive soft tissue may interfere with prosthetic fitting and should be avoided. Overattention to minor dog ears and irregularities may satisfy immediate cosmetic goals at the cost of wound healing and flap viability.² Antagonistic muscle groups should be stabilized to prevent

BOX 115.1

General Principles of Amputation Surgery

- Assess arterial perfusion and bone architecture.
- Handle all tissue with atraumatic technique.
- Excise all nonviable and infected tissue.
- Apply tourniquet to minimize blood loss.
- Eliminate all sharp bone edges and fragments.
- Minimize number of cuts across muscle.
- Transect nerves sharply and allow retraction.
- Minimize use of electrocautery.
- Close wounds under no tension.
- Perform myodesis or myoplasty to stabilize antagonistic muscle groups.
- Use drains to reduce dead space.
- Provide prophylaxis for deep venous thrombosis.
- Administer prophylactic antibiotics.
- Avoid weight bearing until adequate wound healing has occurred.
- Use protective soft and rigid dressings.
- Avoid excessive cosmetic tailoring of wounds.
- Isolate infected or gangrenous tissue with barrier adhesive drapes.

skeletal misalignment, a complication which is both detrimental functionally and cosmetically.³ *Myoplasty*, the suture fixation of antagonistic muscle groups, may help in this regard, in addition to *myodesis*, the direct suturing of the musculotendinous unit to the bone. Excessive periosteal stripping may devascularize the bone, leading to the formation of ring sequestra.

Infected areas should be isolated with the use of mechanical barriers. Open “drainage” or guillotine amputation is sometimes warranted in the setting of gross infection.^{4–8} A two-stage approach, delaying primary closure until a patient is clinically stable, may preserve limb length. Antibiotic coverage should be narrowed based on Gram stain and culture results, with discontinuation as soon as clinically warranted to prevent opportunistic infection such as *Clostridium difficile*.⁹

Protection of the amputation site with use of a rigid or soft dressing may prevent injury in the case of falls. Incisions must be well healed prior to weight bearing. Given their limited mobility, patients are at high risk for developing deep venous thrombosis (DVT) and should receive prophylaxis.¹⁰ Perioperative prophylactic antibiotic use is recommended to limit wound infection following amputation.¹¹

TOE AND RAY AMPUTATION

Anatomy

The bony anatomy of the ankle consists of seven tarsal bones and five metatarsals (Fig. 115.1). The great toe has two phalanges, whereas the other toes have three. Medial and lateral sesamoid bones in the flexor tendons of the first toe provide stability. Joint capsules surround the interphalangeal and metatarsophalangeal hinge joints, and ligamentous and tendinous attachments work in concert with the plantar fascia to maintain structural integrity of the foot.

Technique: Toe Amputation

Toe amputation is appropriate for lesions of the middle and distal toe. A racket incision achieves tension-free closure. So-called for its shape like a tennis racket, the “handle” should lie longitudinally along the dorsal surface of the digit, in the midline for the second through fourth toes and away from the midline on the medial/lateral surfaces for the first and fifth toes (Fig. 115.2).

After incising the skin and soft tissues, the tendinous attachments are divided at the same level as the skin incision and the bone is trimmed back accordingly. If a disarticulation is warranted, a #15 blade is inserted into the joint capsule. Cartilage is excised with a rongeur and the bone edges are filed smooth. Excessive use of electrocautery should be avoided. Interrupted nonabsorbable monofilament sutures are used to close the wound in one layer.

Technique: Ray Amputation

A ray amputation includes resection of the digit and variable length of the associated metatarsal. Ray amputations may be completed with a racket incision, with the “handle” or vertical

portion extending proximal to the metatarsal head (Fig. 115.3). The skin and soft tissues are incised, the tendinous attachments are divided and allowed to retract, and the metatarsal is transected before dividing the remaining soft tissues. Typically, the sesamoid bones are excised, associated flexor tendons are placed on tension and transected, and residual tendon is allowed to retract. Care should be taken to avoid injury to adjacent digital arteries and nerves.

Simultaneous amputation of the first and second rays will significantly alter gait. Isolated first ray amputation is prone to recurrent ulceration in up to 60% of patients.¹² Some surgeons advocate a complete transmetatarsal amputation (TMA) of all remaining toes in this setting but there are no conclusive data governing this decision.¹³ A patient-specific approach is best.

TRANSMETATARSAL AMPUTATION

Anatomy

Proximal to the phalanges are five metatarsals (see Fig. 115.1). They are stabilized by the deep transverse metatarsal ligaments and plantar ligaments distally and the plantar metatarsal

ligaments proximally. The proximal metatarsals articulate with three cuneiform bones and the cuboid laterally. Collectively the tarsometatarsal (Lisfranc) joint connects the midfoot and forefoot.

Technique

TMA is appropriate for wounds involving the entire forefoot or when multiple ray amputations are considered. TMA offers the ability to wear standard footwear with near-normal ambulation. TMA is contraindicated in cases of severe bony deformity of the midfoot and hindfoot which would lead to structural instability.

An incision extends transversely over the dorsum of the foot at the level of the distal metatarsals, coming to corners medially at the first metatarsal head and laterally at the fifth metatarsal head. Next, an incision extends from these corners onto the plantar surface across the base of the toes (Fig. 115.4). The extensor tendons are divided at the skin level, the periosteum is incised, and the metatarsals are divided with a bone saw, each approximately 3–4 mm shorter than the last, moving laterally. A gentle 30- to 45-degree plantar bevel may facilitate liftoff

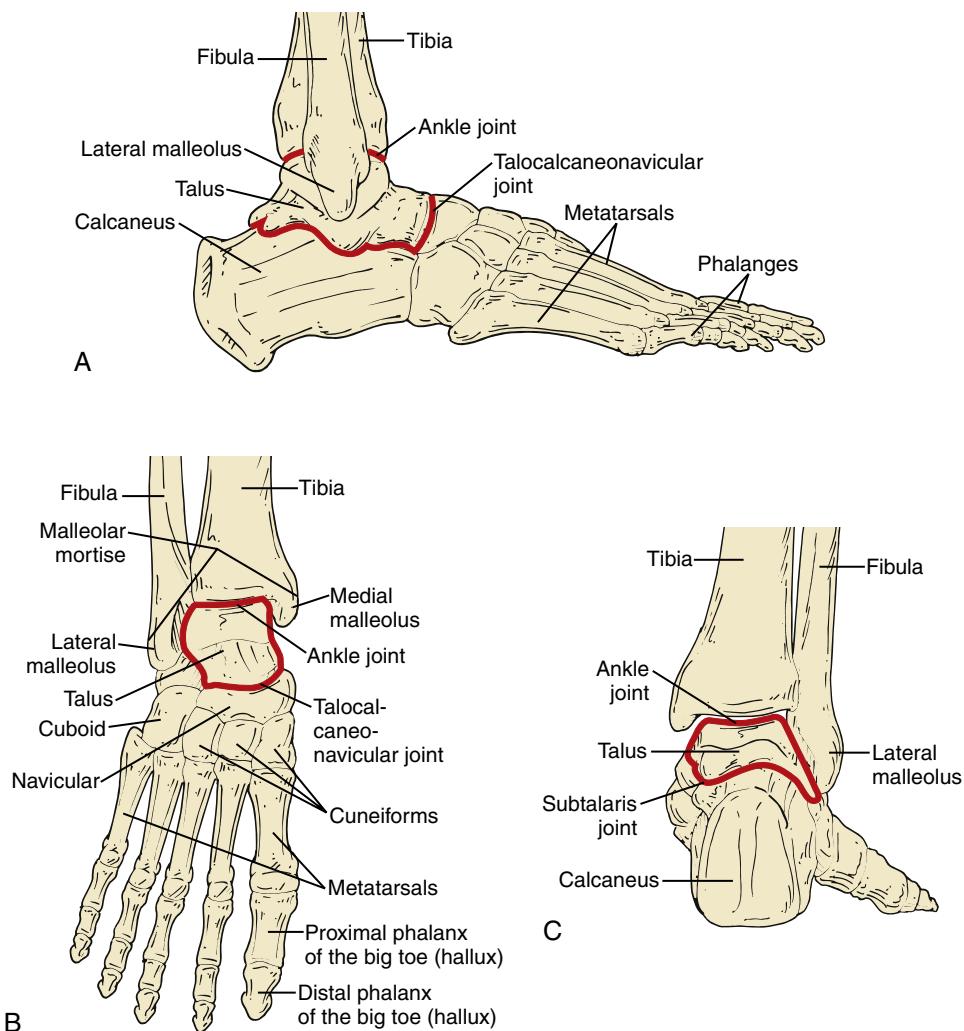


Figure 115.1, cont'd

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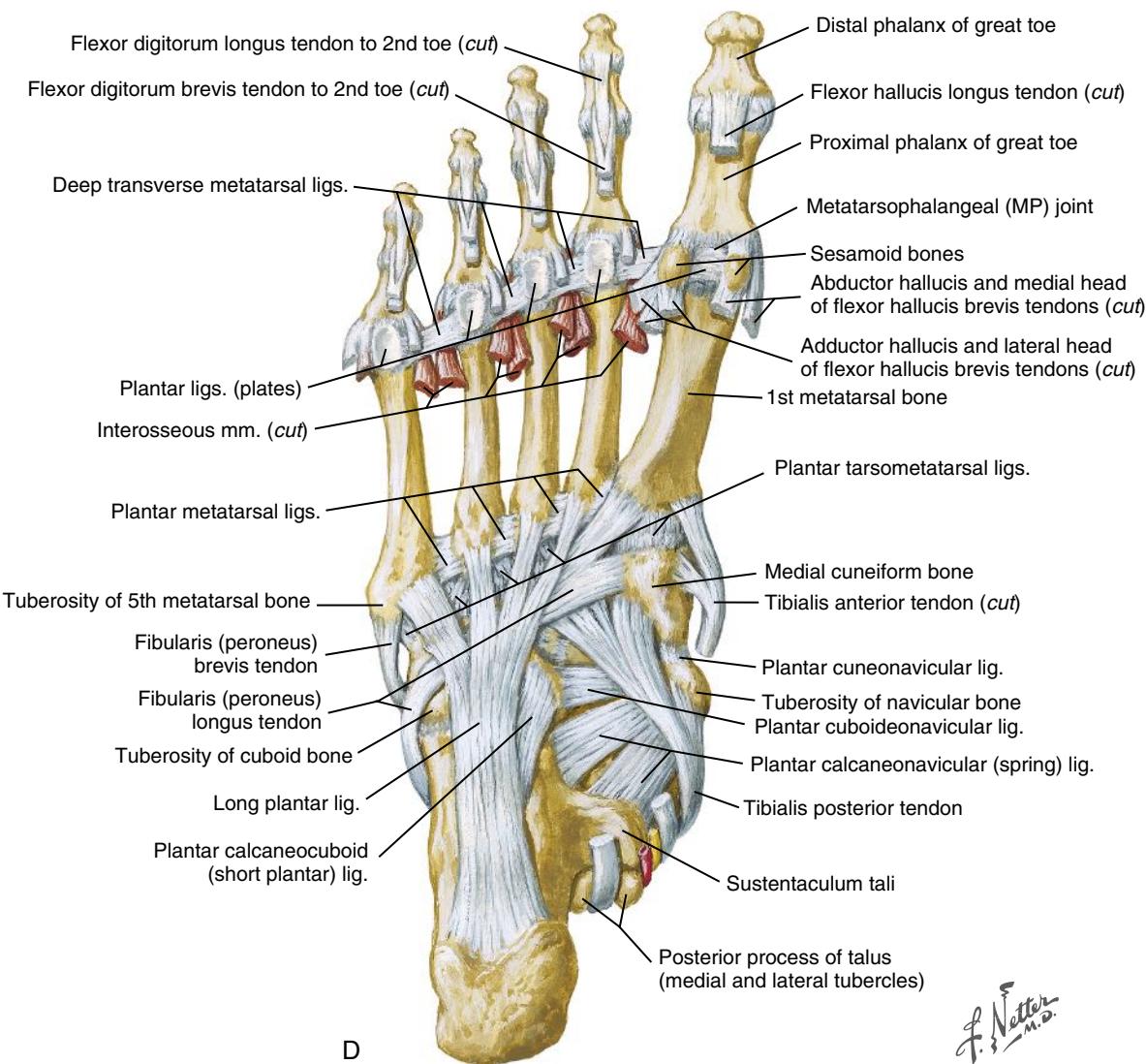


Figure 115.1 Bone Anatomy of the Foot.

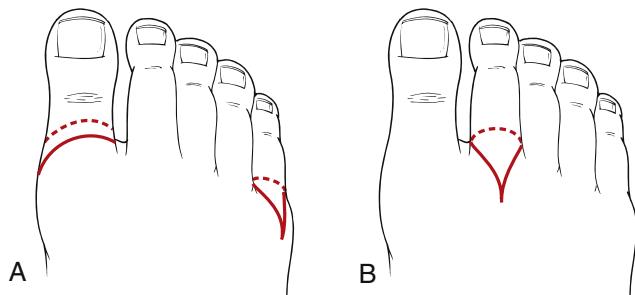


Figure 115.2 (A) Racket incision for first and fifth toe amputation. (B) Racket incision for second, third, and fourth toe amputation.

with ambulation and reduce the risk of future ulceration. After dividing the bones, the plantar myofascial attachments to the metatarsal heads are divided. Care should be taken to stay close to the bones during the formation of the flap to avoid “button-holes”. The poorly vascularized tendons and sheaths in the plantar flap should be excised. To reduce the risk of recurrent ulceration due to equinus deformity, some surgeons recommend Achilles tendon lengthening (ATL) or transection.¹⁴

MIDFOOT AND HINDFOOT AMPUTATIONS

Three proximal foot amputations are occasionally appropriate: Lisfranc tarsometatarsal disarticulation, Chopart midfoot amputation, and Syme amputation (Fig. 115.5).^{15,16} Two rarely performed hindfoot amputations are the Boyd and Pirogoff amputations.^{15,17–19} Hindfoot amputations are performed primarily in children to preserve length and growth centers.

Many surgeons recommend transtibial (below-knee) amputation if TMA cannot be performed or has failed. Others suggest that increased limb salvage rates can be achieved with the use of unconventional foot amputations.^{18,20}

Anatomy

The tibia and the fibula articulate with the talus via the talocrural joint. The ligaments that join these bones are the deltoid, anterior and posterior talofibular, and calcaneofibular ligaments.

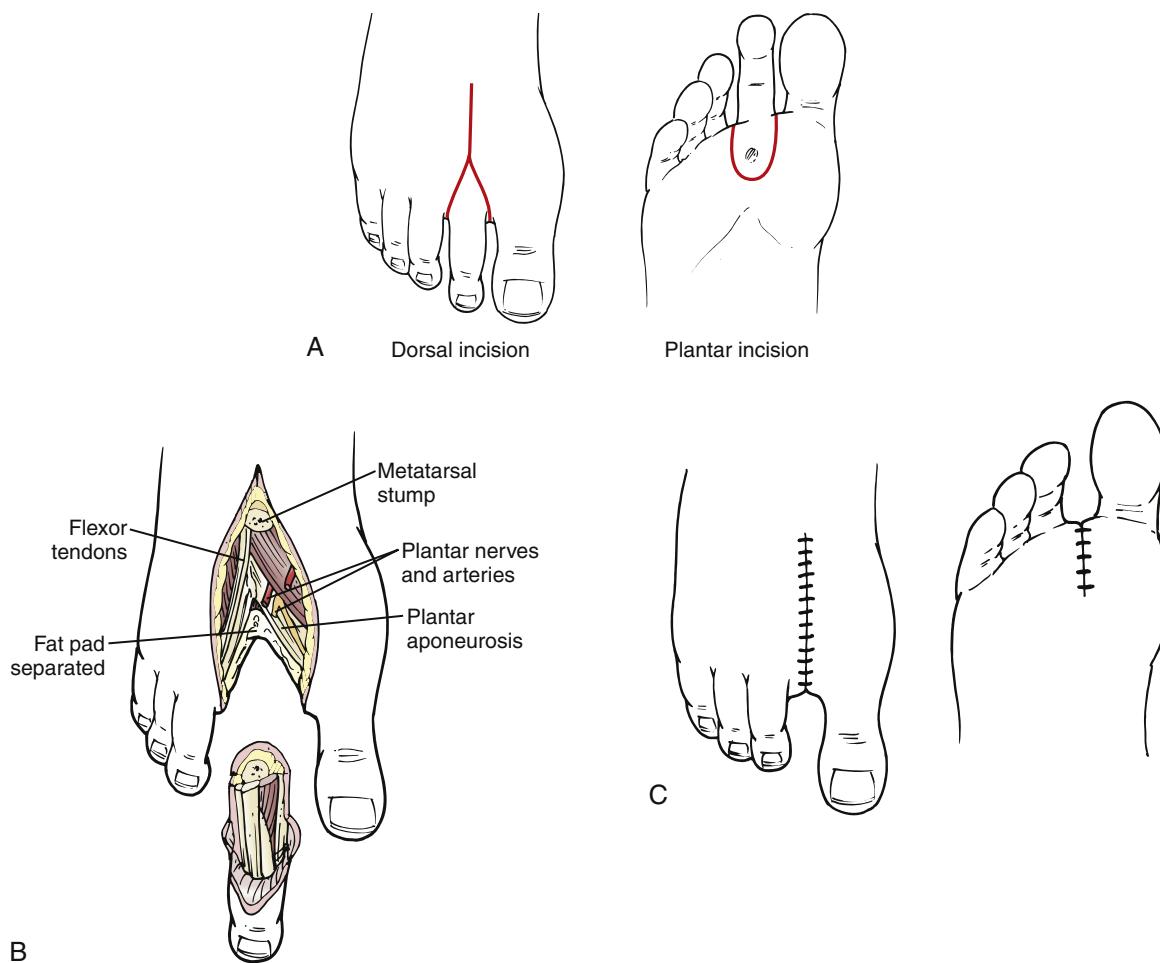


Figure 115.3 Ray Amputation Incision. (A) Note the plantar extension to include a mal perforans ulcer. (B) Transection of the metatarsal shaft. (C) Closure with nonabsorbable suture under no tension.

The talus articulates with the calcaneus at the subtalar joint. The medial and lateral talocalcaneal ligaments and the cervical ligament support this joint. The talocalcaneonavicular joint is a multiaxial joint supported by the talonavicular and plantar calcaneonavicular ligaments. Supination (inversion) at this joint is produced by the tibialis anterior and posterior. Pronation (eversion) is produced by the peroneus longus and brevis. A heavy fibrofatty heel pad firmly adheres to the calcaneus and skin and provides protection during heel strike (see Fig. 115.1).

Because the strong ankle extensor attachments are divided in the performance of midfoot and hindfoot amputation, the Achilles tendon exerts unopposed plantar flexor forces on the residual foot. The Achilles tendon may require division or lengthening to prevent the development of an equinus deformity.

Lisfranc and Chopart Amputations

Lisfranc

Lisfranc first described this amputation in 1815. The incision results in a long plantar flap (see Fig. 115.5). Tendons and synovial sheaths are divided at the level of the skin incision. The first, third, fourth, and fifth tarsometatarsal joints are

disarticulated. The second metatarsal is divided 1 to 2 cm distal to the medial cuneiform.²¹ To reduce the risk of development of equinovarus deformity, Sanders recommended a modification of the Lisfranc amputation that preserves the base of the fifth metatarsal and the insertion of the peroneus brevis.¹⁸ The Achilles tendon is released by either transection or Z-plasty.^{22,23} The plantar fascia on the flap is approximated to the dorsal periosteum with absorbable sutures. The skin is approximated with interrupted monofilament sutures or staples.

Chopart

Described by Chopart in 1814, this amputation involves a long plantar flap similar to that used in the Lisfranc amputation (see Fig. 115.5) and is performed through the talocalcaneonavicular joint and the calcaneocuboid joint. An Achilles tenectomy is recommended. The extensor hallucis longus and the tibialis anterior tendons may be reattached to the talar neck. The extensor digitorum longus may be reattached to the calcaneus.²¹

Postoperative Considerations

Because the Lisfranc and Chopart amputations result in a dramatic alteration in normal foot biomechanics, their durability may be limited. A short-leg plaster cast is applied over the

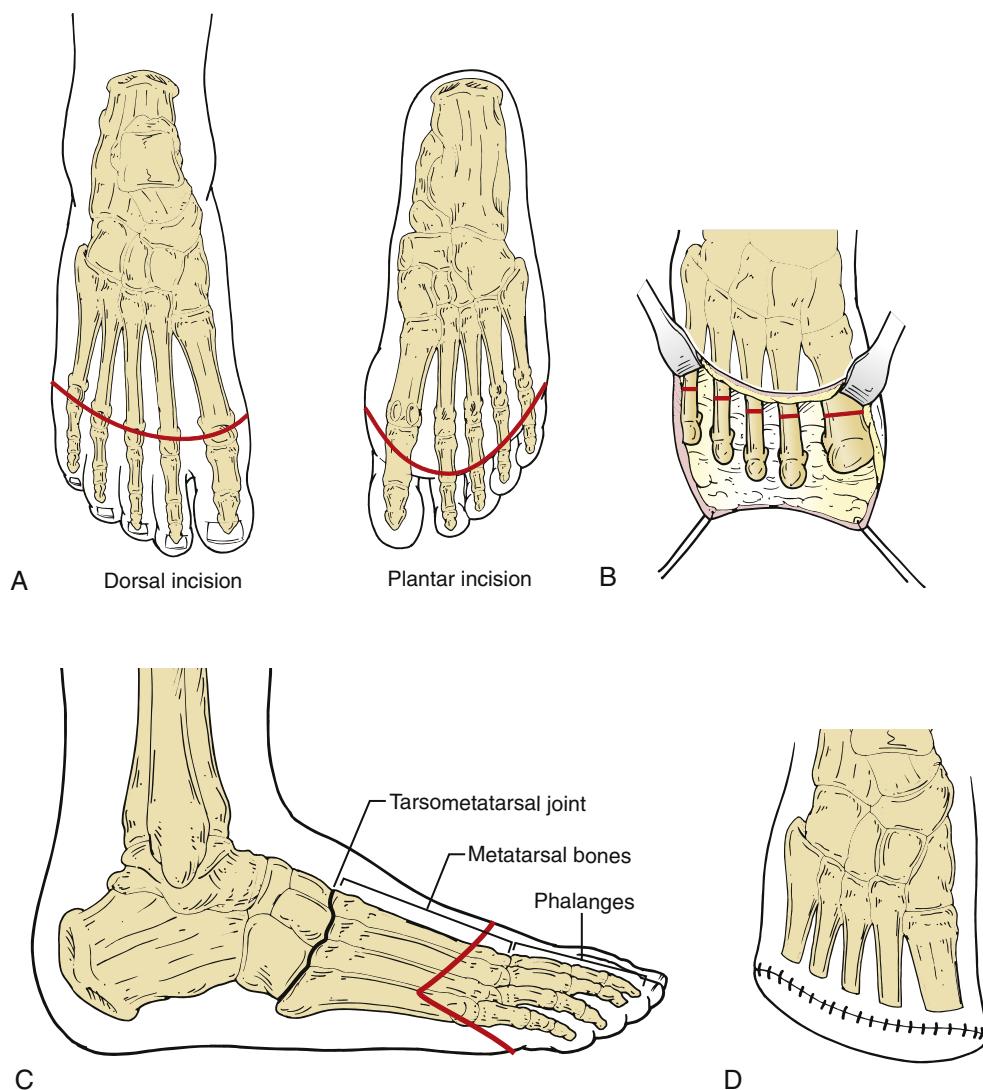


Figure 115.4 Technique of Transmetatarsal Amputation. (A) Dorsal and plantar incisions with disarticulation of the metatarsophalangeal joints. (B) Level of bone transection. (C) Lateral view. (D) Closure with monofilament suture.

sterile dressings on the operating room table. The cast must be molded to ensure that the talus is slightly dorsiflexed in relation to the tibia and that the calcaneal tuberosity is parallel to the long axis of the tibia. The cast is changed weekly to check wound healing. Weight bearing is allowed after 4–6 weeks. Patients with a Lisfranc amputation need little more than a toe filler with an ankle lace-up shoe. Patients with a Chopart amputation need a custom-fitted ankle-foot orthosis with a filler to hold the shoe adequately.

Syme Amputation

Syme first described this amputation in 1843. The anterior incision extends across the ankle just distal to the tip of each malleolus, while the posterior incision extends from the malleoli vertically down and across the sole of the foot (see Fig. 115.6). The extensor tendons are divided at the level of the skin incision.

Next, the dorsalis pedis artery is ligated and divided. The ankle joint capsule is incised while plantar flexing the foot before dividing the medial and lateral ankle ligaments. The tendons of the posterior tibialis and flexor hallucis longus are transected, taking care to avoid injury to the posterior tibial artery. Next, the heel fat pad is carefully dissected by staying close to the calcaneus to avoid buttonholing. Finally, the ankle joint is disarticulated, and the specimen is passed off the table. In a one-stage amputation the malleoli are divided with a saw at the level of the articular surface of the tibia, and the width is reduced by vertical bone excision. Holes are drilled in the medial, anterior, and lateral parts of the distal tibia and fibula to secure the heel pad directly under the tibia. In a two-stage Syme amputation the wound is closed by suturing the heel flap to the dorsal fascia. Six weeks later the malleoli are removed through separate vertical incisions (see Hulnick et al.²⁴ and Richardson²⁵ for a detailed description of midfoot amputations).

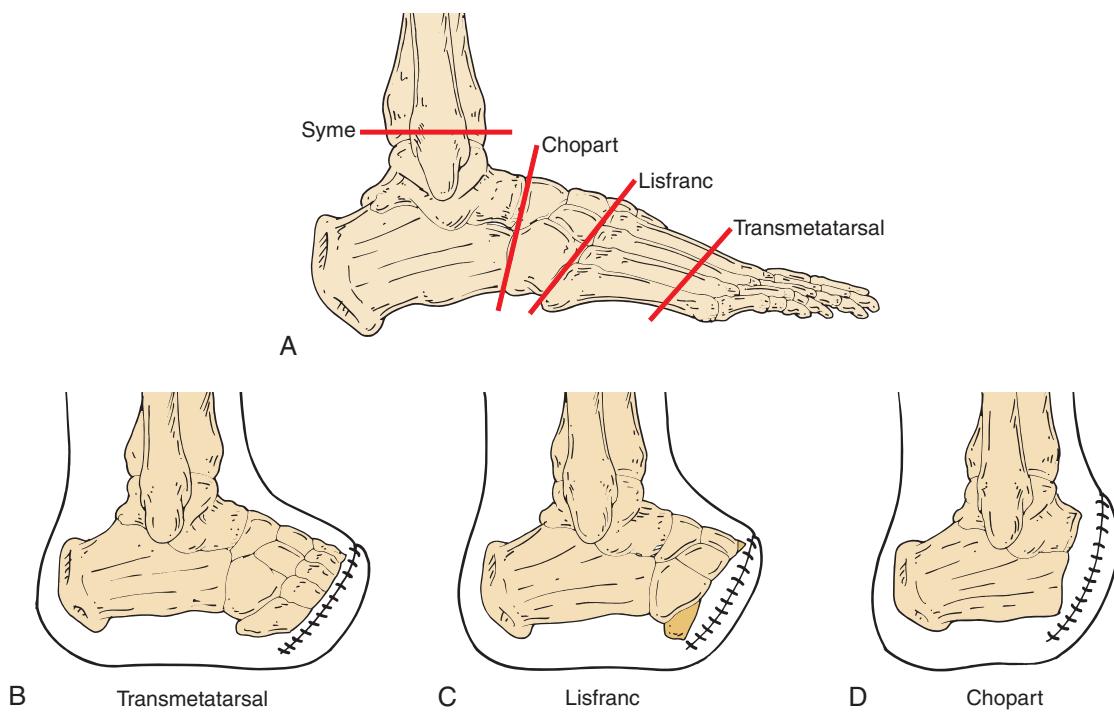


Figure 115.5 Levels of Foot Amputation. (A) Levels of foot amputation. (B) Transmetatarsal. (C) Lisfranc. (D) Chopart.

Postoperative Considerations

The chief advantage of the Syme amputation is the preservation of limb length, which may obviate the need for a prosthesis during brief periods of weight bearing, such as during transfer from a bed to a wheelchair. The disadvantages include the slight leg-length discrepancy, which may lead to biomechanical side effects in more proximal or contralateral joints. Furthermore, the prosthesis is typically bulky at the ankle and less cosmetically appealing than a conventional below-knee prosthesis.

TRANSTIBIAL (BELOW-KNEE) AMPUTATION

Probably no surgical procedure is more prone to individual surgeon preference/bias than below-knee amputation (BKA). The choice of incision, length of bone, use of electrocautery, addition of myodesis or myoplasty, management of major nerves, skin closure techniques and postoperative dressings vary widely among even experienced surgeons owing largely to the absence of objective, randomized data.

Anatomy

The leg contains four muscle compartments. The anterior compartment contains the tibialis anterior, extensor hallucis longus, and extensor digitorum longus muscles, as well as the anterior tibial artery and vein and deep peroneal nerve. The lateral compartment contains two muscles: the peroneus longus and brevis, as well as the superficial peroneal nerve. The superficial posterior compartment contains the soleus, gastrocnemius, and plantaris muscles. Last, the deep posterior compartment contains the flexor digitorum longus, tibialis posterior, flexor

hallucis longus, and popliteus muscles, the posterior tibial artery and veins, peroneal artery and veins, and tibial nerve. The tibial nerve courses adjacent to the posterior tibial artery and veins (Fig. 115.7). Posterior flaps, skew flaps, sagittal flaps, and medial flaps are based on corresponding musculocutaneous perforators; thus it is important to avoid separating the skin and soft tissue from its underlying muscle.²⁶

Technique

Posterior Flap

The posterior-based flap described by Burgess et al.^{27–29} is the most commonly used by vascular surgeons because sural collaterals are usually sufficiently robust to maintain the viability of the gastrocnemius even in the setting of popliteal artery occlusion. Division of the tibia should be at minimum 12 to 15 cm distal to the tibial tuberosity to create the most favorable biomechanics for ambulation with a prosthesis. Insufficient bone length is a major contributor to failure of prosthetic use. To fashion flaps, some advocate using a two-thirds/one-third technique based on leg circumference (Fig. 115.8). The anterior incision of the amputation should be approximately two-thirds the leg's circumference. The length of the posterior flap is one-third the leg circumference and should be shaped in a gentle curve to reduce dog ears.

The skin, subcutaneous tissue, and fascia are incised starting with the transverse portion before extending along the posterior flap. The anterior and lateral compartment muscles are divided next. The periosteum of the tibia is incised and mobilized proximally and the tibia is divided using a bone saw. The fibula is divided approximately 1 to 2 cm proximal to the tibia. Removing too much fibula will result in a conical stump, both unsightly and a poor recipient of a prosthesis. A large

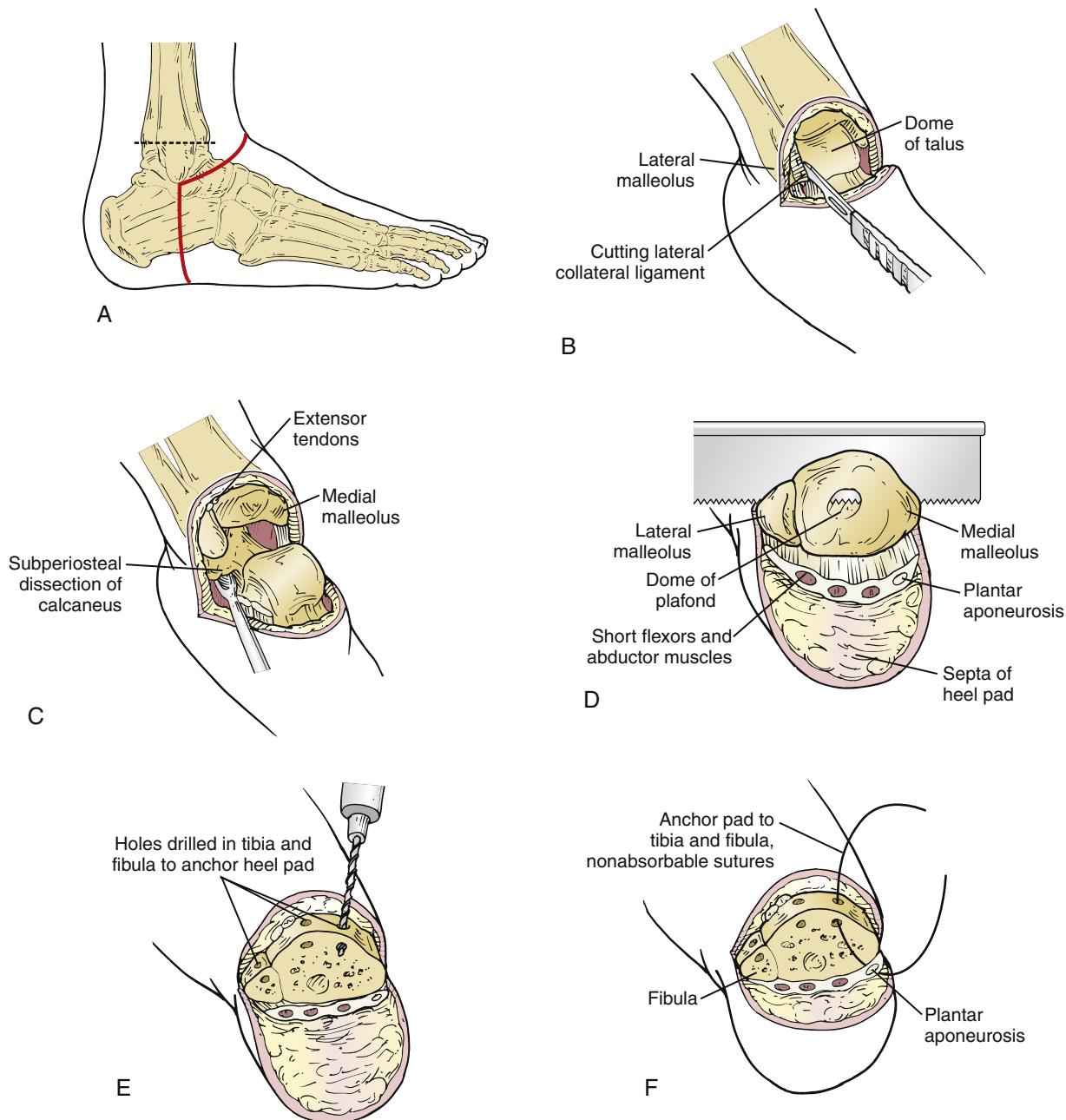


Figure 115.6 Syme Amputation. (A) Skin incision and bone transection level. (B) Exposure of the ankle and division of the ligaments. (C) Soft tissue dissection from the calcaneus. (D) Division of the tibia and fibula. (E) Holes drilled in the anterior aspect of the tibia and fibula. (F) Fascia lining the heel pad sutured to the bone.

amputation knife is used to create the posterior flap. The knife is maintained at a plane deep to the tibia and fibula, dividing the remaining posterior compartment musculature. Major vascular bundles are suture ligated. The tibial and peroneal nerves are sharply divided and allowed to retract proximally. The posterior flap musculature is trimmed of gross excess but allowed to remain sufficiently bulky to cushion impact once fit with a prosthesis. Some surgeons prefer to advance the posterior flap 3 to 4 cm proximal to the tibial osteotomy.³⁰ If warranted, the soleus muscle can be excised up to the level of the tibial osteotomy, but the gastrocnemius and fascia must be preserved.

The anterior tibia is beveled to avoid a sharp edge protruding through the skin. Most surgeons advocate transection of major nerves (saphenous, sural, tibial and peroneal) under traction to allow retraction into the soft tissues to potentially reduce the risk of neuroma formation though there are no objective studies to support this practice.

Some advocate a myodesis (remember “d” for “drill”) of the gastrocnemius. Two holes are drilled into the anterior surface of the tibia, and the gastrocnemius is affixed to the tibia with a nonabsorbable suture in an effort to improve muscle/fascial coverage of the tibia. Bites are taken slightly behind the edge of

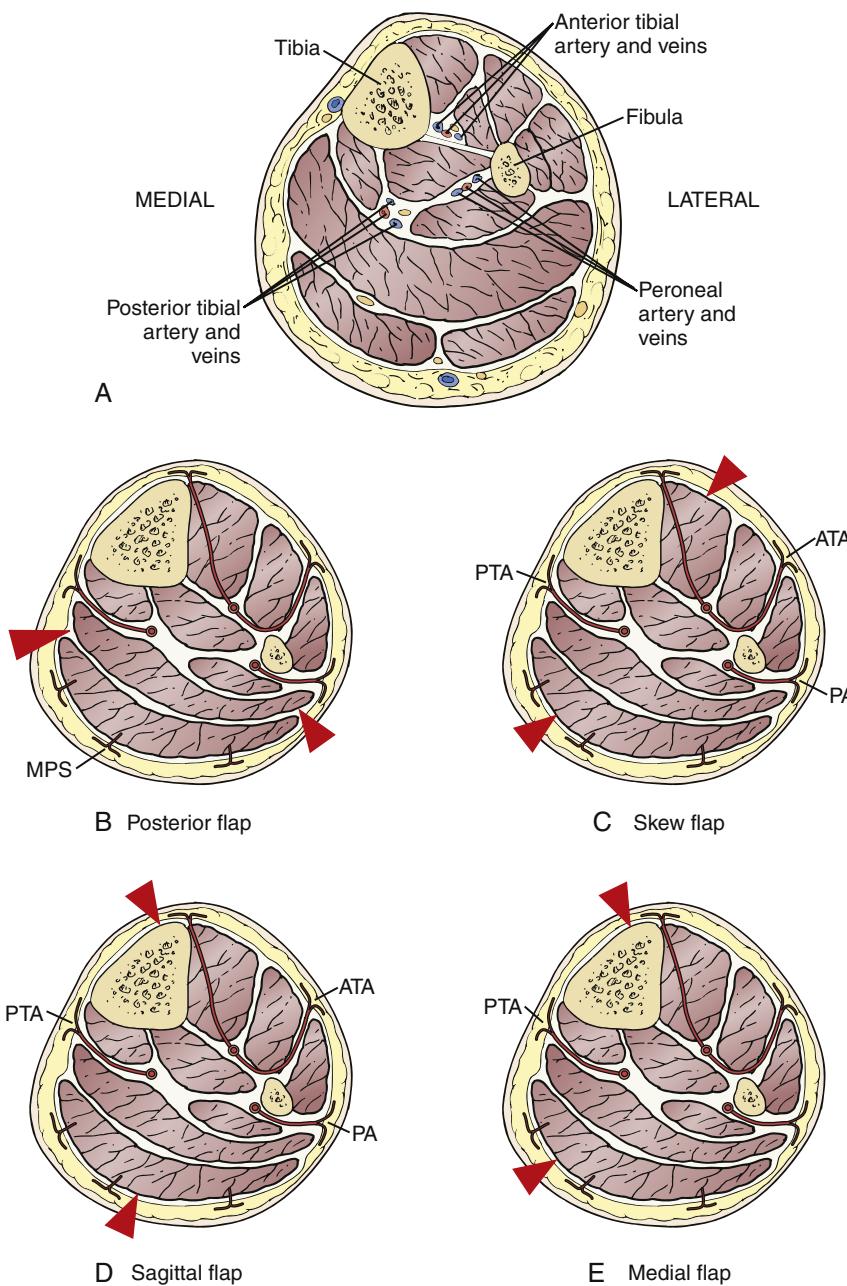


Figure 115.7 Cross-sectional Anatomy and Blood Supply to the Skin at the Level of Transtibial Amputation. Note the location of skin incisions (red arrowheads). (A) Leg cross-section. (B) Posterior flap. (C) Skew flap. (D) Sagittal flap. (E) Medial flap. ATA, anterior tibial artery; MPS, musculocutaneous perforators from the sural artery; PA, peroneal artery; PTA, posterior tibial artery.

the flap through the fascia to create a lip of muscle over the anterior portion of bone. Prior to closure, the wound is irrigated with saline to remove bone dust and debris. The deep fascia is approximated with interrupted absorbable sutures. The skin is closed with staples or interrupted monofilament suture avoiding tightly compressing the flaps.

Sagittal Flap

If creation of a long posterior flap is not possible due to absent or inadequate soft tissue, sagittal or skew flaps may be used. In the sagittal flap technique described by Persson, equal-length

medial and lateral myocutaneous flaps are developed (see Fig. 115.7).³¹ A myoplasty is performed to cover the tibia by suturing the anterior and lateral compartment muscles to the medial component of the gastrocnemius and soleus. A randomized comparison of sagittal versus posterior flaps showed no significant difference in outcome.³²

Skew Flap

In the skew technique, equal anteromedial and posterolateral fasciocutaneous flaps are created (see Figs. 115.7 and 115.9). The posterior muscle flap is identical to the conventional long

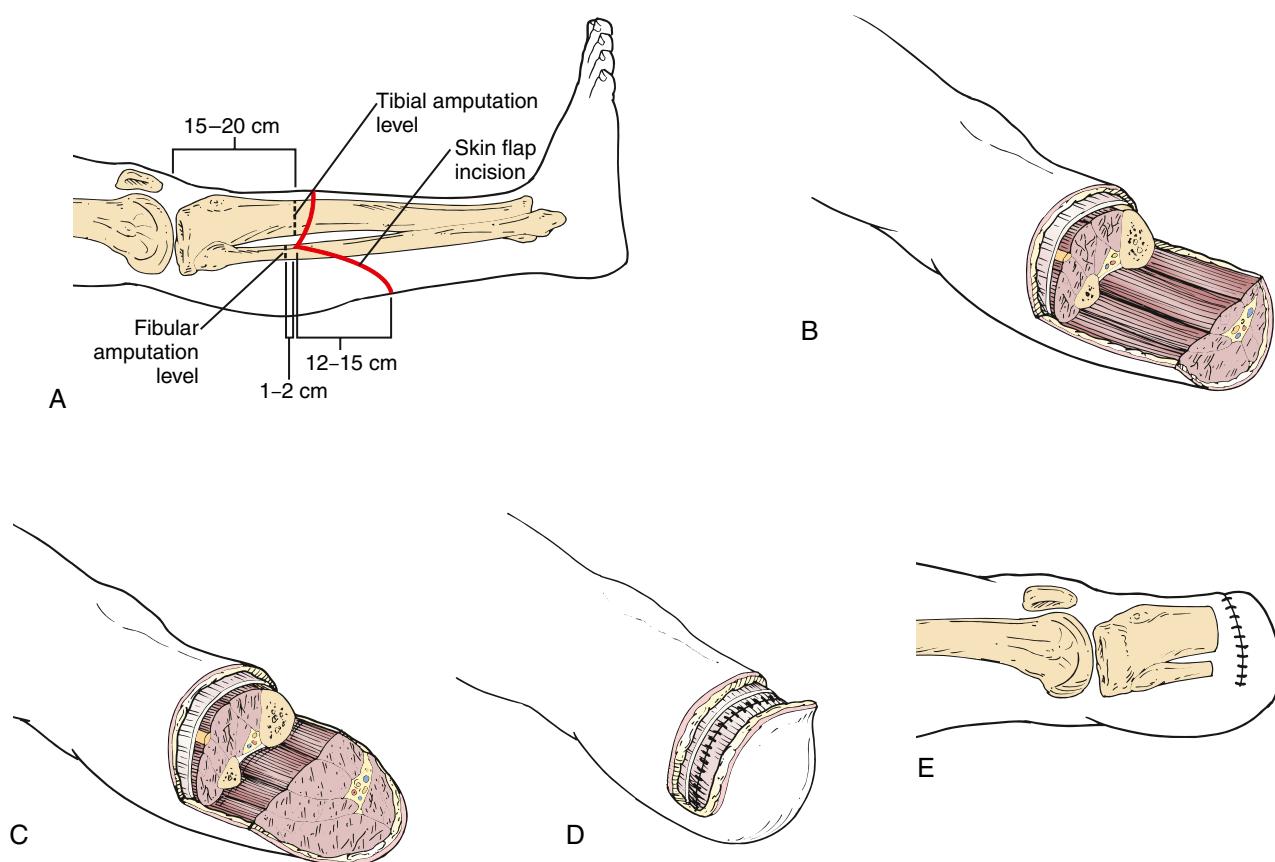


Figure 115.8 Transtibial Amputation. (A) Marking the skin incisions. (B) Fashioning the flaps after bone transection. (C) The soleus muscle is tailored to create a proper flap. (D) The posterior deep fascia is sutured to the anterior deep fascia and periosteum. (E) Closure of the skin flaps.

posterior flap based on the gastrocnemius muscle.³³ The skew technique may be of particular benefit when there is inadequate skin to create a conventional long posterior flap.

Fish-Mouth Flap

Before the development of the long posterior flap, the creation of equal anterior and posterior flaps was the most common transtibial amputation technique. The chief disadvantage is vulnerability of the anterior flap to ischemia.

Medial Flap

A medially based flap technique, described by Jain and colleagues, may be appropriate in selected patients (see Figs. 115.7 and 115.10).³⁴ Based on thermographic imaging, a long medial flap and a shorter lateral flap are designed. A Cochrane review published in 2014 concluded that there was insufficient evidence to establish the superiority of one transtibial amputation technique over the others.³⁵

Ertl Procedure

Tibiofibular bone bridging, known as the Ertl procedure, is thought by some to provide better transmission of energy from the distal femur to the prosthesis. The Ertl procedure uses a bone bridge between the tibia and fibula to provide a more stable weight-bearing surface. The fibula is harvested from the amputation specimen and serves as a bone graft.

Equal length skin flaps are created. The skin and soft tissues are excised, and the anterior muscle is divided. The tibia is divided with a bone saw, and the fibula is first divided approximately 2 to 4 cm distal to this point, depending on the distance from the tibia to the fibula. Next, the fibula is divided at a level of the tibial osteotomy, with care to preserve the peroneal artery and blood supply to the fibula. The posterior flap is then completed. Next, the facing portions of the tibia and fibula are trimmed parallel to accept the fibula bone bridge. The bone graft is affixed either with screws or permanent sutures. A myodesis of the soleus and gastrocnemius to the anterior tibia is completed before reapproximating the soft tissue and skin in two layers.³⁶⁻³⁸ The drawbacks of this operation are: (1) technical complexity; (2) increased length of operation; and (3) the need to postpone weight bearing until the bone graft is well healed (several weeks). The superiority of this technique over traditional transtibial amputation has not been proven,^{39,40} although one series of 32 patients receiving bone bridging of the distal tibia and fibula showed an improved quality of life with improved ambulation and decreased patient frustration.⁴¹

Guillotine Amputation

Patients presenting with severe infection may warrant an initial “debriding” amputation to obtain source control. Revision and flap closure are completed once the patient’s condition is

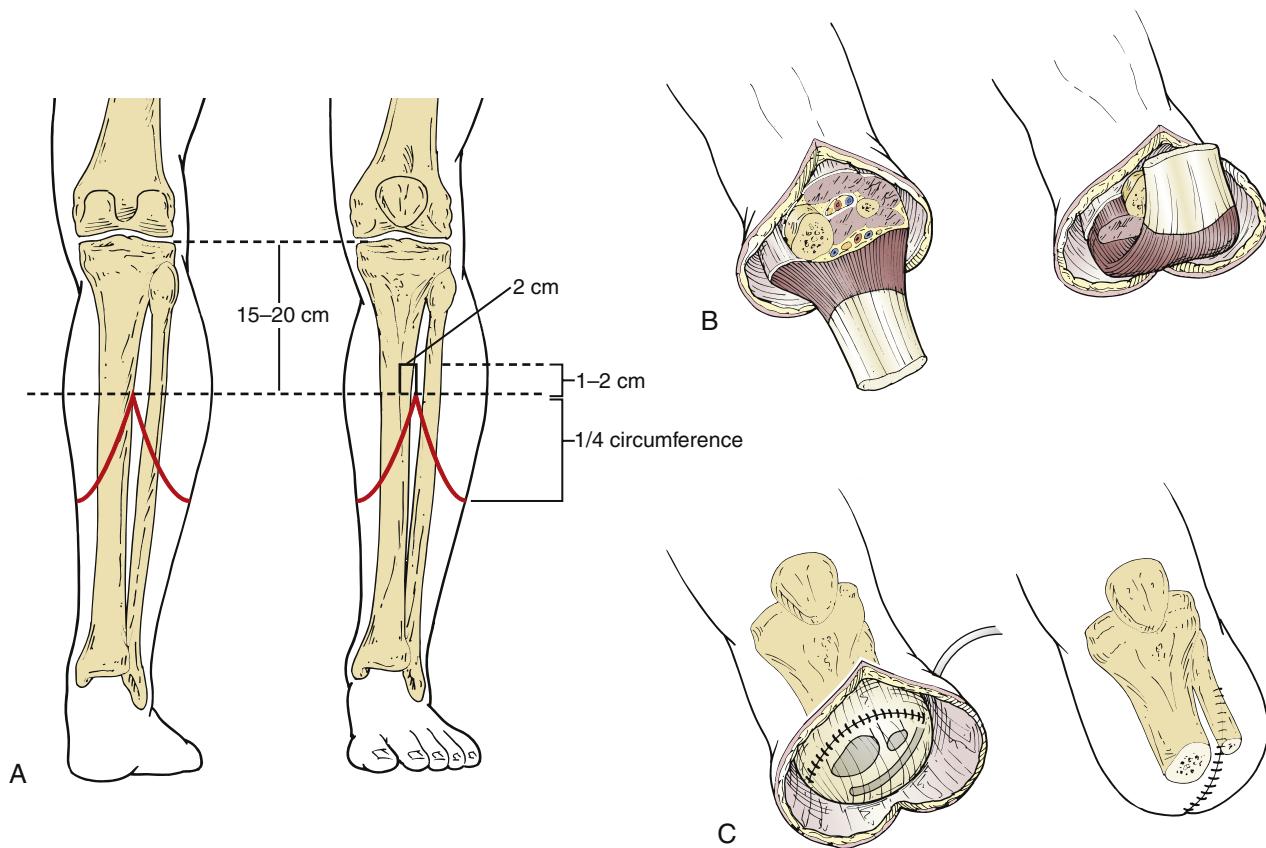


Figure 115.9 Skew Flap. (A) The incisions result in equal anteromedial and posterolateral skin flaps. The tibia is transected to 10–12 cm distal to the joint line. (B) The gastrocnemius muscle flap covers the tibia. (C) The skin is closed with nonabsorbable sutures.

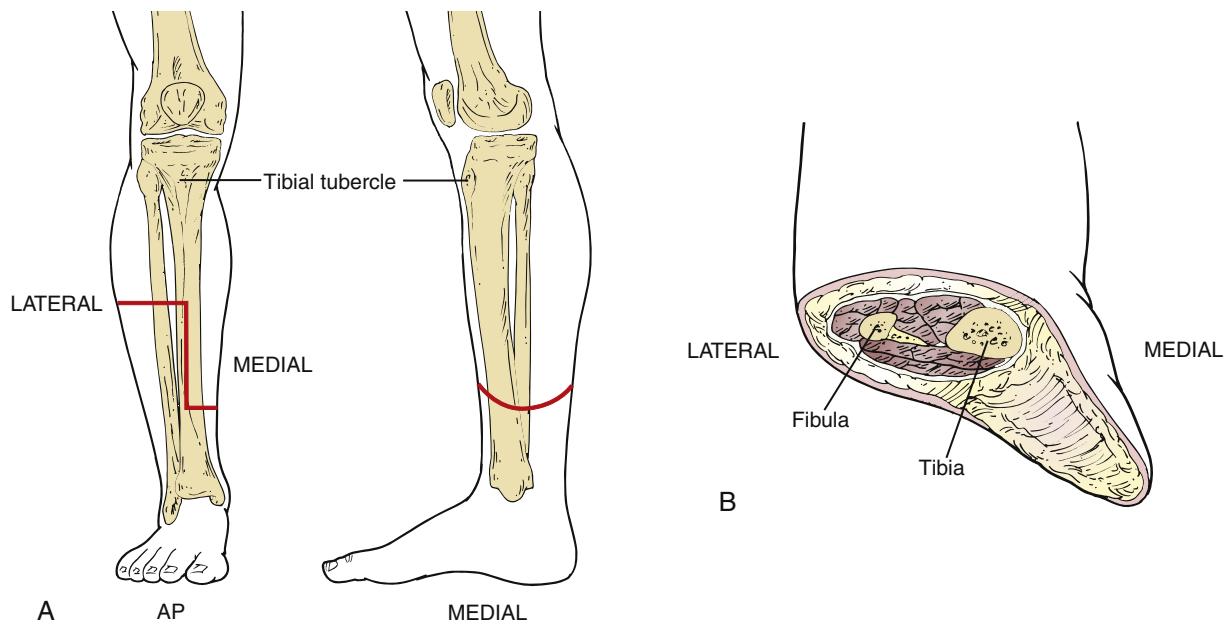


Figure 115.10 (A) Skin incision for a medially based flap. (B) View of the flap after transection. AP, anteroposterior.

more favorable. The literature is mixed regarding the benefit of a two-stage amputation for sepsis. One small trial showed improved results with a two-stage amputation⁴ whereas another trial showed no advantage over using skin wicks in a single stage.⁵

Cryoamputation

Cryoamputation is reserved for patients too ill for anesthesia and may be a treatment for severe gangrenous infection, severe ischemia, or myonecrosis. A tourniquet is applied proximally, and dry ice is packed around the limb. By physiologically

isolating the limb, toxic byproducts and organic acids cannot circulate systemically. After the patient's status improves, a surgical amputation can be completed. Cryoamputation has been associated with improved mortality in comparison with emergency amputation in the frail and elderly.^{42–44} Complications include migration of the frost line above the intended level of amputation and a substantial need for revision.⁴⁵

Postoperative Considerations

There is a tendency for the patient to flex the knee joint postoperatively due to pain, and over time a flexion contracture may occur without proper care. A knee immobilizer (favored by some and reviled by others) may reduce the incidence of contractures and provides some degree of protection in case of falls. Care must be used to avoid excessive pressure on the patella to avoid skin abrasion/ulceration.

Primary healing fails in 20% to 30% of patients. Nehler et al. found only 55% of transtibial amputations were completely healed at 100 days, increasing to 83% at 200 days.⁴⁶ Furthermore, approximately 20% of patients undergoing transtibial amputation need a higher-level amputation.^{46,47}

THROUGH-KNEE AMPUTATION

Anatomy

Through-knee amputation requires the removal of the tibia, fibula, and articular surface of the distal femur. Of particular note is the treatment of the patellar ligament (also known as

the patellar tendon), cruciate ligaments, and tendons of the hamstring muscles, because these structures are sutured to each other (myoplasty) in a through-knee amputation. The patellar ligament is an extension of the quadriceps tendon, which stabilizes the patella and attaches distally to the tibial tuberosity. The hamstring tendons collectively are derived from the semitendinosus, semimembranosus, and biceps femoris muscles.

Technique

In patients with good rehabilitation potential who are not suitable candidates for transtibial amputation, a through-knee amputation may be an acceptable alternative. Through-knee amputation offers higher rates of successful ambulation when compared with transfemoral amputation. Some have actually advocated for primary through-knee amputation rather than transtibial amputation in selected patients.⁴⁸ However, 10% to 15% of patients undergoing through-knee amputation will require a higher level of amputation.⁴⁹

We recommend a technique originally described by Mazet in which the distal femur is preserved and condyles are trimmed squarely (Fig. 115.11).^{50,51} An alternative is the modified Gritti–Stokes amputation, which involves transection of the articular head of the femur with preservation and fixation of the patella as an end-cap to the leg. A fish-mouth incision is fashioned with its corners at the level of the mid condyles of the femur. The anterior flap is extended to the level of the tibial tuberosity and the posterior flap is extended to be the same length. Next, the skin is incised and the medial and lateral collateral ligaments are divided. The patellar ligament is

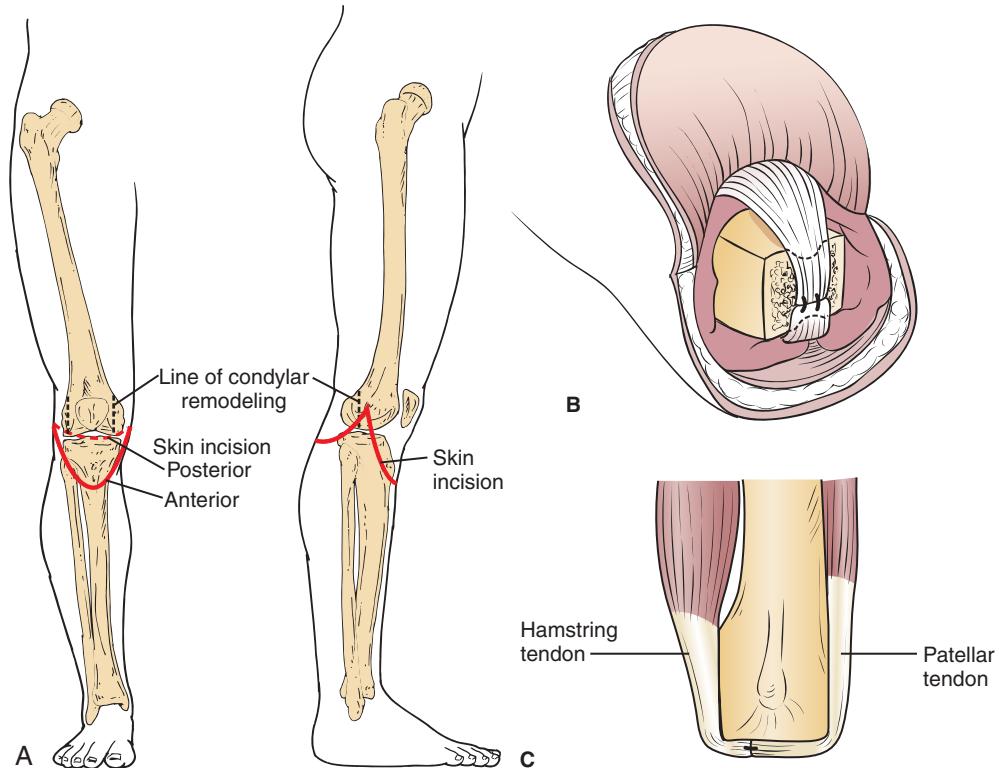


Figure 115.11 (A) Fish-mouth incision for through-knee amputation. (B and C) The patellar tendon is sutured directly to the residual cruciate ligament.

divided from its attachment to the tibial tuberosity, preserving its length and then it is retracted proximally. The skin and deep fascial elements are dissected off the knee capsule before excising the knee capsule and dividing the cruciate ligaments. The popliteal artery and veins are suture ligated, and the common peroneal and tibial nerves are transected sharply under tension and allowed to retract. The popliteus and gastrocnemius muscles are divided along with the remaining tendons from their insertion sites; then the leg is removed. By dissecting very closely to the patella during its removal, the anterior skin flaps are preserved and buttonholing is avoided.

After the knee joint is disarticulated, the goal is to create a flat weight-bearing surface for prosthetic fitting. The menisci are removed, and the lateral one-third of the lateral condyle and medial half of the medial condyle of the femur are trimmed using a bone saw. The posterior surface is squared. The edges are smoothed with a rasp or bone saw. Next, the hamstrings are approximated to the patellar ligament while incorporating the cruciate ligaments in the bite. Finally, the fascia and skin are closed in two layers.

TRANSFEMORAL (ABOVE-KNEE) AMPUTATION

Anatomy

The thigh has three muscle groups: anterior, middle, and posterior. The anterior muscle group consists of the quadriceps femoris, sartorius, and tensor fascia latae. The medial group consists of the adductor longus, brevis and magnus, gracilis, and pectineus muscles. Posteriorly are the hamstrings: biceps femoris (long and short heads), semitendinosus, and semimembranosus. Of note, the adductors insert into the postero-lateral femur along the linea aspera. The adductor magnus also inserts onto the adductor tubercle, a bony prominence on the medial epicondyle of the femur.

Technique

The femur is typically divided at the junction of the middle and distal one-third, or approximately 12 cm proximal to the femoral condyles, but if necessary division can be more proximal as long as tissue coverage exists. A fish-mouth incision is used, creating equal anterior and posterior flaps, although orientation can be varied (Fig. 115.12). After incising the skin and soft tissue, the superficial femoral artery and femoral vein are divided and controlled with suture ligature. The muscles are divided in the same plane, unless intending to perform a myodesis (see later). The femur is transected proximal to the corners of the fish-mouth incision using a mechanical saw and rough edges are filed as needed. The sciatic nerve is stretched, divided, and allowed to retract.

There is a tendency for the hip flexors to abduct and flex the thigh because the adductor muscles are no longer attached and able to oppose this motion. After creating flaps and incising the skin and soft tissue, muscles are then identified. The quadriceps is detached proximal to the patella, leaving some

of its tendinous portion intact. The vastus medialis is reflected laterally off the intermuscular septum to expose the adductor magnus. The adductor magnus is sharply divided at its attachment to the adductor tubercle on the medial epicondyle and it is reflected medially to expose the femoral shaft. The vessels traversing the Hunter canal are ligated. The remaining gracilis, sartorius, semimembranosus, and semitendinosus are divided approximately 1 to 2 cm distal to the point of transection of the femur. The femur is exposed and cut with a mechanical saw, two to three holes are drilled into the lateral cortex, and one to two holes drilled into the posterior cortex of the remaining femur, approximately 1 to 2 cm from its end. The adductor magnus is wrapped over the end of the bone, with the femur held in maximal adduction then anchored using the lateral holes. Anterior and posterior sutures are used to prevent the muscle from sliding off the bone. The quadriceps muscles are wrapped over the end of the femur and sutured posteriorly, and the remaining posterior muscles are anchored posteriorly to the newly affixed adductor magnus.^{52,53} Although reliable studies of myodesis have not been performed, it may benefit patients more likely to ambulate with an above-knee prosthesis.

Postoperative Considerations

The threat of wound contamination is of higher concern with transfemoral amputation. Dressings are left in place at a minimum of 4 to 5 days unless clinically compelled to remove earlier.

Patients with above-knee amputation (AKA) use 50% more energy to ambulate than those with below-knee amputation (BKA), and less than 10% of elderly vascular amputees ambulate effectively after transfemoral amputation.⁵⁴

HIP DISARTICULATION

Anatomy

The hip joint is a ball-and-socket joint stabilized by a fibrous capsule, acetabular labrum, ligament of the head of the femur, iliofemoral, ischiofemoral, pubofemoral, and transverse acetabular ligaments. Anterior to the hip joint are the rectus femoris, iliopsoas, and pectineus muscles. Anterior to these muscles are the tensor fascia lata and sartorius. Posterior to the joint are the piriformis muscle, obturator internus and externus, superior and inferior gemelli, and quadratus femoris. These are among the other muscles of the hip and thigh not immediately adjacent to the hip joint also associated with ambulation.

Technique

The patient is positioned in a semilateral position. An anterior racket incision or a long posterior flap incision may be used (Fig. 115.13).⁵⁵ The anterior racket incision starts 2.5 cm medial to the anterior superior iliac spine, extends toward the pubic tubercle, and continues posteriorly distal to the ischial tuberosity and gluteal crease. The incision is continued

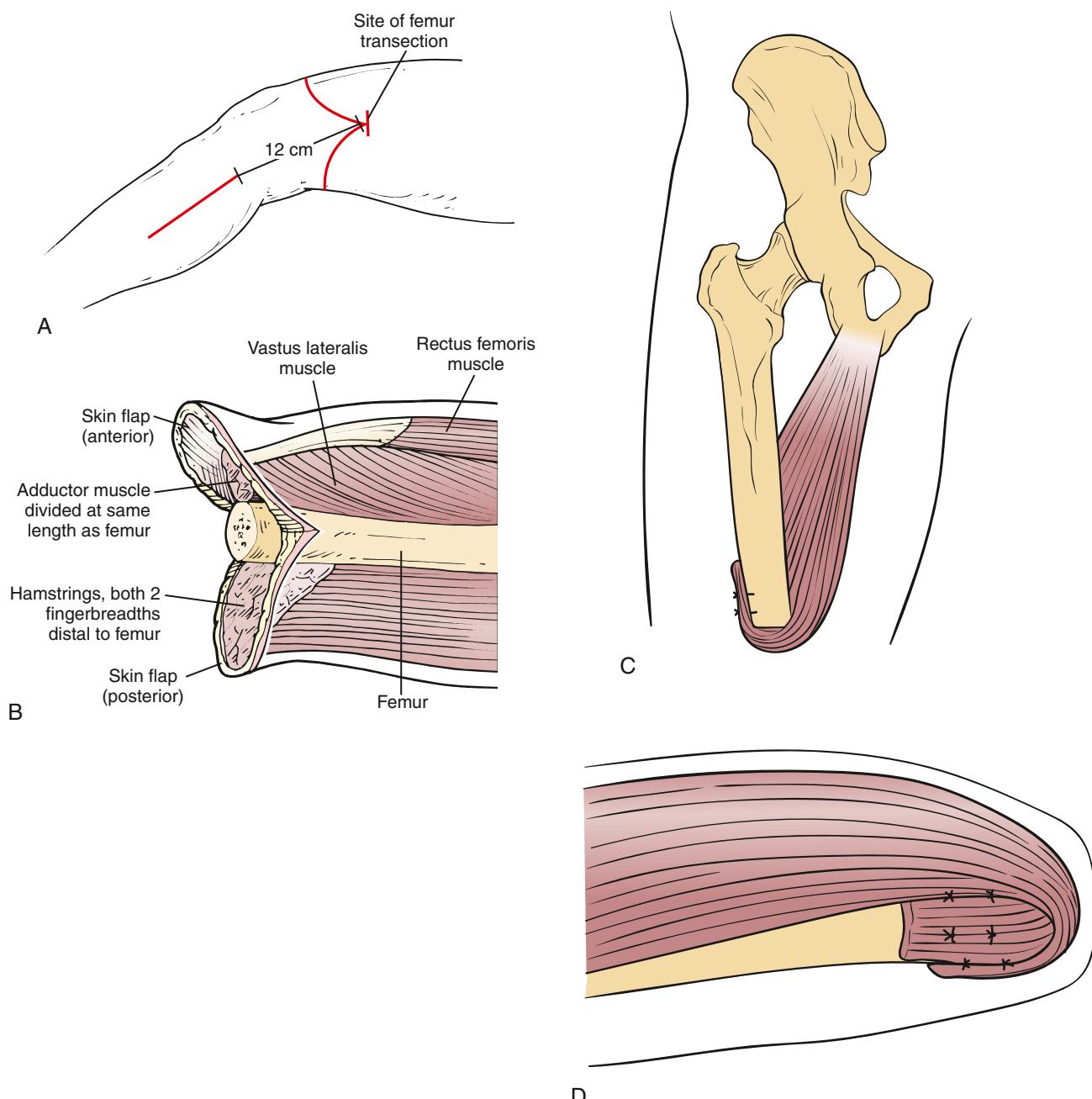


Figure 115.12 (A) Fish-mouth incision for long transfemoral amputation. (B) Cutaway view of transfemoral amputation. (C) Fixation of adductor magnus to the distal femur, performed in maximum adduction. (D) The quadriceps muscle is then anchored to the distal femur with the hip extended.

anteriorly, medial to the greater trochanter and the anterior inferior iliac spine before joining the incision at its origin. The skin and soft tissues are incised down to the external oblique aponeurosis and deep fascia of the thigh. The femoral vessels are suture ligated and the femoral nerve transected and allowed to retract. Next, the muscles of the hip joint are divided, starting with the sartorius at its origin and iliopsoas at its insertion site. The pectineus is divided at its origin on the superior pubic ramus. The gracilis muscle and three adductors are divided at their origins on the pubic rami. The obturator neurovascular bundle is divided, and the obturator externus muscle is divided from its insertion to the trochanteric fossa. The hamstrings are

transected at the ischial tuberosity before dividing the tensor fasciae latae, gluteus maximus, and rectus femoris before dividing the remaining muscles attached to the greater trochanter. To complete the amputation, the ligamentous attachments and capsule of the hip joint are divided. The sciatic nerve is transected and allowed to retract and the specimen is passed off. The posterior quadratus femoris is sutured to the anterior iliopsoas and the lateral gluteus medius is sutured to the medial obturator externus. One may elect to place closed suction drains in the subcutaneous space. Closure is in two layers: the gluteal fascia is approximated to the inguinal ligament and the skin is closed loosely with staples.⁵⁵

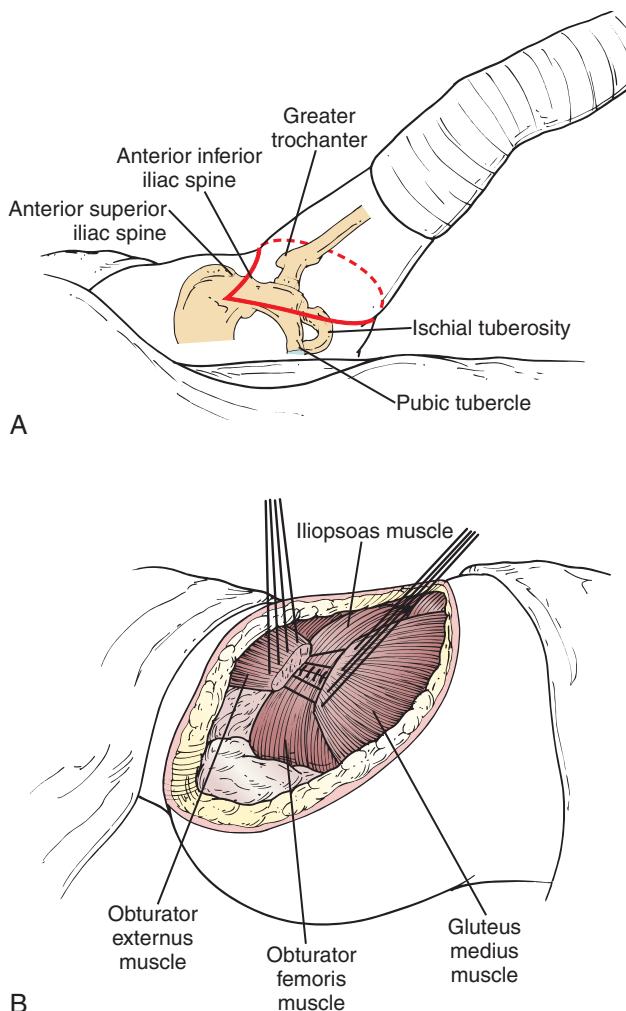


Figure 115.13 (A) Racket incision for hip disarticulation. (B) Two-layer myoplasty over the acetabulum.

Dressings

The choice of postoperative dressings should be based on the simultaneous goals of protecting the wound from stool and urine soiling, preventing injury from falls and absorbing drainage. We have found the use of vacuum sponge (Prevena) systems to be very effective. An alternative for very proximal amputations (AKA and hip disarticulation) is to use iodine-impregnated adhesive dressing.

PRINCIPLES OF POSTOPERATIVE CARE

In our practice, operative dressings are left in place for 5 days unless a clinical indication (e.g., fever, bleeding) warrants removal.^{56,57} Some advocate for application of an immediate postoperative prosthesis (IPOP), reporting effective prosthetic ambulation at an earlier time when compared with conventional practice.^{58,59} Drawbacks of IPOP include the need for a skillful multidisciplinary team, its lack of being universally available, and the inability to examine the wound when in place.^{57,60,61}

Attention should be paid to control of blood sugar in the physiologic range and to maintaining adequate nutrition.

Operative Mortality

In the modern era, 30-day operative mortality ranges from about 2% to 20% for major lower extremity amputations.^{2,62–65} For minor amputations at the ankle or below, operative mortality drops to 2%–4%.^{46,47,66,67} Most lower extremity amputations are performed for ischemia and diabetes, with trauma and malignancy accounting for less than 10% each.^{68–70} The most common causes of death following lower extremity amputation are cardiac complications (46%), sepsis (14%), and pneumonia (11%).⁷¹ Overall 30-day mortality in two large retrospective studies was approximately 12% after AKA and 6% after BKA.^{65,71} Mortality following amputation has not changed significantly in the modern era despite improvements in anesthetic and critical care (Fig. 115.14).⁷²

Many additional observational studies have sought to identify the predictors of operative mortality after lower extremity amputation. A study of more than 9000 patients used the ACS NSQIP database to perform a retrospective review of BKA and AKA patients.⁶⁵ In patients undergoing AKA, 30-day mortality was more often associated with the following risk factors in decreasing order: hemodialysis dependence, thrombocytopenia, total dependent functional status, age greater than 80 years, steroid use, congestive heart failure, preoperative sepsis, body mass index less than 18.5 kg/m², and dyspnea. In patients undergoing BKA, 30-day mortality was more often associated with the following risk factors, in decreasing order: age greater than 80 years, DNR status, hemodialysis dependence, totally dependent functional status, sepsis, and thrombocytopenia.⁶⁵ In another study of 30-day mortality after BKA, renal failure increased the risk of death by more than threefold to 62%.⁷³ Guillotine amputation for sepsis was associated with a 14.3% mortality compared with 7.8% in patients undergoing elective amputation.⁶¹

The most recent retrospective study of 30-day mortality for AKA and BKA included over 14,000 male patients within the Veterans Affairs Surgical Quality Improvement Program data set and established a weighted risk score for perioperative mortality with the lowest risk patients having a 30-day mortality of 2.2% and the highest risk patients having a 30-day mortality of 19.8% percent. The variables with the highest weighted risk score included "do not resuscitate" status and severe congestive heart failure. Other variables included age greater than 80, creatinine greater than 1.5 g/DL, AKA (vs. BKA) and dependent living status. Coronary artery disease and chronic obstructive pulmonary disease without other risk factors placed patients into a low-risk low-mortality group in this study.⁷⁴

LONG-TERM SURVIVAL

The prevalence of major lower extremity amputation attributable to vascular disease in the United States was approximately 500,000 in 2005, with an expected increase by 50% by the year 2020.⁷⁵ One-year survival rates are lower in patients receiving a higher-level amputation (Table 115.1). The approximate 1-year survival following BKA is 65% to 80% versus 50% following AKA (Fig. 115.15).^{47,64,71,72,76} From another perspective, the median survival was reported as 1 year for transfemoral

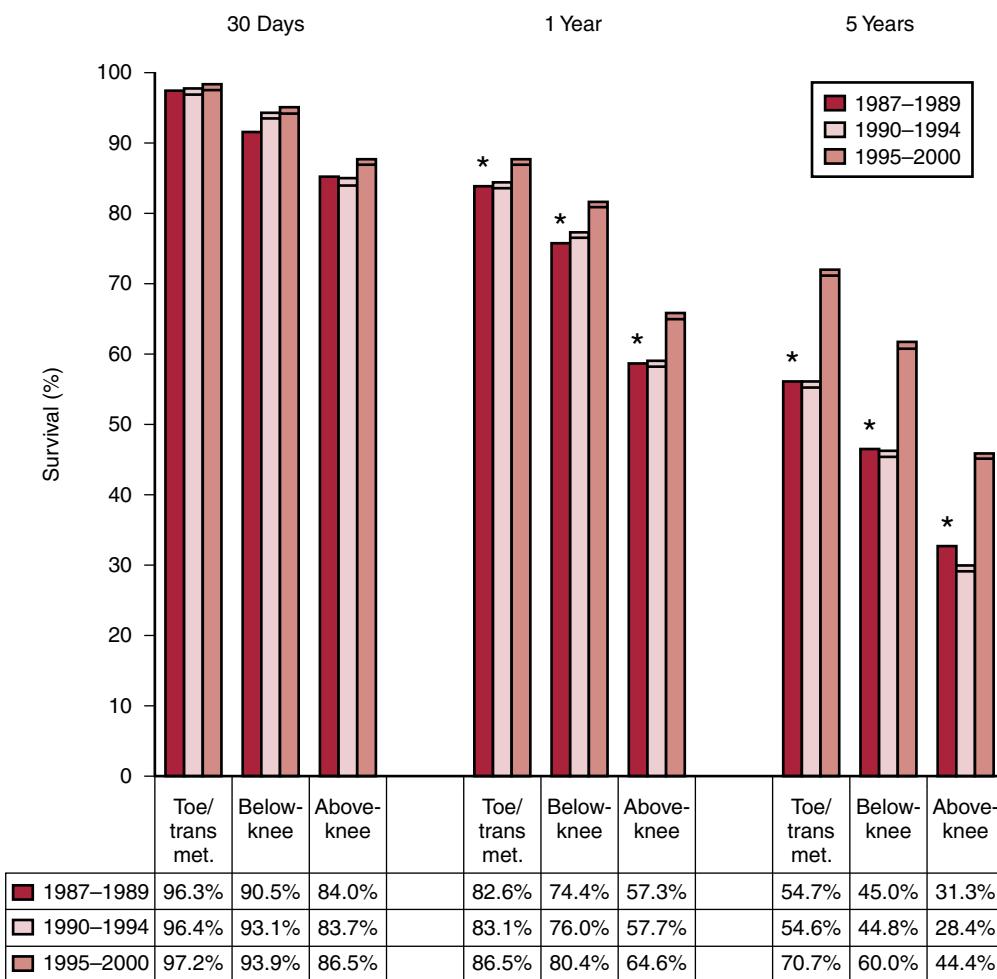


Figure 115.14 Bar graph showing survival at 30 days, 1 year, and 5 years following foot (toe/transmetatarsal), below-knee, and above-knee amputations during three periods (1987–1989, 1990–1994, and 1995–2000). (* $P < 0.001$ when post-1995 is compared with pre-1995.) (From Sandnes DK, Sobel M, Flum DR. Survival after lower-extremity amputation. *J Am Coll Surg*. 2004;199:394–402.)

amputation and 2.4 years for transtibial amputation.⁷⁷ Predictably, patients with diabetes and renal failure fare worse.^{71,77} Of 390 British patients undergoing lower extremity amputation, diabetic patients' median time to death was 27.2 months versus 46.7 in nondiabetics.⁷¹ Amputation patients on dialysis had a 1-year survival of 51.9%, amputation patients not on dialysis but with a serum creatinine greater than 2 mg/dL had a 1-year survival rate of 55.9%, and non-dialysis-dependent patients had a 1-year survival rate of 75.4%.⁷¹ Overall, long-term survival has improved following major lower extremity amputation.^{62,72}

FUNCTIONAL OUTCOME

After toe, ray, and transmetatarsal amputations, near-normal ambulation with conventional footwear is likely. Shoe fillers and simple orthoses allow for ambulation in a majority of patients.^{12,17,66,67,78,79}

Following transtibial amputation for vascular disease, bipedal ambulation with a prosthesis is unfortunately not universal. Two recent reports indicate only approximately 25% of major lower extremity amputees ambulate with a prosthesis

outside the home.^{46,80} These patients were unable to use a prosthesis for a variety of reasons, including mental illness, cardiopulmonary insufficiency, inadequate balance, and stump problems.^{46,81} A prospective study of 297 patients reported that those who received care in an acute inpatient rehabilitation facility had better functional outcome at 6 months than patients who were treated at home or in a skilled nursing facility.⁸² Taylor and coworkers identified significant preoperative factors independently associated with not wearing a prosthesis. In order from greatest to least risk, these patients were nonambulatory before amputation (odds ratio [OR] 9.5), AKA (OR 4.4), homebound but ambulatory (OR 3.0), older than 60 years (OR 2.8), diagnosed with dementia (OR 2.4), end-stage renal disease (OR 2.3), or coronary artery disease (OR 2.0).⁸³ Older transfemoral amputees rarely (<10%) ambulate successfully with a prosthesis.^{46,80,84} Dialysis-dependent renal failure is a strong predictor of nonambulatory status.

Despite the fact that few vascular amputees ambulate with a prosthesis outside the home, most maintain their preoperative living status. Highly motivated patients – as evidenced by a commitment to a strict rehabilitation program, including smoking cessation and weight loss – are more likely to

TABLE 115.1 Thirty-Day Mortality, 1-Year Survival, and Reamputation Rates

Series	Year	Number of Patients	30-DAY MORTALITY (%)		1-YEAR SURVIVAL (%)		REAMPUTATION RATE	
			BKA ^a	AKA ^a	BKA	AKA	BKA to AKA (%)	Contralateral Major Amputation (%)
Kazmers ^b	2000	8696	9.4	16.1				
Feinglass et al. ^c	2001	4061	6.3	13.3	77	59		
Mayfield et al. ^d	2001	5180	7.0	11.1				
Abou-Zamzam et al. ⁶³	2003	131					19.6	10.7 (at 3 years)
Nehler et al. ⁴⁶	2003	172					19	
Cruz et al. ⁸⁴	2003	296	12	17			12	17 (at 7 years)
Aulivola et al. ⁷¹	2004	959	5.7	16.5	74.5	50.6	9.4	19.8 (at 11 years)
Sandnes et al. ⁷²	2004	6919	6.1	13.5	80.4	64.6		
Subramaniam ^e	2005	954	4.2	17.5	78.2	62.1		
Ploeg et al. ⁶⁴	2005	122	5.2	17.8			14.3	
Dillingham et al. ⁴⁷	2005	3565			64.5	49.6	9.4	9.4 (at 1 year)
Stone et al. ¹⁹	2007	508	3.6	13.6			11.5	21 (at 5 years)
Nelson et al. ⁶⁵	2012	9368	6.5	12.8				

^aAKA, above-knee amputation; BKA, below-knee amputation.

^bKazmers A, Perkins AJ, Jacobs LA. Major lower extremity amputation in Veterans Affairs Medical Centers. *Ann Vasc Surg*. 2000;14:216–222.

^cFeinglass J, et al: Postoperative and late survival outcomes after major amputation: findings from the Department of Veterans Affairs National Surgical Quality Improvement Program. *Surgery*. 2001;130:21–29.

^dMayfield JA, et al: Survival following lower-limb amputation in a veteran population. *J Rehabil Res Dev*. 2001;38:341–345.

^eSubramaniam B, Pomposelli F, Talmor D, Park KW. Perioperative and long-term morbidity and mortality after above-knee and below-knee amputations in diabetics and nondiabetics. *Anesth Analg*. 2005;100:1241–1247.

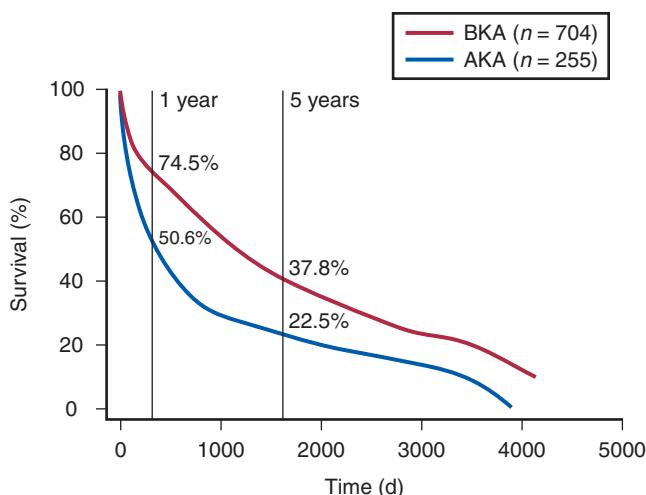


Figure 115.15 Long-term survival following below-knee amputation (BKA) and above-knee amputation (AKA). (From Aulivola B, Hile CN, Hamdan AD, et al. Major lower extremity amputation: outcome of a modern series. *Arch Surg*. 2004;139:395–399.)

achieve long-term success.⁸⁵ In addition, patients with financial resources that allow participation in a well-organized rehabilitation program are more likely to be successful. Taylor and coworkers identified the following statistically significant preoperative factors that were independently associated with a failure to maintain an independent living status (in decreasing

order of influence): age 70 years or older (hazard ratio [HR] 4.0), age 60 to 69 years (HR 2.7), level of amputation (HR 1.8), homebound ambulatory status (HR 1.6), and dementia (HR 1.6).⁸³ In the United States, Medicare reimbursement for a prosthesis is based on adequate patient motivation as well as the ability to achieve a defined functional state classified as a “K level” (Table 115.2).⁸⁶

REAMPUTATION

Following an initial toe amputation, approximately 50% of patients eventually undergo additional ipsilateral or contralateral amputations. Following foot or ankle amputation, nearly 35% of patients progress to a higher-level amputation within 1 year.⁴⁷ Wound problems develop in 20% to 30% of patients following transtibial amputation.^{46,71,84} Only half of these amputations are salvaged at the transtibial level. In addition, reamputation to the transfemoral level has been reported in 9.4% to 19.6% of prior transtibial amputees.^{46,47,63,64,71,84} It has also been reported that 9.4% to 17% of transtibial amputees undergo contralateral major amputation within as little as 12 months.^{47,63,71,84,87} Not surprisingly, the risk of ipsilateral reamputation at a higher level is inversely related to the level of the index amputation. Diabetic patients are almost twice as likely to have reamputation as are nondiabetic patients.^{76,88} The 1-, 3-, and 5-year ipsilateral reamputation rate for diabetic

TABLE 115.2

K Levels, A Classification System Created by the US Centers for Medicare and Medicaid Services Used to Stratify Potential Functional Ability in Amputees

Level 0:	Does not have the ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility.
Level 1:	Has the ability or potential to use a prosthesis for transfer or ambulation on level surfaces at fixed cadence. Typical of the limited and unlimited household ambulator.
Level 2:	Has the ability or potential for ambulation with the ability to traverse low level environmental barriers such as curbs, stairs or uneven surfaces. Typical of the limited community ambulator.
Level 3:	Has the ability or potential for ambulation with variable cadence. Typical of the community ambulator who has the ability to traverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic use beyond simple locomotion.
Level 4:	Has the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels. Typical of the prosthetic demands of the child, active adult, or athlete.

patients are as follows: for toe amputees, 22.8%, 39.6%, and 52.3%, respectively; for ray amputees, 28.7%, 41.2%, and 50%, respectively; for midfoot amputees, 18.8%, 33.3%, and 42.9%, respectively; and for major amputees, 4.7%, 11.8%, and 13.3%, respectively. In a study analyzing factors that predict long-term resource use and survival after major amputation, the authors noted that complicated diabetes, renal failure, and undergoing index BKA were all associated with increased additional amputation-related procedures.⁸⁹

COMPLICATIONS

Local

Bleeding

Reoperation for postoperative bleeding is reported in 3% to 8% of major lower extremity amputations.^{46,62} Frequently, patients undergoing dysvascular amputations are on antiplatelet therapy, which may increase the likelihood of developing a hematoma. Despite this elevated risk, patients should still receive DVT prophylaxis, unless contraindicated.

Infection

The likelihood of wound infection following major lower extremity amputation ranges from 13% to 40%.^{5,9,90} An increased risk of wound infection is associated with diabetes, preoperative wound infection, malnutrition, malignancy, advanced age, lack of insurance, wound hematoma, and prior prosthetic bypass grafts. Complete removal of synthetic graft material at the time of amputation can decrease the rate of stump infection.⁹¹ A recent study reported wound infection or disruption in healing to be 10.4% after BKA and 7.2%

after AKA. In this study, patients with elevated international normalized ratio (INR) and patients aged 50 to 59 were more likely to develop wound complications after a BKA, whereas current smokers and obese patients were more likely to develop wound complications after AKA.⁹²

Superficial infections can initially be treated by administration of broad-spectrum antibiotics and removal of skin sutures. Deeper infections necessitate more aggressive drainage and debridement. Vacuum dressings may be particularly effective in this setting.²²

Direct falls onto an amputation stump may result in hematoma, infection and wound dehiscence requiring operative re-intervention or higher level of amputation. Ancillary services including physical and occupational therapy, in addition to adequate patient supervision remain important to ensuring an optimal outcome.

Contracture

Flexion contractures at the hip and knee joint develop in 3% to 5% of major lower extremity amputations. A fixed flexion contracture at the knee that exceeds 15 degrees prohibits effective prosthetic ambulation. After a significant contracture develops, it may be impossible to correct with physical therapy or surgery.⁹³ A rigid, removable dressing should be applied to prevent knee contractures. An aggressive postoperative knee exercise program should be initiated as soon as possible. Hip flexion contracture may be limited by positioning the patient in the prone position for brief periods.

Systemic

Cardiac and Pulmonary

Myocardial infarction remains the most common cause of death following lower extremity amputation. In a study of 788 patients, 10.2% of patients experienced a cardiac complication: congestive heart failure (4.2%), myocardial infarction (3.4%), and arrhythmia (2.6%).⁷¹ Antiplatelet agents and statins should be continued perioperatively, and one should aim to maintain adequate perfusion while avoiding over-resuscitation in the perioperative and postoperative phases. Clinical suspicion of an adverse cardiac event should remain high.

Following amputation, patients are at risk for respiratory complications, including pneumonia.

Venous Thromboembolism

Following lower extremity amputation, the risk of DVT is up to 50%.^{10,94–96} Low-molecular-weight heparin administered prophylactically lowers this risk to 10%. It is our practice to prefer low-molecular-weight heparin for chemoprophylaxis, although unfractionated heparin is preferred in patients with severe renal impairment or weight less than 45 kg.

Renal Failure

Acute blood loss, general anesthesia, and any other cause for hypotension and end-organ malperfusion may put the patient at risk for acute kidney injury. New-onset renal failure following amputation ranges from 0.6% to 2.6%.^{46,71}

Stroke

The incidence of stroke after major amputation ranges from 0.28% to 1.4%.^{46,62} Stroke is a rare cause of perioperative death behind infection, cardiac event, and pulmonary embolus.⁹⁷

Psychiatric

Posttraumatic stress disorder is common (20%–22%) after amputations for combat or accidental injuries. For vascular amputations the incidence is less than 5%. Risk factors for major depressive disorder include young age at the time of amputation, pain, neurotic personality, unhealthy lifestyle, and poor coping skills.^{98,99} In addition, 16% of a sample of 239 patients undergoing vascular disease-related amputation experienced suicidal ideation.¹⁰⁰

Pain

Chronic pain is reported by up to 95% of amputees.¹⁰¹ Pain may be confined to the residual limb or may be perceived as so-called phantom pain originating from the amputated extremity. Ischemic stump pain must be differentiated from pain due to musculoskeletal (e.g., bone spurs, chronic osteomyelitis) or neurologic sources (e.g., neuroma or neurospinal pain). Chronic ischemic stump pain may be difficult to detect by physical examination alone but is confirmed by a transcutaneous oxygen tension less than 20 mm Hg. Chronic infection, particularly related to residual prosthetic graft material, may also cause pain. Neuroma can develop at the site of transection of virtually any peripheral nerve. The pain is usually well localized and can be transiently or permanently blocked with anesthetic injection. Pressure points that develop over bone spurs or pathologic bone formation should be eliminated. Depression appears to complicate the treatment of pain in many amputees.¹⁰¹

True phantom pain is a complex, poorly understood pain syndrome. The incidence of phantom pain widely varies in the literature from 5% to 85%, depending on the diagnostic criteria.^{102,103} Inadequate control of both preoperative and postoperative pain may increase the risk of chronic amputation pain.¹⁰⁴ Gabapentin may be effective as a component of multimodality treatment of phantom pain.

Recently, Targeted Muscle Reinnervation (TMR) has been recommended to improve residual limb function and prosthetic use, and to decrease phantom pain.¹⁰⁵ The technique, which may be performed at the initial amputation or as a secondary surgery, involves co-apting major nerves such as the tibial nerve to a functional muscle.^{105–107} Although larger datasets are warranted, early reports indicate reduced residual limb pain and improved prosthetic use. Multimodality pain management is the cornerstone of a successful amputation rehabilitation program.¹⁰⁸

LOOKING AHEAD

Despite our increased understanding of surgical technique and outcomes, a true replacement for an amputated limb or digit

is still not within sight. At present, artificial intelligence is being explored to better predict appropriate level of amputation in ischemic limbs.¹⁰⁹ Prosthesis technology is continuing to improve and the concept of targeted muscle reinnervation is starting to take hold. A paradigm shift toward functional limb restoration will come about as many disciplines converge upon the centuries-old technique of limb amputation.^{105–107,110–112}

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CHAPTER 116

General Considerations of Diabetic Foot Ulcers

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INTRODUCTION

Diabetes and its subsequent complications, including diabetic foot disease, is a rapidly growing global health pandemic and a major financial burden on healthcare systems worldwide. The International Diabetes Federation estimated that over 463 million people suffer from diabetes in 2020 and that the total number of people with diabetes is predicted to rise to 578 million by 2030 and to 700 million by 2045. China, India and the USA remain the top three countries with the largest number of diabetic patients and diabetes was the seventh leading cause of death in 2010.¹ Diabetes is the leading cause of foot pathology, causing foot ulcerations from neuropathy, infection, and ischemia. Indeed, most nontraumatic amputations in the

United States and Canada are secondary to diabetic foot ulcers.^{2,3} Among people within the United States, up to 15% have active ulcers and 1 in 4 have a lifetime risk of developing a diabetic foot ulcer.⁴ Infection occurs in approximately half of diabetic foot ulcers, and many of these require amputation. As such, diabetic foot ulcers are one of the most costly aspects of diabetes care, and ulcer-related complications are the leading cause of hospitalization for diabetic patients.⁵ Even if a diabetic foot ulcer is treated, the recurrence rate of an ulcer ranges from 35% at 1 year to 77% at 5 years.⁶ This has led to a growing risk of amputation among diabetic patients, because 85% of patients presenting with a nonhealing foot ulcer are at risk for a subsequent amputation.⁷

EPIDEMIOLOGY

Beyond their devastating complications, such as amputation, diabetic foot ulcers have also been associated with poor quality of life outcomes and a significant financial burden, both to the patient and to the economy through direct costs and lost productivity. In 2012 the financial cost of diabetes within the United States was over \$245 billion, including \$176 billion in direct medical costs and \$69 billion in indirect costs related to disability and loss of productivity.⁸ The reduced mobility, multiple prolonged hospitalizations, clinic visits, and the deteriorating quality of life lead to cardiovascular stress and an increased risk of mortality compared with the general population. In fact, patients with a diabetic foot ulcer have an annual mortality rate approaching 10%, with an increase to 20% annually if an amputation is performed. Diabetic patients who undergo amputation have a median incidence of mortality at 27 months postoperatively, compared with 47 months among nondiabetic patients with amputation.⁹ In all, the 5-year relative mortality rate for those with diabetes who undergo a major limb loss is 70%.¹⁰

On average, treating diabetic foot ulcers has been estimated at \$8000 to \$17,000 in medical expenditures and those patients who subsequently undergo an amputation require \$40,000 to \$60,000, depending on the extent of the amputation and the associated hospital stay.¹¹ Limb amputations are also predictors of further deterioration in the patient's health. Among patients who have undergone a major lower extremity amputation, up to 40% will undergo amputation of the contralateral limb within 3 years.¹²

It has been well documented that socioeconomic, racial and ethnic disparities in healthcare exist. This is especially true with regards to the growing rate of diabetes around the world and the disproportionate outcomes between ethnic, racial groups and socioeconomic class. African Americans, Hispanics, and Native Americans have a higher prevalence of diabetes than non-Hispanic whites. Consequently, the incidence of diabetic foot ulcers and amputations are disproportionately higher in African Americans, Hispanics, and Native Americans. In 2008, the incidence of diabetic foot ulcers among Medicare beneficiaries was 6.0% for whites, 6.3% for African Americans, 6.4% for Hispanics, and 7.0% for Native Americans.¹³ The incidence of diabetes-related amputations in African Americans and other minorities was more than double that of whites.¹⁴ Medicare data from 2008 show that American Indian/Alaska Natives had an incidence rate double that of non-Hispanic whites.¹⁵ The level and severity of the amputation was also noted to be more significant between these groups. The lower extremity amputation rate in low-income neighborhoods is almost double that of higher-income neighborhoods.¹⁶ These drastic differences in outcomes is thought to be secondary to more advanced disease upon presentation, more severe comorbidities and access to medical care.

PATOPHYSIOLOGY

The etiology of diabetic foot ulceration is a well-understood, but multifactorial and complex process (Fig. 116.1). Major risk factors associated with diabetic foot ulcer formation are diabetic peripheral neuropathy and peripheral arterial disease (PAD), which act either in isolation or concurrently. Other important

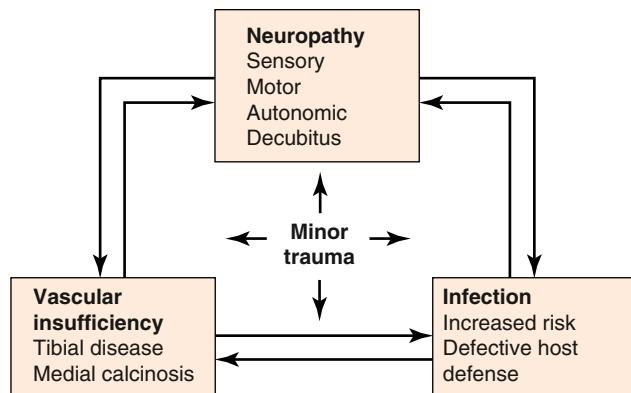


Figure 116.1 Multifactorial Etiology of Diabetic Foot Pathology.

risk factors include soft tissue infection, biomechanical abnormalities, peripheral edema, plantar callus formation, nephropathy, poor glucose control, age, and a prolonged diabetic course.¹⁷ Abnormal foot biomechanics often results from structural foot deformities combined with the limited joint mobility and bony abnormalities found in diabetic patients. Trauma due to poorly fitting footwear also frequently plays a major role in ulcer formation. Ulceration of the heel often combines decubitus or pressure forces with ischemia, resulting in a difficult management issue.

Diabetic Neuropathy

Diabetes results in both somatic and autonomic neuropathy. The onset of somatic neuropathy is insidious and progressive, eventually resulting in the complete loss of foot sensation and placing the patient at a higher risk of unperceived foot trauma and ulceration.¹⁸ Examples include puncture wounds while walking barefoot, burn wounds, and iatrogenic or self-induced trauma while cutting nails or grooming the skin. Furthermore, loss of sensation places the patient at a higher risk of injury when donning improperly fitted shoes.¹⁹ Somatic neuropathy also leads to muscle wasting and eventual flexor-extensor muscle imbalance, weakening of the anterior calf muscles, and the development of an equinus deformity. The forefoot is the most common site of neurotropic ulceration as a result of those diabetes-induced muscle imbalances.²⁰ Patients with isolated diabetic somatic neuropathy have been found to be at a sevenfold increased risk of foot ulceration compared with other patients.²¹

Sympathetic autonomic nerve dysfunction results in reduced sweating accompanied by dry, fragile skin that is at a higher risk of cracking and fissure formation. This neuropathy can also result in arterial-venous shunting and impaired microvascular regulation of the skin.²² As such, the insensitive diabetic foot may appear warm and well perfused, resulting in a false sense of security by both the patient and the provider as to the risk of diabetic ulcer formation.¹⁸

Peripheral Arterial Disease

Arterial disease contributes to the development of 50% of diabetic foot ulcers and plays a role in 70% of the mortality among diabetic patients.^{17,23} Arterial occlusive disease may be present in isolation or in combination with neuropathic disease in up to

TABLE 116.1

Summary of the Classification System of Diabetic Foot Infection by the International Working Group on Diabetic Foot Infection

Grade	Clinical Signs of Infection
1	None
2	Local process involving skin and subcutaneous tissue Erythema (if present) <2 cm No sign of systemic infection
3	Local process deeper than skin and subcutaneous tissue Erythema >2 cm Local abscess, osteomyelitis, septic arthritis, fasciitis No sign of systemic infection
4	Signs of systemic infection (>2 of the following): Temperature >38°C, or, <36°C Heart rate >90 bpm Respiratory rate >20 breaths/min tcPO ₂ <32 mm Hg WBC >12, or >10% bands

Signs of local infection: swelling, induration, erythema, tenderness, warmth, purulent discharge.

45% of lower extremity ulcerations.²⁴ Although femoral artery disease occurs in an equal incidence with the nondiabetic population, infrapopliteal occlusive disease with heavy calcification is the classic picture of diabetic arterial disease. In addition, despite the basement membrane affected at the capillary level in those with diabetes, microvascular disease precluding revascularization in diabetic patients has been disproved. Diabetic patients are at a higher risk of digital artery disease with palpable pedal pulses that nonetheless can result in digital ulceration and subsequent impaired healing and gangrene. Despite the relatively common occurrence of an incomplete pedal arch in diabetic patients, tibial revascularization, especially to the angiosome in which the ulceration is located, is possible in the vast majority of diabetic patients to overcome foot ischemia.²⁵

Soft Tissue Infection

Diabetic foot ulcers may present with or without infection with a classification proposed by the Infectious Diseases Society of America, including a PEDIS (perfusion, extent, depth, infection and sensation) score to guide assessment of severity and subsequent therapy (Table 116.1). A wound culture should be obtained when signs of an infection, such as purulence, cellulitis in the adjacent skin, malodor, and tissue necrosis, are present. However, ulcers that are otherwise clean and free from any local or systemic signs of infection should not be swabbed or cultured.²⁶ In the absence of a clinical suspicion of an active infection, a culture swab will likely report mixed skin flora that are not associated with an active infection, and unnecessary treatments might be prescribed. When a soft tissue culture is desired, samples obtained surgically or by curettage of the wound bed are more sensitive and specific in identifying the causative organisms and guiding therapy than swabbing the wound or drainage. In addition, diabetics have elevated serologic concentrations of adhesion molecules that bind monocytes, leukocytes, and platelets to the endothelium and impair its function, leading to

diminished skin perfusion and healing, resulting in a reduced ability to deliver antibiotics to sites of infection.^{27,28}

Muscle and Bone Abnormalities

The changes in biomechanical forces that result from diabetic bony deformities create points of pressure that may eventually lead to ulceration (Fig. 116.2). These forces, combined with limited joint mobility, lead to structural deformities such as hallux valgus, claw toes, and abnormalities of the metatarsophalangeal joints. This process is exacerbated by neuropathy-induced lack of sensation in the diabetic foot. Muscular weakness can result in functional imbalances between the tendons of the foot with subsequent hammer-toe development that is vulnerable to shoe trauma at bony prominences. The contracted toes also induce increased pressure at the plantar aspect of the metatarsal heads. In addition, Charcot changes and midfoot collapse due to neuro-osteoarthropathy, as well as restricted foot motion due to flatfoot deformities, equinus, and knee or back issues, may all add to the biomechanical stress experienced by the foot, worsen the degree of ulceration, and prevent adequate healing.²⁹

PRESENTATION AND DIAGNOSIS

Patient History

A detailed medical and surgical history should be obtained from every diabetic patient with a foot ulcer to determine how the patient's diabetes is managed, whether the ulcer appeared suddenly or secondary to a traumatic incident, whether the patient traveled recently or acquired new footwear, and to determine the wound's duration and any noticeable changes in its appearance and character. Any previous wounds should also be documented, as well as any wound care treatments that the patient has received. Wounds that are accompanied by systemic symptoms suggestive of infection, such as malaise or cold sweats, should be treated without delay. Risk factors for diabetic foot ulceration, such as a history of peripheral neuropathy, symptoms of arterial disease, and bony deformities, as well as any previous vascular, orthopedic, or plastic surgical interventions, should also be documented.

Physical Examination

The diabetic foot physical examination must include dermatologic, neurologic, vascular, and musculoskeletal assessments (Table 116.2).³⁰ The skin of patients with advanced diabetic disease is usually dry and brittle because of peripheral neuropathy. Areas of hyperkeratosis indicate pressure points that are often accompanied by preulcerative or ulcerative changes (Fig. 116.3). Preulcerative changes may be subtle and can appear as pinpoint hemorrhages or shallow hematomas within the dermis. A waxy appearance of the callus may indicate fluid beneath the lesion and should be palpated for fluctuance. A hyperkeratotic lesion suspicious for underlying ulceration should be sharply debrided to inspect the underlying skin.

Inspection of the foot may reveal the sequelae of motor neuropathy, such as atrophy of the intermetatarsal musculature and

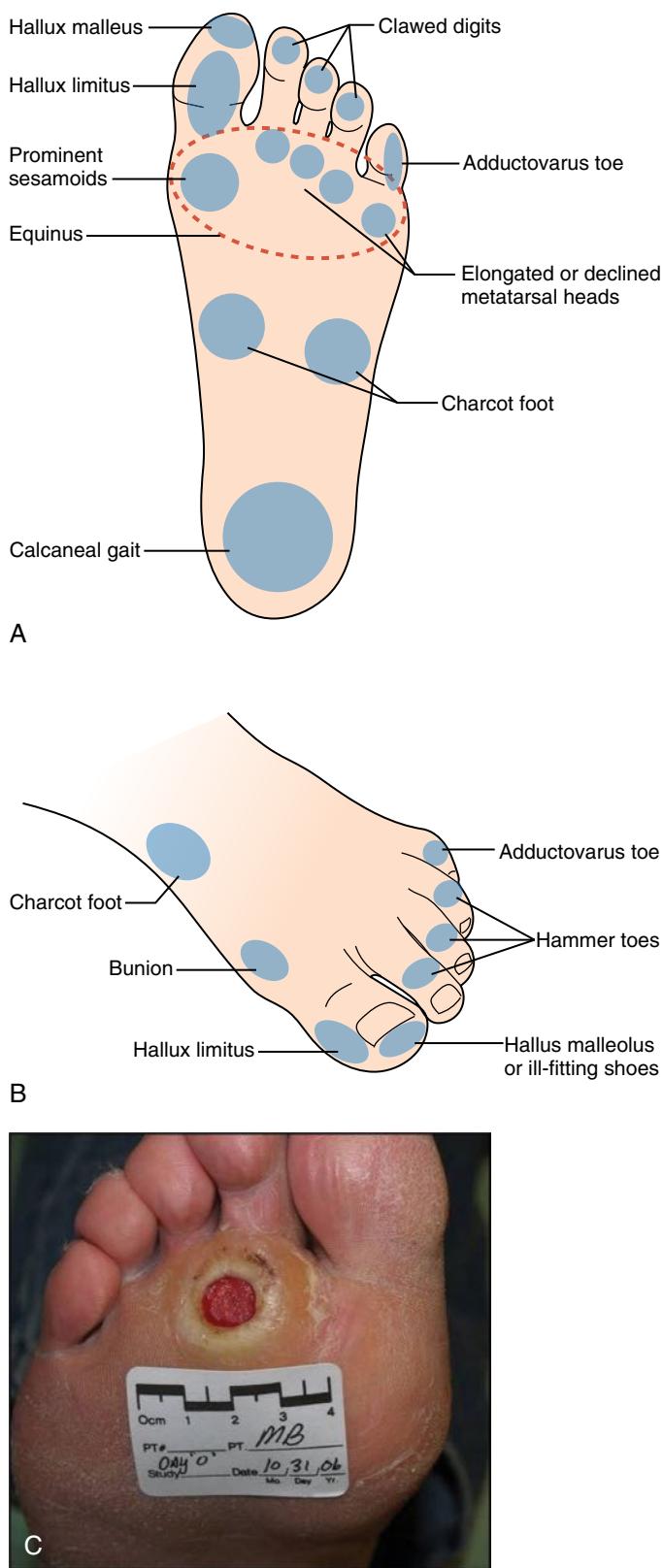


Figure 116.2 Locations of skin lesions on the diabetic foot with corresponding biomechanical etiologies related to the plantar (A) and dorsum (B) surfaces with an example of a diabetic dorsal foot wound (C). (C, Courtesy Vickie Driver, MD)

hollowing of tissue between the metatarsals and arch of the foot. The patient should also be examined for Charcot neuropathic osteoarthropathy, also known as “Charcot foot.” The classic, but late, presentation of a “rocker bottom foot” in these patients creates severe midfoot plantar pressures and subsequent ulceration.³¹ A unilateral, hot, swollen foot should be considered an acute presentation of Charcot foot until proven otherwise.³² Early offloading and immobilization can prevent further damage and prevent a rocker bottom foot (Fig. 116.4). Acute Charcot foot can often be misdiagnosed as cellulitis, osteomyelitis, deep venous thrombosis, or gout.

Sensory testing using a Semmes–Weinstein monofilament (10g) is a predictive and easily reproducible test to assess the neuropathic risk of foot ulceration and amputation in diabetic patients.³³ Failure of the patient to perceive more than 4 or more of the 10 test sites has been associated with a 15-fold increase in the risk of plantar ulceration.³⁴ Testing perception of vibration with a 128-mHz tuning fork is also predictive of ulceration risk, although this test is less reliable than the Semmes–Weinstein test.²¹

Lower extremity arteries, including the femoral, popliteal, and tibial arteries, should be palpated to detect a pulse. However, palpation is affected by factors such as the patient’s body habitus, peripheral edema, and blood pressure fluctuations, as well as the examiner’s level of experience. As such, clinical decision making should not be based solely on the presence or absence of palpable pulses without further noninvasive vascular testing. An ankle–brachial index (ABI) measurement is often obtained at the time of the initial clinical evaluation but may be falsely elevated due to the prevalence of medial arterial calcification in the tibial arteries of the diabetic foot.^{35,36}

Diabetic Ulcer Evaluation and Classification

The diabetic ulcer should be visually inspected for the presence of viable tissue, drainage, purulence, odor, and surrounding erythema. The wound dimensions, location, and the number of ulcers should also be carefully documented. Mixed arterial/venous ulcers should also be suspected with appropriate vascular lab testing. A sterile probe should be used to interrogate the wound for any abscesses, tendons, or bone. Encountering bone using the probe places the patient at a high index of suspicion for osteomyelitis.³⁷

Numerous diabetic foot ulcer classification systems have been developed and used for clinical and research purposes. The Wagner classification is the first such system and was initially developed for pressure wounds rather than diabetic ulcers. This system has limited sensitivity and specificity and has limited clinical application.³⁸ The University of Texas Classification System and the PEDIS ulcer classification were subsequently developed to correlate wound characteristics with clinical outcomes (Table 116.3).^{36,37} The WIFU (Wound, Ischemia, foot Infection) classification system, as advocated by the Society for Vascular Surgery, is the most recent foot ulcer staging system that has been clinically validated by several investigators (Fig. 116.5).^{39–41}

Radiologic Investigations

Numerous imaging modalities are available for the workup of diabetic foot ulcers. Foot X-rays should be obtained to rule out

TABLE 116.2 The Essential Components of a Diabetic Foot Exam

Vascular	Neurologic	Dermatologic	Musculoskeletal
Palpate pedal and lower extremity pulses Look for distal hair growth on feet, toes Assess capillary filling time in the toes	Test for loss of protective sensation by Semmes–Weinstein monofilament, biothesiometry, or electronic tuning fork Look for muscle atrophy of the feet	Note the ulcer depth, tissue in the wound bed, if bone is palpable Look for signs of infection around a wound (erythema, purulence) Inspect for other preulcerative lesions (blisters, calluses, corns)	Inspect for deformities Look for signs of Charcot foot (collapsed arch or hot, red swollen foot) Check the dorsiflexion of the ankle and the great toe joint

Adapted from Miller JD, Carter E, Shih J, et al. How to do a 3-minute diabetic foot exam. *J Fam Pract.* 2014;63:646–656.



Figure 116.3 Diabetic foot ulceration with dry, brittle skin in an area of pressure.

bony deformities, and, if infection is suspected, evaluate for subcutaneous gas. When ulcer healing does not progress at a satisfactory rate, other imaging studies that should be considered include computed tomography (CT), magnetic resonance imaging (MRI), labeled white blood cell scans, single-photon emission computed tomography (SPECT), and positron emission tomography (PET) scans to rule out osteomyelitis or soft tissue infections. Although PET and labeled white blood cell scans have been shown to have the highest diagnostic accuracy in confirming or excluding the diagnosis of osteomyelitis, they are time-consuming and expensive tests and many clinicians will preferentially order MRIs first for the workup of osteomyelitis.⁴²

MANAGEMENT

General Principles

The decision to treat a diabetic foot ulcer in an outpatient setting or as an inpatient in the hospital often hinges on the patient's

presenting clinical status. Septic patients with severely infected wounds require admission for urgent surgical management to limit the spread of the infection and tissue destruction. Conversely, patients with stable, chronic issues can be managed in the outpatient setting. Outpatient care consists primarily of wound management through local wound care and coordination of appropriate diagnostic testing and consultations. Serial wound clinic visits for dressing changes and debridement of the wounds is often required for many patients. A myriad of topical dressings exists from which to choose based on the wound etiology, availability, and cost. In addition to debriding and maintaining a moist and healthy wound bed, diabetic foot ulcers should also be treated with culture-directed antibiotics, if infected. It is sometimes possible to accomplish these goals with a dressing that serves multiple purposes: control of infection and inflammation, moisture balance, and the provision of pressure relief.

Wound Debridement

The purpose of debriding a diabetic foot ulcer is to alter the environment of the wound and to promote healing by removing abnormal tissue, such as hyperkeratotic epidermis and necrotic dermal tissue, foreign debris, and bacteria.⁴³ In addition to removing nonviable tissue, debridement converts a stagnant wound into an acute healing wound by releasing platelet growth factors, inhibiting proteinases, and limiting the action of bacterial biofilm.⁴⁴ Different modalities for debriding a wound include sharp, surgical, enzymatic, autolytic, mechanical, and intraoperative with ultrasonic and hydrosurgical devices. Because the majority of these patients are neuropathic, aggressive debridement can usually be carried out with minimal discomfort. If the patient is anxious or an extensive debridement is required, a local anesthetic block or sedation in an operating room setting may be helpful.

Sharp debridement at the bedside may suffice for small wounds, but larger wounds often require repetitive debridement, with the goal of a well-perfused wound bed and quantitative cultures less than 10^5 /g tissue before closure. In Sinkin's series of 193 wounds in Charcot foot patients, the average number of debridements prior to attempted closure was four.⁴⁵ Exposed bone needs to be debrided to stippled punctate bleeding, and bone cultures should be obtained. The bacteria most likely to be involved in diabetic osteomyelitis are skin organisms, frequently *Staphylococcus aureus* and sometimes resistant strains.⁴⁶ Copious pulse lavage irrigation should be performed at the end of each debridement.

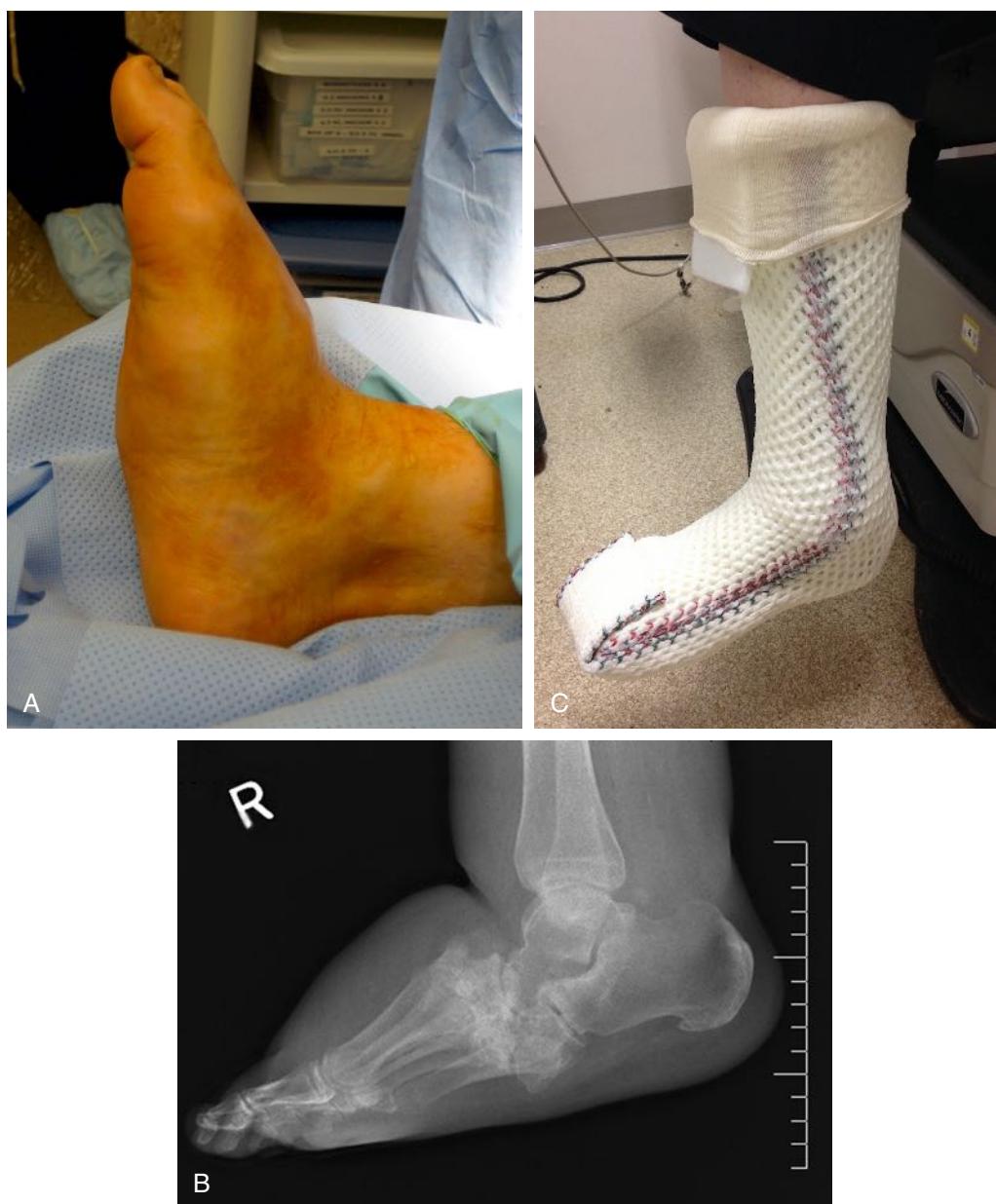


Figure 116.4 Charcot foot; typical “rocker bottom” appearance (A), characteristic X-ray (B), and offloading with total contact cast (C).

TABLE 116.3 Wagner and Texas Classification Systems of Diabetic Foot Ulcers

WAGNER METHOD		UNIVERSITY OF TEXAS METHOD	
Grade	Details	Grade	Details
0	No open foot lesion	0	Presence of preulcer or postulcer epithelialization
1	Presence of superficial ulcer, partial or full thickness	1	Superficial ulcer not penetrating tendon, bone or joint
2	Ulcer extends to ligaments, tendon, joint capsule or deep fascia without abscess or osteomyelitis	2	Ulcer penetrating through to tendon or capsule
3	Presence of deep ulcer with abscess, osteomyelitis	3	Ulcer penetrating to bone or joint
4	Gangrene localized to the forefoot or heel	A	Noninfected and nonischemic ulcer
5	Extensive	B	Infection present
		C	Ischemia present
		D	Both infection and ischemia are present

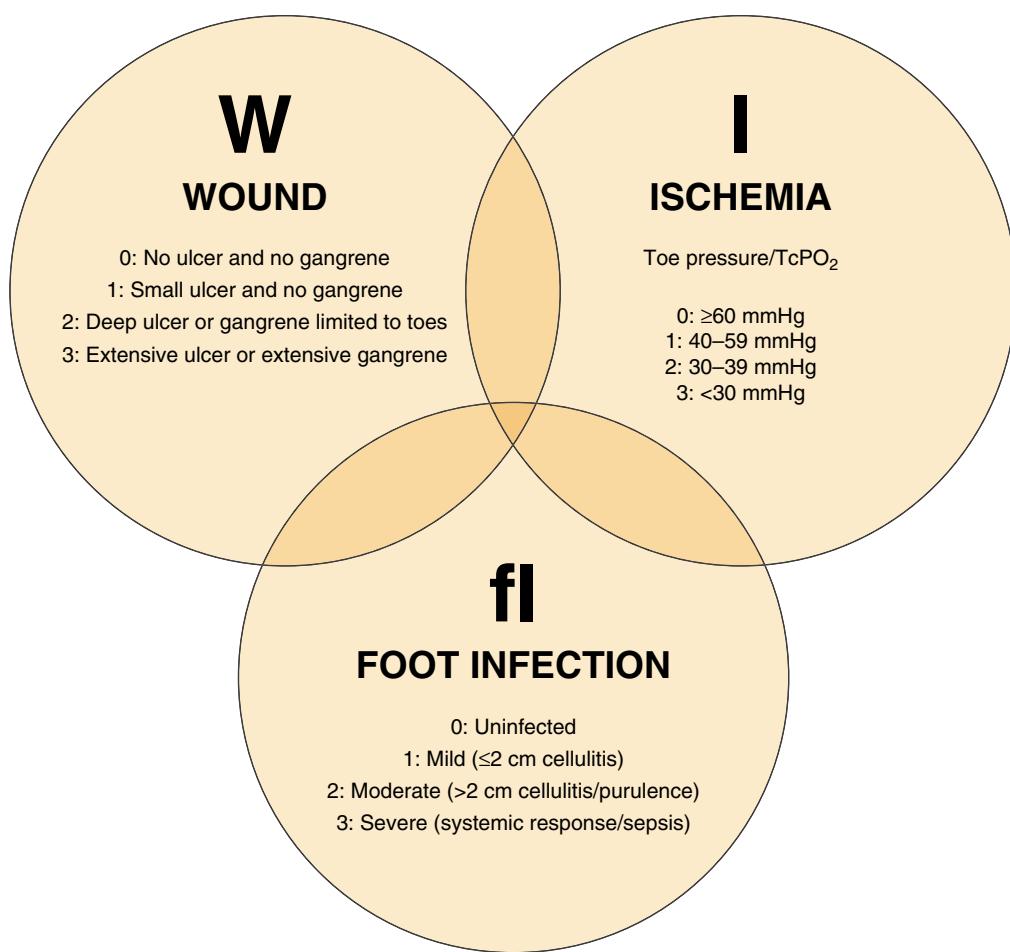


Figure 116.5 SVS WIfI Classification System. $TcPO_2$, transcutaneous oxygen pressure.

Between debridements, wounds may be covered with moist dressings, silver-containing dressings, or creams or treated with negative-pressure therapy. Zhang and colleagues reported that negative-pressure therapy was more likely to shrink or heal ulcers compared with standard therapy and did so in a shorter period of time.⁴⁷

Offloading

The foot must also be offloaded to minimize pressure on the wound and to prevent ulcers from recurring. The likelihood of healing increases with the effectiveness of offloading and the compliance of the patient.⁴⁸ Offloading modalities include postoperative shoes, wedge shoes, healing sandals, braces, boots, and total contact casting. Although level one evidence for these individual modalities is sparse, a meta-analysis showed greater wound healing efficacy with the use of total contact casting and irremovable cast walkers.⁴⁹ Multilayer customized offloading orthoses and fillers at sites of partial foot amputation are available to stabilize the position of the foot within the shoe. It is necessary to balance and offload pressure from both prior and potential ulceration sites.⁵⁰ Referral to an orthotist for prescription footwear and orthoses is recommended because the at-risk patient will need monitoring and adjustment of the devices. The patient may also benefit from additional bracing or splinting to offload

pressure and will need to have these devices replaced regularly for the rest of their lives.

Patient Education

Due to the initial indolent course of diabetic foot ulcers but their potentially devastating complications, it is advisable to educate patients and their families on the nature of the disease to maximize the likelihood of compliance with medical optimization and wound care. Patients should also recognize the signs and reasons to seek urgent medical attention, such as a spreading soft tissue infection or gangrenous changes on the foot, because many patients with diabetic foot ulcers are insensitive in their feet because of diabetic neuropathy. The Society for Vascular Surgery has recognized the importance of involving patients in their plans of care, and its diabetic foot guidelines recommend that patients and their families be educated about preventive foot care and undergo interval foot inspections by physicians or advanced practice providers at least annually.⁵¹

Advanced Wound Treatment Modalities

There is an ever-growing list of advanced wound treatment modalities such as bioengineered cultured cell grafts, allografts, collagen xenografts, and amniotic membranes. There is evidence to support the use of these products for wounds that

have demonstrated a decreased rate of healing, but the quality of the evidence is variable, and the choice of product is often based on practitioner preference.^{52,53}

There is also a role for negative-pressure wound therapy (NPWT) in the management of diabetic foot ulcers, as well as in the postoperative setting after amputation or delayed primary closure as a bridge to delayed grafting. A recent study reported that NPWT improved wound granulation, reduced the time to wound closure, and reduced the incidence of subsequent minor amputations.⁵⁴

SOFT TISSUE SURGERY FOR THE DIABETIC FOOT

Diabetic patients with foot ulceration and tracking abscesses, wet gangrenous changes, gas in the tissue on plain film radiographs, or systemic signs of sepsis require urgent surgical attention. A thorough incision and drainage of any abscesses or infectious tracks must be aggressively performed in the operating room, along with an appropriate exploration of fascial compartments and layers of the foot, because abscesses originating from a forefoot ulcer can track up to the ankle or lower leg. Amputation of digits or portions of the foot may be necessary due to gangrene or to limit the advancement of infection. If the viability of any of the patient's foot tissue is questionable, then one might consider limiting the amount of tissue that is resected, to preserve later closure options. Any resected tissue or bone should be cultured and sent for a pathology evaluation. Patients will often subsequently require multiple procedures to resect necrotic wound edges and debride the wound to promote granulation.

After treating the foot infection, the focus of care should be directed towards the need for revascularization and primary or secondary wound closure. Because of the complex altered physiology of these wounds, as well as additional systemic issues in diabetic patients, wound closure is slow and multiple interventions are frequently required. However, with meticulous attention to detail, closure rates of up to 80% have been reported.⁵⁵ Defining principles of successful wound closure include infection control, wound debridement, adequate perfusion, offloading of pressure, and moisture balance. Small superficial wounds may heal either without additional intervention or with the application of cell-based materials such as Dermagraft, Apligraft, or keratinocyte allografts.⁵⁶ Antibiotic-impregnated bone beads might also be used to enhance the treatment of any residual osteomyelitis.⁵⁷

Local Tissue Flaps

Local flaps for wound closure should be designed according to the foot's actual blood supply. A Doppler exam to determine areas of antegrade and retrograde flow is an important guide. Flaps should contain arterial perforators detected by Doppler signal, designed in the direction of antegrade flow to the local flap. The significant advantage of using local skin flaps is the concept of "replacing like with like": replacing defects with similarly specialized skin. The downside to local flaps is the limited

amount of specialized skin available to close wounds, limiting the size of wounds that can be handled in this manner. If there is a bone abnormality causing the ulcer to form, the bone must be addressed and corrected to minimize the chance of recurrence. Blume described such an approach with 67 cases of one-stage ulcer debridement and closure together with correction of underlying bone abnormalities. Results with this single-stage approach included 97% healing, 54% without complication, and 88% without recurrence at 2.5 years. Forefoot wounds healed more quickly than midfoot or rear-foot wounds, and deep wounds healed slower than superficial wounds, with a longer hospital stay. This suggests that local skin flaps in selected patients can be very successful. Double plantar rotation flaps can also be designed to either side of the defect for closure of small (<2 cm) central plantar forefoot ulcers.⁵⁸

Free (Microvascular Transfer) Flaps

Free flaps supply a large amount of tissue and can allow for aggressive debridement because the size of the wound is less constraining than with pedicled flaps. However, the flap should not disturb the vascular supply of the foot, so arterial end-to-side anastomoses are a better choice than end-to-end anastomoses to maintain prograde flow in the native circulation. Microvascular transfers frequently require secondary procedures such as debulking and tissue re-inset to improve aesthetics and function. Because of flap bulk, getting shoes to fit can be very difficult. All successful series report aggressive debridement of nonviable tissue, revascularization when necessary to provide normal oxygen tension, control of medical problems, gradual protected weight bearing, correction of underlying bony abnormalities before or during the flap procedure, and control of infection. Deconditioned patients with multiple, poorly controlled medical problems are better treated with local tissue closure options.

Prevention of Recurrent Soft Tissue Defects

Prevention of wound recurrence is as important as the initial closure of the wound. Unfortunately, the risk of recurrent ulceration remains high, ranging from 35% at one year to 77% at five years, despite improvements in diabetic foot management.⁶ The continued presence of those factors leading to initial ulcer formation such as neuropathy or arterial disease contributes significantly to this recurrence rate. Ulceration of the plantar surface correlates with increased sole and midfoot pressures with ambulation. Shortening of the Achilles tendon by contraction or chronic tightness can significantly contribute to increased plantar foot pressures. Diabetic Achilles tendons examined with electron microscopy demonstrate increased collagen density and structural disorganization.⁵⁹ Elevated glucose levels may lead to abnormal cross-linking between collagen fibrils and increasing tendon stiffness. Colen and colleagues looked at diabetic wound closure comparing those that were done in conjunction with a surgical offloading procedure such as Achilles tendon lengthening versus those that did not have the tendon lengthened.⁶⁰ At nearly 3 years' follow-up, 2% of the patients with Achilles tendon lengthening recurred as

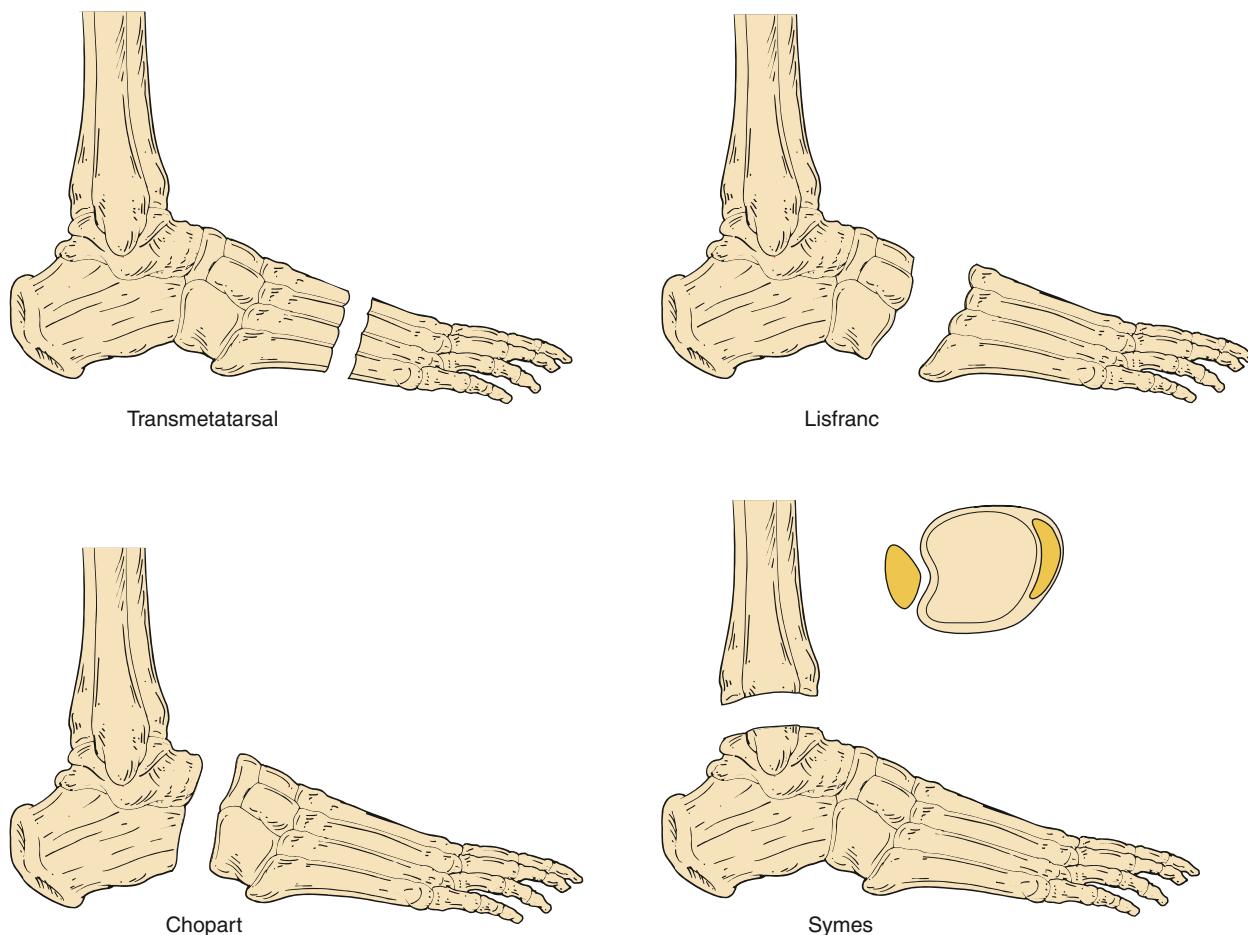


Figure 116.6 Types of midfoot amputation available for optimal maintenance of diabetic limb function: Lisfranc, Chopart, and Symes.

opposed to 25% of those without tendon lengthening. Patients who cannot dorsiflex the ankle past neutral or have forefoot pressures of more than 100 lb/in² are considered at increased risk of recurrent ulceration. Achilles tendon lengthening can often be performed percutaneously to achieve neutral or within 5 degrees of dorsiflexion in an effort to prevent recurrent foot ulceration. Another offloading procedure that is promising in patients with recalcitrant digital ulcers secondary to hammer toes is tenotomy of the digital flexor tendon. This allows the pulp of the toe to take weight again offloading the sole of the foot. Tenotomy can be performed in an outpatient setting without the need for further immobilization. The quality of evidence for tenotomy is low at this time but the benefits may outweigh the potential risks.

AMPUTATION

When wound closure is not possible, because of the size and extent of the wound, location, or irreversible ischemia, then some variant of foot amputation may be required. Proper choice and optimal performance of amputation, such as partial or complete ray, transmetatarsal, midfoot amputations, are critical components of diabetic foot management (Fig. 116.6).

With current advances in revascularization and wound care treatments, a partial foot amputation may be possible where a below- or above-knee amputation would previously have been thought more likely. Although amputations often carry a social stigma and are associated with significant psychological suffering to the patient, they may also result in rapid healing, shorter hospitalizations, lower risk of reinfection or recurrence of a wound, and an acceptable functional outcome. After the patient's amputation site is healed, the focus of treatment should become the prevention of ulcer recurrence at the site of amputation through appropriate offloading and patient education, as previously discussed.

Patients often benefit from a course of physical therapy postoperatively because many patients with advanced diabetic foot ulcer wounds demonstrate impaired ambulation in a prolonged non-weight-bearing state and are physiologically deconditioned. Outpatient or acute inpatient rehabilitation and physical therapy can be useful in helping patients regain muscle strength, improving gait and balance, and returning to an active lifestyle that is essential to controlling the patients' underlying medical and vascular pathologies. Finally, the patient will need ongoing care by multidisciplinary medical and surgical teams to mitigate the risk of future diabetic ulcer complications.

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TABLE 116.4**Noninvasive Vascular Studies in the Diabetic Foot and their Interpretations**

Test	Normal	Mild Disease	Moderate Disease	Severe Disease
ABI	0.9–1.1	0.7–0.9	0.4–0.7	<0.4 or >1.1
TBI	>0.7	0.5–0.7	0.35–0.5	<0.35
PVR Waveforms	Triphasic	Biphasic	Biphasic	Monophasic
tcPO ₂	>40 mm Hg	20–40 mm Hg	20–40 mm Hg	<20 mm Hg
SPP	>50 mm Hg	30–50 mm Hg	30–50 mm Hg	<30 mm Hg

ABI, ankle-brachial index; PVR, pulse volume recording; SPP, skin perfusion pressure; TBI, toe-brachial index; tcPO₂, transcutaneous oxygen.

PERIPHERAL ARTERIAL DISEASE AND THE DIABETIC FOOT

Lower extremity arterial disease in diabetic patients is characterized by tibial artery involvement and the sparing of the microvascular circulation.⁶¹ In the past, clinicians often discounted the utility of revascularization for diabetic patients with lower limb ischemia. It was reasoned that, because the etiology of diabetic arterial disease was secondary to the occlusion of the microvascular circulation, bypass surgery would not improve flow within the microcirculation and would undoubtedly fail. However, this belief has been discredited, and lower extremity revascularization with open or endovascular interventions can contribute in a significant way to limb preservation in this patient population. The indications for treating arterial occlusive disease in diabetics are similar to nondiabetic patients: lifestyle limiting claudication, rest pain, and tissue loss that is associated with nonhealing ulcers and gangrenous changes.

Vascular Lab Workup

ABI + TBI
PVR
tcPO₂
SPP
PPG

Diabetic patients with tissue loss or nonhealing ulcers without palpable pedal pulses should undergo further testing for underlying arterial disease. Although ABI measurements are a standard component of the vascular workup, these values, as previously mentioned, are often unreliable in diabetics because of medial calcinosis of the tibial vessels. However, the digital arteries are often spared the heavy calcification that occurs in the tibial arteries, and their measurements of flow more accurately reflect foot perfusion. As such, toe-brachial index (TBI) measurements may be more useful in diabetic patients with a suspected falsely elevated ABI.⁶² A TBI greater than 0.6 is predictive of tissue healing.*

Alternative tests that might also be useful in the workup of diabetic foot ulcers include pulse volume recordings (PVR), photoplethysmography (PPG), and transcutaneous oxygen tension (tcPO₂), and skin perfusion pressure (SPP) measurements. Healing is unlikely to occur if the PVR amplitude is less than 5 mm or the PPG is less than 50 mm Hg.⁶³ Furthermore, wound healing is likely with a tcPO₂ greater than 40 mm Hg. A regional index can be calculated to account for variations in systemic arterial oxygen availability. To calculate this index, the foot tcPO₂ measurement is divided by a tcPO₂ reference point, usually chosen at the chest. A patient with a tcPO₂ index greater than 0.6 is likely to heal a wound, whereas a value less than 0.4 is unlikely to

heal.⁶⁴ SPP measurements less than 30 mm Hg are predictive of nonhealing and greater than 50 mm Hg are predictive of healing. A summary of these noninvasive vascular studies and interpretive guidelines is presented in Table 116.4. Further noninvasive imaging, such as CTA and MRA, is often the next step for arterial imaging based on the vascular lab assessment. However, fine detail and definition of the tibial and pedal arteries is required to plan diabetic revascularization; therefore, arteriograms are often obtained to assist with operative planning, with CO₂ angiography considered in the setting of renal insufficiency (Fig. 116.7). Images from a CTA or MRA can allow a focused arteriographic approach that can often be combined with an endovascular therapeutic intervention if appropriate. In our experience, this occurs in approximately 60% of arteriographic studies performed for diabetic limb preservation.

Endovascular Interventions in the Diabetic Patient

Endovascular interventions continue to play an increasingly prominent role in the treatment of diabetic foot ulcer patients. However, tibial artery occlusive disease remains a challenge for a catheter-based approach. Several authors have demonstrated comparable outcomes after endovascular revascularization in diabetics and nondiabetics, with lower long-term primary patency rates in diabetic patients, but equivalent secondary patency and limb preservation rates.⁶⁵ Arterial runoff may be an important factor in determining the efficacy of endovascular interventions. Faglia and colleagues reported on 420 diabetic patients who underwent tibial angioplasty and found that the lack of a patent tibial artery at the end of the study resulted in a 62% amputation rate, compared with 1.7% in patients with at least one patent artery to the foot.⁶⁶

Different modalities are available for revascularization, including standard tibial angioplasty with dedicated wires, standard balloons, and drug-eluting balloons, as well as pedal arch reconstruction with the “pedal loop” technique. The pedal loop technique involves traversing lesions in the pedal arch to establish blood flow to the foot in a prograde or retrograde manner.⁶⁷ Data of the role of stenting and drug-elution technologies in tibial artery revascularization remain limited. Although one study reported that infrapopliteal stenting can be successful, with restenosis rates of 20% at 1 year and greater than 70% primary patency, functional limb preservation was better for those patients undergoing proximal below-knee angioplasty compared with tibial stenting.⁶⁸

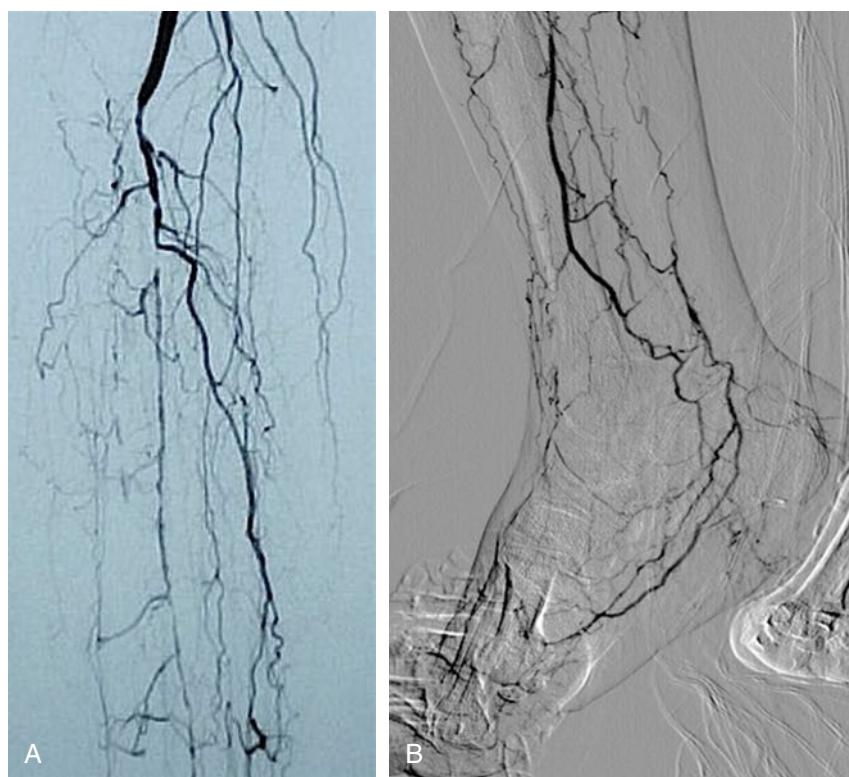


Figure 116.7 Lower extremity arteriogram with the tibial artery occlusive disease typical of a diabetic pattern (A) and the importance of adequate foot views to delineate distal targets for revascularization; in this case the distal peroneal and medial and lateral plantar branches (B).

Surgical Bypass in the Diabetic Patient

For diabetic ulcers to heal, it has been axiomatic to restore pulsatile blood flow to the foot. Although the femoropopliteal arterial segment is commonly affected in diabetics, tibial artery occlusive disease is the classic distribution in diabetic patients, leading to limb-threatening ischemia.⁶⁹ In our experience, functioning in a limb preservation program with a large volume of diabetic revascularization, approximately 25% of patients with limb-threatening ischemia who present with significant wounds and tissue loss are best treated by surgical bypass as the initial method of revascularization. We have found that diabetics with more extensive tissue loss ($>2 \text{ cm}^2$) heal faster and more completely after bypass, compared with endovascular therapy. Due to the preponderance of tibial artery involvement, distal targets can include the medial and lateral plantar branches and other inframalleolar arteries (Fig. 116.8). Due to the patient's diabetic tibial distribution, a popliteal–distal bypass can often be considered because the proximal arterial tree is spared from flow-limiting occlusive disease. Use of the popliteal artery for inflow limits the length of the bypass to optimize long-term patency, as well as the length of the autogenous conduit needed for the bypass (Fig. 116.9).

Several investigators have established the superiority of lower extremity bypass with autogenous vein compared with other conduits. If vein can be used as a conduit for bypass in diabetic patients, then a patency and limb salvage rate similar to nondiabetic patients can be obtained.⁷⁰ Pomposelli and colleagues analyzed a cohort of 1000 bypasses, 92% of which were in diabetic patients, and reported a primary patency of 57% and 38% at 5 and 10 years, respectively.⁷¹ A large prospective study of vein bypass grafts for critical limb ischemia

(PREVENT III) evaluated bypasses in 1404 patients, 64% of whom were diabetic and 75% of whom presented with tissue loss.⁷² The authors reported a primary patency of 61% at 1 year and a reduced amputation-free survival at 1 year for a high-risk cohort, as determined by factors including age greater than 75 years and a history of dialysis, significant coronary artery disease, anemia, and tissue loss at presentation. However, up to 30% of diabetic patients do not have adequate saphenous vein for bypass to distal tibial targets. In reoperative patients, this figure increases to 50%.⁷³ In such patients, alternative conduits for bypass, such as the lesser saphenous vein, arm vein, composite veins, and a polytetrafluoroethylene (PTFE) graft with a distal vein patch with or without a distal arteriovenous fistula, should be considered. Furthermore, although these alternative conduits are not equivalent to intact great saphenous vein for tibial bypass, they can be effective for limb preservation.^{74–77}

Lower extremity bypasses in diabetic patients are not without risk. There is a certain perioperative morbidity associated with bypass surgery that approaches 20%, with a 10% incisional complication rate for vein grafts. These pulmonary, cardiac, and renal complications can delay recovery and add to hospital stay and cost. Indeed, although diabetes is not a risk factor for vein graft failure, it has been associated with increased risk of long-term mortality and limb loss in patients with critical limb ischemia when compared with nondiabetic patients.⁷⁸

Endovascular Versus Bypass for Diabetic Revascularization

An appropriate revascularization strategy should be customized for diabetic patients according to their anatomy and comorbidities. The Bypass versus Angioplasty in Severe Ischemia of

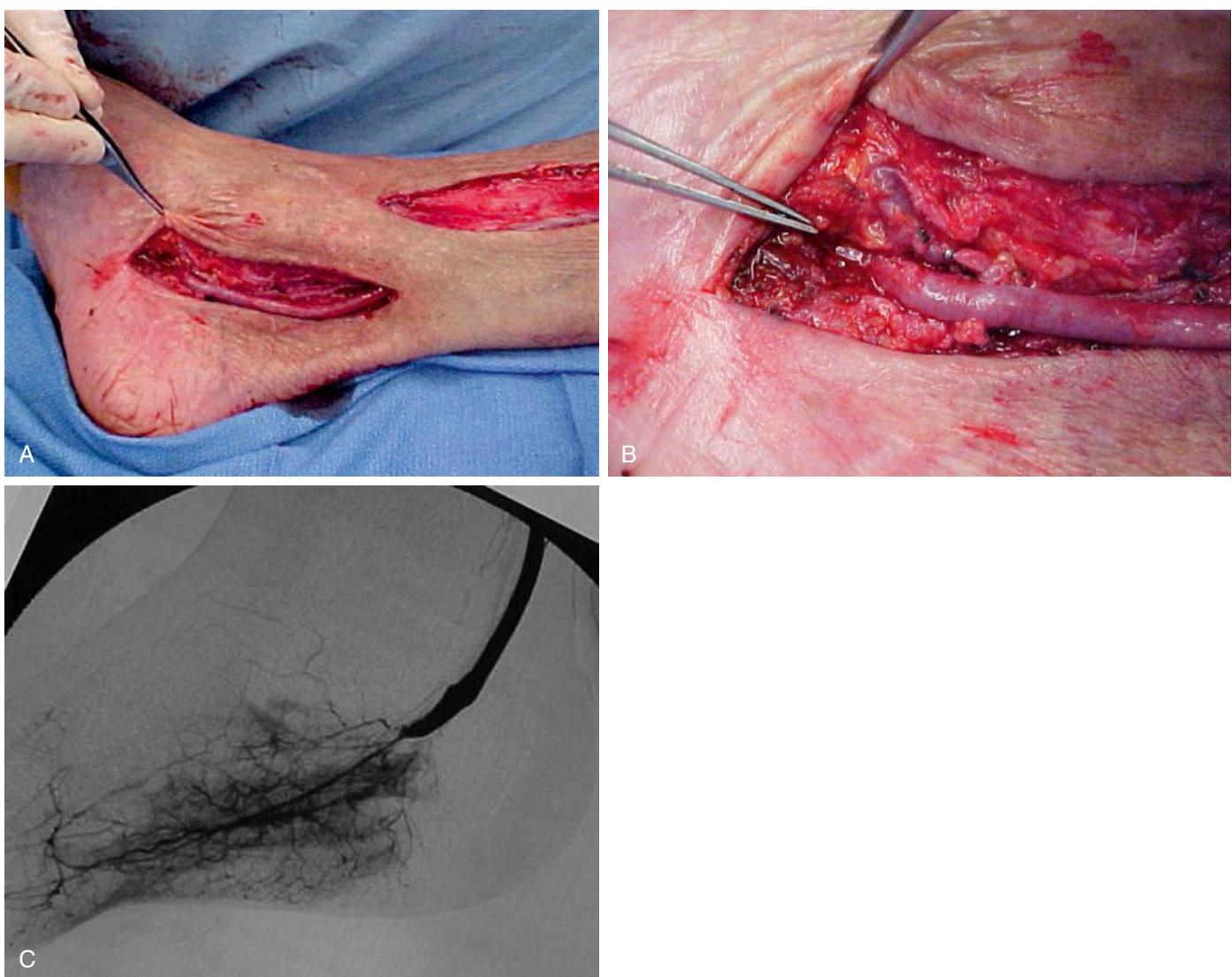


Figure 116.8 Distal bypass to the medial and lateral plantar branches of the posterior tibial artery as required in the diabetic patient (A) with the distal anastomosis (B), completion arteriogram (C).

the Leg (BASIL) trial attempted to compare endovascular intervention with surgical bypass.⁷⁹ Among the 452 patients randomized to bypass or endovascular intervention, perioperative morbidity was higher with surgery, but amputation-free and overall survivals were similar in both groups at 1 year. However, at the 2-year interval, surgery was associated with a reduced risk of amputation and death. The authors concluded that angioplasty should be used first for patients with a life expectancy of ≤ 2 years and that bypass is preferred when a vein conduit is available. However, the generalizability of these results to diabetic patients is limited because only 42% of the patients in the study were diabetic. We hope that the ongoing BEST-CLI and BASIL 2 trials shed more light on the optimal revascularization strategy for diabetic patients.

Hinchliffe et al. published a review of revascularization for the treatment of diabetic foot ulceration from 1980 to 2010.⁸⁰ Outcomes were similar, with a 1-year limb preservation rate



Figure 116.9 Incisions associated with a popliteal–distal bypass in the diabetic patient with proximal extension of the skin incision to harvest optimal vein and limit the distal limb harvest incision through chronically ischemic tissue.

BOX 116.1**Organizational Structure of a Multidisciplinary Team to Optimize Outcomes and Financial Viability in the Care of the Diabetic Foot**

Structure of a limb preservation program
 Physician team
 Physician champions
 Staff
 Space
 Diagnostic imaging
 Vascular therapy
 Endovascular
 Open surgery
 Soft tissue therapy
 Wound care
 Reconstruction and amputation

Hyperbaric O₂
 Rehab/PMR program
 EMR
 Educational activities
 Physicians
 Patients
 Research
 Coordinator
 Database
 Statistician
 Marketing
 Financial analysis

of 85% after bypass and 78% following angioplasty. However, loss of patency was not always associated with amputation, because the initial intervention allowed for wound healing and sufficient collateralization to maintain tissue integrity, despite subsequent failure of the revascularization. Therefore although prospective, randomized data comparing surgical bypass with endovascular revascularization specifically for diabetic foot ulcer patients are lacking, similar limb preservation rates can be achieved when the physician's best judgment is used to develop an individualized revascularization plan for each patient.

MULTIDISCIPLINARY LIMB PRESERVATION PROGRAMS

A successful limb preservation program requires a coordinated effort of physicians, nurses, allied health professionals, and administrators dedicated to the preservation of functional limbs. Such a multidisciplinary approach should take advantage of protocol-driven care, involving a full complement of diagnostic and therapeutic modalities that combine revascularization with soft tissue reconstruction and medical support.⁸¹ Unfortunately, there continues to be geographic and demographic variation in the care delivered to patients at risk of losing a limb from diabetes.⁸² There are also a variety of approaches to diabetics with limb-threatening ischemia: approximately 25% undergo primary amputation, 25% receive medical therapy, and only 50% undergo any attempt at revascularization.

The Society for Vascular Surgery and the American Podiatric Medical Association have stressed the importance and prospective benefits of multidisciplinary care for diabetic foot ulcer patients.⁸³ Benefits to the patient include a reduction in time for vascular assessment, wound healing, institution of treatment for infection, and the time to final correction of podiatric and orthopedic deformities. Enhanced follow-up and increased surveillance of revascularization procedures contribute to patient outcomes. Advantages for the physicians include the ability to efficiently manage complex patients with help from the appropriate medical specialties, an expected increase in patient referrals, the ability to obtain leadership roles both regionally and nationally, the development of an important clinical area to enhance the identity of the institution, and

the infrastructure for clinical research and trials. Evidence is available that a multidisciplinary program can bestow these advantages, including a significant reduction in the incidence of major leg amputations (Box 116.1).^{50,84}

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Systematically evaluates the benefits and harms of advanced wound care therapies for nonhealing diabetic, venous and arterial ulcers. Although most of the data is poor, compared with standard care, some advanced wound care therapies may reduce time to healing and the proportion of ulcers healed.

Hinchliffe RJ, Andros G, Apelqvist J, et al. A systematic review of the effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral arterial disease. *Diabetes Metab Res Rev.* 2012;28(suppl 1):179–217.

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Diabetic Foot Abnormalities and their Management

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INTRODUCTION

Diabetic foot ulcers (DFUs) are often erroneously thought to be a minor complication of diabetes. Diabetic foot ulcers usually start as an innocuous blister from rubbing on a shoe that is too tight, or at the site of an old callus on the sole of the foot. In reality, diabetic foot ulcers are the start of a cascade of events that contribute to repeated infections, hospitalizations, surgeries and amputations. In fact, 10%–50% of DFUs end in some type of amputation. Diabetes detrimentally affects every system in the body. Manifestations in the foot exemplify the systemic disease process with the development of peripheral sensory neuropathy, motor neuropathy, autonomic neuropathy, limited joint mobility, structural foot deformity (e.g., hammertoes and hallux valgus), Charcot arthropathy, and macro and micro-angiopathy¹ (Fig. 117.1). DFUs usually develop at the site of pressure areas on the sole of the foot that are exposed to repetitive injury (walking activity) or at the site of constant pressure at bony prominences (e.g., hammertoes or bunion deformities) from tight shoes. Patients with diabetes are often severely impaired hosts. Neuropathy eliminates the perception of pain and unrecognized injuries until infection damages enough tissue to cause pain. Immunopathy increases the risk of infection and a poor inflammatory response.^{2,3} Macro- and micro-angiopathy impede the response to both infection and normal reparative processes. The purpose of this chapter is to discuss the components related to the diabetic foot.

PERIPHERAL NEUROPATHY

Peripheral neuropathy is one of the most important components in diabetic foot ulcers and infections. Peripheral neuropathy is a progressive pathologic process that develops in the environment of diabetes, prolonged poor glucose control and microvascular disease.^{4,5} Glycation-induced metabolic and vascular changes of nerve fibers result in sensory, autonomic, and motor neuropathy in the lower extremity. Neuropathy plays a devastating role in the cascade of events that lead to ulceration, infection, and amputation.⁶ Patients often present with a combination of small and large fiber neuropathy. Small fiber neuropathy is usually diagnosed based on symptoms of burning, tingling, and radiating electrical pain.^{7,8} Clinical assessment is based primarily on the patient's inability to perceive temperature differences, so it is not often evaluated. Large fiber neuropathy generally presents with symptoms of numbness, tingling, and formication. Patients will often complain that their feet feel cold when they feel warm to their spouse or in the clinic. Large fiber neuropathy is easily assessed in the clinic with a 128-Hz tuning fork, 10-g monofilament, or Achilles deep tendon reflexes.^{8–10}

Large fiber sensory neuropathy is often so severe that patients lack sufficient peripheral sensation to protect their feet from injury. This is referred to as "loss of protective sensation" (LOPS). Initially, diabetic peripheral sensory neuropathy with the "loss of protective sensation" begins distally in the toes and progresses to the ankle and legs. Large fiber neuropathy is one of the + postural instability & ↑ falls.

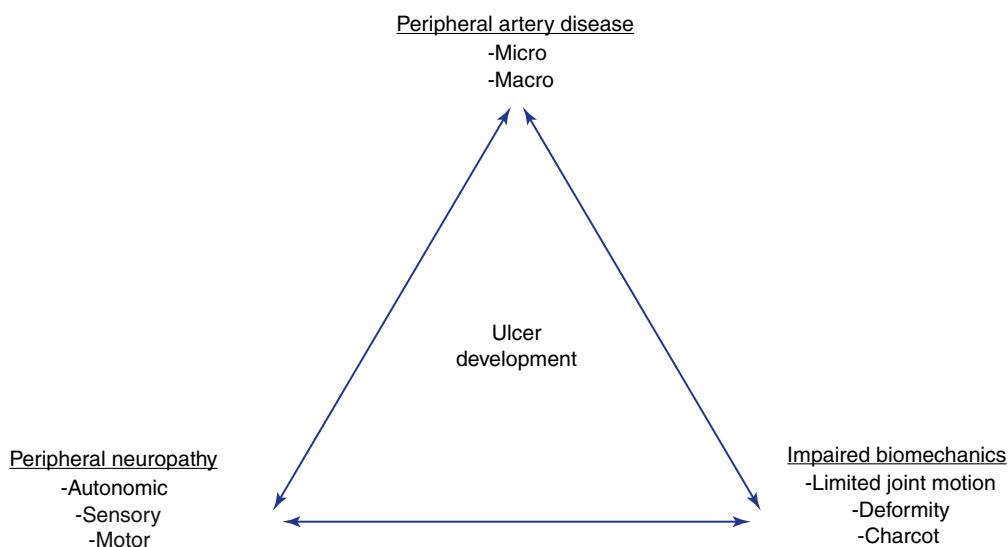


Figure 117.1 The triad of peripheral neuropathy, patho-biomechanics, and peripheral vascular disease lead to diabetic foot ulcers.

sentinel disease processes that leads to diabetic foot ulceration. LOPS provides an environment for foot injury without being recognized by the patient. For example, in people with normal sensation, a sharp object such as a tack is reflexively identified and the foot is spontaneously withdrawn, avoiding further injury. In an environment of sensory neuropathy, the patient will not withdraw the foot. The tack is unrecognized, resulting in repetitive damage to deep structures. Foreign materials such as dirt and fabric are pushed into deep tissue that creates abscess and necrosis. Because of neuropathy, there is a longer time after a puncture event before the patient seeks medical care¹¹ and the risk of surgery and amputation are much higher among people with diabetes and neuropathy. Patients with diabetes are 5 times more likely to require multiple surgeries and 46 times more likely to have an amputation as a result of an infected puncture wound.^{12,13} Patients with large fiber neuropathy have postural instability and an increased risk of falls and associated trauma.¹⁴

Autonomic peripheral neuropathy is related to the increase in sympathetic tone in the diabetic lower extremity. Dysregulation can lead to arterial-venous shunting, small vessel ischemia, and changes in the soft tissue turgor.^{15,16} Xerosis, with its loss of moisture balance and elasticity, can lead to developing fissure or tears in the skin.¹⁷ Further, chronic edema applies tension on the compromised soft tissue envelope, increasing the susceptibility of minor tissue injury, causing breaks in the skin leading to an ulceration.¹⁸

There is no established treatment for large fiber neuropathy. The symptoms of small fiber peripheral neuropathy (paresthesias, burning, pins and needles, tingling, radiating pain) are often treated off-label with oral medications including antidepressants, antiarrhythmics, and anticonvulsants such as gabapentin.¹⁹ In addition, vitamin supplements with L-methylfolate, methylcobalamin, and pyridoxal 5'-phosphate and topical medications including topical clonidine and capsaicin formulations have shown efficacy to reduce symptoms.^{20,21} There are two FDA-approved drugs for painful neuropathy (pregabalin and duloxetine). Both have demonstrated reduction in pain and improved sleep compared to placebo.



Figure 117.2 Intrinsic minus foot with muscle wasting.

Motor neuropathy in the lower extremity leads to muscle atrophy and imbalance of opposing muscle groups. Motor neuropathy is especially apparent in the smaller intrinsic muscles of the hands and feet. Even in people without diabetes, an imbalance of the extensors and flexors; evertors and invertors; and the abductors and adductors can cause capsular laxity and bony mal-alignment, joint subluxation, and structural foot deformity. With severe motor neuropathy, patients' hands can develop a "monkey paw" or an "intrinsic minus" foot, the atrophy of intrinsic muscles (Fig. 117.2). In the foot, motor neuropathy contributes to the development of forefoot deformities such as hammertoe and hallux abductovalgus, which are reported to be major contributors of ulceration (92% related to neuropathy, and 77% related to deformities)²² (Figs. 117.3 and 117.4). For example, the intrinsic flexors, interossei, and lumbricals in the foot normally stabilize the toes against the metatarsal heads in the stance and propulsive phases of the gait cycle. When the intrinsic muscles atrophy, the balance of the stronger long flexors and extensors causes the toes to contract and eventually to dislocate dorsally at the metatarsophalangeal joints. This imbalance and deformity can literally push the head of the metatarsals through the bottom of the foot.

Surgical decompression of the peroneal and tibial nerves may have a role if the disease is not advanced.^{23,24} Wieman



Figure 117.3 (A) Hammertoe with ulcer on the weightbearing surface of the distal toe. (B) Multiple digital deformities.



Figure 117.4 (A) Decreased dorsiflexion of the metatarsophalangeal joint. (B) Resultant ulcer on the plantar aspect of the hallux interphalangeal joint.

and colleagues decompressed the posterior tibial nerve by excising the flexor retinaculum at the level of the medial malleolus in 26 patients.²⁵ Within 1 month, 92% of patients reported their pain had subsided. Macare van Maurik's group performed decompression prospectively on 42 patients whose contralateral limb served as the control. Randomization was performed to determine which leg received surgical intervention. At 3 months there was a significant improvement in pain in the postoperative leg that was maintained for 12 months.²⁶ There are currently few prospective studies and long-term effectiveness of the procedure is yet to be measured.

PERIPHERAL ARTERIAL DISEASE

Perfusion is arguably the most critical element in diabetic foot ulcer healing, amputation level selection, and limb salvage.

Tools to measure functional perfusion to determine wound healing are an unmet need in the diabetic foot. Traditional arterial Dopplers are unreliable because of Monckeberg medial calcific sclerosis. Often, arteries in the foot and ankle are not compressible. Toe pressures and waveforms may be more helpful, however many patients have had previous amputations and do not have toes to evaluate. There have been a number of new technologies such as hyperspectral imaging (HSI) and the SPY fluorescence imaging system that have been met with enthusiasm but are still being evaluated. Early proof of concept studies with hyperspectral imaging indicated the technology could be used to predict DFU healing. However, subsequent studies have reported contradictory results. Nouvong and colleagues reported the results of a prospective cohort study of 54 patients with 73 diabetic foot ulcers over a 24-week period.²⁷ She reported the sensitivity, specificity, positive predictive value

was 80%, 74% and 90%. Likewise, Khaodhia evaluated 23 patients with 34 DFUs and reported the sensitivity, specificity, and positive and negative predictive values of the HT index for predicting healing were 93%, 86%, 93%, and 86%, respectively.²⁸ In contrast, Jeffcoate and colleagues evaluated 43 patients with DFUs. They found a negative association with HSI and healing at 12 weeks and a positive association at 24 weeks.²⁹ Indocyanine green angiography in the SPY system may help to evaluate the effectiveness of vascular interventions but the technology does not provide quantitative measurements, so it is difficult to compare patients and quantify results.³⁰ There is no evidence that indocyanine green angiography is useful to determine wound healing or amputation level selection.

Another pertinent concept relates to angiosomes, the anatomic areas that are vascularized by a source artery. The three major vessels (posterior tibial, peroneal, anterior tibial arteries) feed specific areas of the lower extremity. Several reports have stated that there is a correlation between the ulcer site and the angiosome that is compromised.³¹ However, there are redundancies inherent in the foot with arterial-to-arterial connections that may compensate for occlusive disease in one or more vessels. Successful healing of ulcers through indirect revascularization implies that in many cases, these redundancies exist and may be adequate.^{32,33} Current consensus is that angiosome-targeted revascularization should be performed when possible (direct revascularization), because it enhances wound-healing.

When patients present with infection, surgical excision of the infection needs to be achieved before revascularization to reduce the risk of graft or stent infection. Ischemic ulcers on the other hand should not be debrided until revascularization has been performed, unless there is concern for underlying infection. While necrotic areas or frankly gangrenous digits will ultimately require some sort of amputation, this must be performed at a level where perfusion is adequate for healing. As long as there is no significant infection, debridement and amputation for dry necrosis should also be delayed until after revascularization. However, because this is an impaired host, local signs of infection are often blunted and it may be difficult to determine if there is underlying soft tissue or bone infection. The Wagner classification system is the oldest in use specifically

for diabetic foot ulcers but does not take ischemia into account until the ulcer has progressed to gangrene.³⁴ The University of Texas classification system builds on this and encompasses depth, infection, and ischemia³⁵ with some overlap between the two systems (Table 117.1).

BIOMECHANICS

The foot is a complex structure with 26 bones and multiple articulations; intrinsic and extrinsic tendon insertions; fascia and ligaments that are both flexible and rigid. There is a redundant network of lymphatics, veins, arteries, and nerves, encased in a resilient soft tissue envelope. The complications associated with diabetes impart a devastating toll on foot function. Amputation often causes biomechanical changes in the foot that contribute to adaptive, progressive structural deformities, tendon imbalances, and limited joint mobility. After amputation, the risk of recurrent ulcers, infections, and amputations increases dramatically.^{36,37}

Structural changes occur in the diabetic foot that alter the underlying biomechanics. Stiffening of soft tissue structures, including tendons, ligaments, and joint capsules, leads to a limitation of range of motion across joints, joint subluxation, and dislocation.^{38,39} Deformity and limited joint motion is thought to be caused by atrophy of intrinsic muscles of the foot from peripheral motor neuropathy and advanced glycation end products that induce changes in the collagen of tendons. This process can lead to shortening of the tendon and loss of elasticity. Patients subsequently develop deformities such as hammertoes or equinus deformity, the limitation of dorsiflexion at the ankle joint.⁴⁰ Limited joint mobility often contributes to compensatory gait changes. For instance, to compensate for equinus, patients abduct and pronate their foot in gait. This causes increased pressure and shear on the ball of the foot, leading to plantar forefoot ulcerations under the metatarsal heads.^{41–43}

Callus distribution is a reliable method of identifying areas of pressure and shear forces that are often associated with foot ulceration.^{44,45} Alterations in gait patterns (i.e., shuffling, antalgic, wide base, unsteady) imply an underlying abnormality.^{46,47}

TABLE 117.1 Combined University of Texas and Wagner Classification Systems

Stage	GRADE			
	0	I	II	III
A	Pre- or post-ulcerative lesion. Completely epithelialized (Wagner 0)	Superficial wound not involving tendon, capsule, or bone (Wagner 1)	Wound penetrates to tendon or capsule (Wagner 2)	Wound penetrates to bone or joint
B	Infection	Infection	Infection	Infection (Wagner 3)
C	Ischemia	Ischemia	Ischemia	Ischemia (Wagner 4/5)
D	Infection and ischemia	Infection and ischemia	Infection and ischemia	Infection and ischemia

Adapted from Wagner FW, Jr. The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle*. 1981;2(2):64–122; and Lavery LA, Armstrong DG, Harkless LB. Classification of diabetic foot wounds. *J Foot Ankle Surg*. 1996;35(6):528–531.

Limited joint range of motion and structural deformities like bony prominences or joint contractures are signs of mal-alignment. Reducibility of any mal-aligned joint articulation is a key feature when examining the deformity. As the term implies, a reducible deformity is one that can be placed back into an anatomical position. A semi-reducible deformity cannot be completely realigned into an anatomical position, and a non-reducible deformity is a fixed deformity that cannot be reduced at all. Typically, there is a progression from a reducible to a rigid deformity, and the options become more limited as the deformity progresses.

Offloading

Offloading is the term to describe devices used to protect the foot and reduce pressure and shear and is an important aspect of healing DFUs. When pressure and shear are related to structural deformities or limited joint mobility, surgery can be used to correct deformities and improve joint motion. Conservative methods focus on the concept of offloading focal areas of pressure and distributing it across a wider surface area, changing gait patterns, and reducing the number of steps taken during the course of treatment. Offloading can be achieved through padding, orthotics, braces, over the counter fracture boots, and total contact casts.⁴⁸

Offloading is among the most important treatments to heal DFUs, especially when they occur on the sole of the foot. The total contact cast (TCC) is the most effective offloading technique to heal plantar ulcerations.^{49,50} Retrospective cohort studies and prospective randomized controlled trials report very similar results. When patients are treated with TCCs about 70%–90% of patients heal in an average of approximately 42 days. Unfortunately, TCCs are not commonly used. Many clinicians do not have the facilities or training to successfully use this approach.

Other methods, including walker boots, healing sandals, and bespoke shoes and insoles, are used with less success.^{51,52} Removable cast boots are often referred to as CAM walkers (Controlled Ankle Motion walker). These are over-the-counter devices originally designed for fractures. There are now several brands that are designed specifically to treat diabetic foot ulcers. Most studies report that 22%–79% of ulcers heal using this approach. In contrast, healing sandals and therapeutic shoes heal about 21% to 58% of DFUs in 12-week studies.^{50,53–56} One of the reasons that TCCs may be effective is because of the forced compliance that exists with a cast. Other techniques allow patients to remove their offloading device as they please. Many patients will not use special shoes or braces when they are at home.

Surgical Correction

Surgical correction can be conducted to heal an ulceration that has not healed with traditional approaches or when ulcers recur, despite using standard prevention approaches. The goal of the surgery is to produce a rectus, balanced foot. Soft tissue corrections largely focus on tendon lengthening and should

be reserved for reducible or semi-reducible deformities. For example, Achilles tendon lengthening has been demonstrated to reduce peak plantar pressures experienced in the forefoot by as much as 27%.^{57–59} Randomized controlled studies and cohort studies of Achilles tendon lengthening report 93% to 100% DFU healing within 12 weeks.^{57,60,61} Once the biomechanical abnormality has been addressed, the ulcer healing rate is high, the time to heal is short, and the incidence of reulceration is significantly less compared with patients treated with TCC alone. For the latter patients, the pressure and shear which caused the ulcer are only modified during the period of TCC therapy and remain as pathologic forces to cause reulceration after TCC removal if no other means of offloading is utilized.

Digital flexor tendon releases have been utilized as a simple method to correct contracture of the long flexor tendons. This procedure reduces pressure over the dorsal aspect of the interphalangeal joints and over the distal tip of the toes.⁶² Bony procedures include exostectomies (simple removal of bony prominences) and joint realignment through resectional arthroplasty and are typically used for non-reducible deformity.^{59,63} Tendon balancing and skeletal reconstruction (e.g., TAL and midfoot arthrodesis) are often done in combination. Therapeutic shoes and insoles and bracing to offload the foot are still necessary after the surgery. The goal of all of these options is to optimize function while minimizing new ulcer formation or ulcer recurrence.

THE DIABETIC FOOT ULCER

There are multiple DFU treatment strategies.^{64–73} Each treatment modality serves a purpose including: drainage control, edema management, infection/biofilm eradication, or direct wound-healing stimulation. Each modality has its own advantages and limitations with some level of evidence supporting efficacy. The number and diversity of treatment strategies reveal the lack of consensus for a singular algorithm. Further, the treatment rendered reflects the diversity of healthcare providers and their level of training and experience that care for DFUs (e.g., nurses, physical therapists, podiatrists, surgeons, and nonsurgical physicians). Regardless, certain fundamentals of wound care should be applied prior to implementation of any advanced therapies. These fundamentals include: (1) ensuring or establishing adequate perfusion; (2) providing optimal offloading; (3) controlling/treating acute infection and biofilm formation; and (4) optimizing the patient's metabolic and nutritional status. It is also important to recognize that antibiotics and dressings serve to optimize the wound environment and do not directly heal wounds. In general, the chronic ulcer must be converted to an acute wound for healing to occur. Ulcers should be debrided regularly in clinic with plans for definitive surgical closure or coverage once the ulcer is deemed "appropriately prepared" (i.e., not infected, perfusion maximized).

Minor or major amputation is a viable option for the treatment of chronic ulcerations, especially when it can improve function and prevent reulceration.^{74,75} The decision for amputation is easier in the environment of infection or ischemia where there is an obvious need to remove necrotic or infected

tissue. The biomechanical consequences of surgery and amputation should be anticipated. The goal is to provide a functional amputation stump. For example, a transmetatarsal amputation (TMA) should maintain the anatomical parabola of the metatarsals. This allows for an even distribution of pressure at the planter stump to prevent future breakdown. The TMA results in a durable, functional foot when patients receive bespoke shoes and insoles and regular foot evaluation to prevent reulceration.^{76,77}

CHARCOT NEUROARTHROPATHY

Charcot neuroarthropathy (CN) can be considered an end stage sequela of pathologic diabetic foot processes that has devastating clinical and economic consequences (Fig. 117.5). CN has been reported to increase healthcare costs by 17.2% and results in an increase of hospital length of stay.⁷⁸ There is a paucity of published prevalence reports; however, it is estimated 0.5% to 8% of patients with diabetes develop CN.^{79,80} The prevailing theory involves demineralization of the bone, causing instability. In the environment of profound peripheral neuropathy where the patient bears weight and ambulates, fractures and dislocations occur in the joints of the foot and/or ankle. An acute traumatic event or the cumulative effect of minor trauma can incite a CN episode. CN progresses through four stages: Stage 0 – clinical stage presenting with warm, swollen, often painful foot; Stage 1 – fragmentation/destruction, bony cysts, and erosion; Stage 2 – joint subluxations; Stage 3 – arch collapse and coalescence; and Stage 4 – consolidation.⁸¹ The key to the treatment of CN is early recognition and immobilization with non-weight-bearing. As it progresses through its stages, further destruction can occur. Once the fractures are consolidated, custom braces and shoes are usually required to accommodate the residual deformity, prevent reulceration, and provide stability. Surgical reconstruction may be necessary to realign the foot and ankle into a rectus position. Surgical

complication rates can be high with resultant major amputation rates as high as 31%.⁸² Chapter 119 (Podiatric Care of the Diabetic Foot) discusses Charcot foot in more detail.

THE IMPAIRED HOST

Patients with diabetes have a blunted local and systemic inflammatory response with four times the hospital admission rate and five times the complication rate compared to patients without diabetes.⁸³ Classic signs of infection such as rubor, calor, dolor, and tumor are absent or diminished, even in acute severe infections. Criteria used to define infection like the systemic inflammatory response syndrome (SIRS), which includes fever, tachycardia, tachypnea, and leukocytosis, are normal in many patients with severe limb-threatening infections.^{84–86} The proposed mechanism for the high rate of wound chronicity and infection in these patients is that hyperglycemia is associated with leukocyte dysfunction.⁸⁷ Neutrophils demonstrate delayed chemotaxis, poor phagocytosis and adhesion, and impaired myeloperoxidase function.^{88,89} Subsequently, microbes can escape the innate immune system and have a nutrient source, which allows the development of either senescent multi-species microbiome or acute infection.⁹⁰

Chronic foot ulcers that are not infected have normal clinical presentation but high levels of pro-inflammatory cytokines^{91,92} with a microbiome composed of bacteria and fungi.⁹³ Studies that visualized biofilm under scanning electron microscopy have shown their presence in 100% of chronic diabetic foot ulcers, though the effect of biofilm on the healing of chronic wounds has not been fully elucidated.^{94–96}

INFECTION

Infection is one of the most important complicating factors in the diabetic foot and is usually the underlying cause of hospitalization and amputation. International experts recommend



Figure 117.5 Charcot neuroarthropathy with characteristic rocker bottom deformity and plantar midfoot ulcer.

TABLE 117.2

Combined Foot Infection Severity Classification from the Infectious Diseases Society of America and the International Working Group on the Diabetic Foot

No Infection	Diabetic foot ulcer without signs of infection
Mild soft tissue infection	Infection limited to skin or superficial subcutaneous tissues without local complication or systemic illness. ≥2 manifestations: <ul style="list-style-type: none">• Local swelling or induration• Erythema (extending ≤2 cm from ulcer)• Local tenderness or pain• Local warmth• Purulent discharge
Moderate soft tissue infection	Systemically stable patient with ≤1 of the following: <ul style="list-style-type: none">• Erythema (extending ≥2 cm from ulcer)• Lymphangitis• Spread beneath fascia• Deep tissue abscess• Gangrene. Can involve muscle, tendon, or joint. Does not involve bone.
Severe soft tissue infection	Systemically unstable patient with the above criteria AND 2 of: <ul style="list-style-type: none">• Temperature >38°C or <36°C• Heart rate >90 beats/min• Respiratory rate >20 breaths/min or PaCO₂ <32 mmHg• White blood cell count >12,000 or <4000 or ≥10% immature forms (bands)
Moderate bone infection	Any bone infection of the foot without systemic involvement.
Severe bone infection	Systemically unstable patient with the above criteria AND 2 of: <ul style="list-style-type: none">• Temperature >38°C or <36°C• Heart rate >90 beats/min• Respiratory rate >20 breaths/min or PaCO₂ <32 mm Hg• White blood cell count >12,000 or <4000 or ≥10% bands

Adapted from Lavery LA, Ryan EC, Ahn J, et al. The Infected Diabetic Foot: Re-evaluating the Infectious Diseases Society of America Diabetic Foot Infection Classification. *Clin Infect Dis*. 2020;70(8):1573–1579; and Bus SA, Lavery LA, Monteiro-Saunders M, et al. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev*. 2020;36(Suppl 1):e3269.

that the diagnosis of infection is based on clinical signs and not based on swab cultures of an ulcer.⁹⁷ On the other hand, as a group, patients with diabetes represent severely impaired hosts and may not express the normal signs of inflammation such as erythema, swelling and local warmth.

The portal for infection in the diabetic foot is typically an ulcer, or infection is seeded through a puncture wound. Hematogenous spread of infection to the foot is uncommon.⁹⁸ As acute infections evolve, deep abscesses and osteomyelitis ensue. Diabetic foot infections (DFI) are typically bacterial and can be monomicrobial or polymicrobial. The most common bacterial pathogens are *Staphylococcus* and *Streptococcus*.^{99–101}

The International Working Group on the Diabetic Foot (IWGDF) has updated their Diabetic Foot Infection Classification (Table 117.2).⁹⁷ The new classification includes six categories that separate moderate and severe bone infections based on SIRS criteria.^{84,102} The Infectious Diseases Society of America (IDSA)¹⁰³ and IWGDF^{1,104} have previously supported distinctly different treatments for soft tissue and bone infections. A separate tier for osteomyelitis supports not only the difference in treatments, but the poor clinical outcomes associated with osteomyelitis.^{85,105,106} Patients with osteomyelitis require surgery more often, they have more procedures, more amputations, have longer treatment with antibiotics, and higher rates of recurrence.^{85,106,107}

Treatment of acute infections usually requires parenteral antibiotics and surgery for decompression, excision of infection, and amputation. Empiric antibiotic coverage is broad, and then therapy is targeted based on culture and sensitivities from deep tissue and bone. Surgical decompression and amputation may require multiple operating room visits until all nonviable tissue is excised, at which point a plan for definitive closure or coverage can be implemented.

The role of biofilm in clinical infection, osteomyelitis and wound healing is controversial. Biofilms are multispecies colonies of relatively senescent communities of bacteria that are encased in a glycocalyx shell that inhabit wounds, implantable medical devices, surgical material (e.g., suture), artificial joints, and orthopedic implants. Planktonic bacteria may leave the biofilm to begin other colonies or to seed acute infections. Due to the low metabolic activity of biofilm, antibiotic therapy is typically ineffective; thus physical disruption of the biofilm is often necessary.^{108,109} Disruption can be accomplished through other methods beyond excisional debridement such as ultrasound, or antiseptics.^{110–112}

Osteomyelitis

Osteomyelitis has been identified in patients with diabetes up to 20% in an outpatient setting and 67% for patients hospitalized for DFI.^{113,114} The majority of cases of osteomyelitis in the foot and ankle are by contiguous spread, with the nidus being the ulcer. Thus, in many settings, there is a correlation of osteomyelitis with the clinical finding of a positive probe to bone.^{115,116} The combination of clinical findings suggesting infection, bony fragmentation identified on plain radiographs, and focal areas of increased signal intensity on magnetic resonance imaging establish the diagnosis of osteomyelitis. The gold standard to diagnose osteomyelitis is bone biopsy for culture and histology.^{117,118}

The utility of laboratory biomarkers in patients with diabetes to diagnose and monitor reinfection has been demonstrated in several studies.^{119–121} Erythrocyte sedimentation rate (ESR) of 60 mm/h and C-reactive protein (CRP) 7.9 mg/dL have been identified as optimal cutoff points to differentiate osteomyelitis from soft tissue infection.¹²² Biomarkers can also be used for the monitoring of osteomyelitis treatment and reinfection of bone. There is a very high rate of reinfection in people admitted to the hospital for soft tissue infection (>30%) and bone infection (>50%) within a year after hospital discharge.⁸⁵

TABLE 117.3 Bespoke Shoes and Insoles to Prevent Recurrent Diabetic Foot Ulcers

	Pressure-Based Insole N = 130	Custom-Made Insoles N = 171	Custom-Made Insoles N = 298	Manufactured Shoes N = 69	Insoles N = 92	Rocker Sole Shoes N = 51
Study duration	RCT 18 months ¹³⁰	RCT 18 months ¹²⁸	RCT 12 months ¹³¹	RCT 12 months ¹³⁰	RCT 12 months ¹³²	RCT 6 months ¹³³
Treatment group ulceration (%)	9.1% Pressure-based insole	38.8% Custom-made insoles	11.5% Custom-made insoles	27.7% Manufactured shoe and insoles	14-15% Extra depth shoe, custom and prefab	23% Rocker sole shoes
Control group ulceration (%)	45.3% Standard of care	44.2% Standard of care	38.6% Standard of care	58.3% Self-selected	17% Self-selected	64% Standard of care

Prevention of recurrent diabetic foot ulcers. Expanded from Bus SA, Lavery LA, Monteiro-Soares M, et al. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev.* 2020;36(Suppl 1):e3269.

ESR >73.5 mm/h, CRP >1.5 mg/dL, procalcitonin >0.034 ng/mL, interleukin 6 (IL-6) >6.56 pg/mL, IL-8 >13.3 pg/mL, and monocyte chemoattractant protein 1 (MCP) >42.5 pg/mL are all predictive of reinfection.¹¹⁹ ESR and CRP are inexpensive and readily available for monthly monitoring during the post-operative period.

PREVENTION

There is a tremendous opportunity to change the trajectory of diabetic foot complications by understanding and implementing prevention practices.^{97,123} Since most patients that are treated by vascular surgeons have a history of a foot ulceration, amputation or vascular intervention, their patients will usually fit the highest risk profile. There is no evidence that the first foot ulceration can be prevented or that it would be cost effective to do so, because the incidence of DFUs in the general population is 2%–7% per year. There is essentially no research that specifically addresses this segment of the population. Most of the research in this area has been done on recurrent foot ulcerations, because the rate of reulceration is so high.¹²⁴ Preventing ulcer recurrence requires a multidisciplinary team that usually includes vascular surgery, podiatry, diabetes educator, and a pedorthotist. The crux of prevention is understanding the role of biomechanics (limited joint range of motion and structural deformity) in the etiology of DFUs. The main interventions for preventing reulceration includes foot-specific education, regular foot clinic evaluation, and therapeutic shoes and insoles.^{125,126}

Once a patient has developed a foot ulcer and it heals, 50%–80% of patients will have another foot ulcer within a year, if they don't receive some type of prevention.¹²⁷ Appropriately fitting shoes and insoles can prevent reulceration. In randomized clinical studies, patients treated with “therapeutic shoes and insoles” showed a two- to four-fold reduction in reulceration compared to patients with “self-selected shoes” (Table 117.3).^{125,128,129} After healing, patients should not wear the same shoes in which they developed their ulcer.

CONCLUSIONS

Unfortunately, many complications of diabetes are manifested in the foot. The management of these complications follows a predictable course of multiple hospitalizations, operations, and progressive limb loss. Early recognition and identification of the at-risk diabetic foot can curtail this downward spiral by a specialized and dedicated diabetic foot team.

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Wound Care

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Based on a previous edition chapter by William A. Marston

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The prevalence of diabetes and obesity has increased significantly, which has led to complications such as stroke, peripheral vascular complications, and chronic nonhealing wounds.^{1,2} In most medical communities, surgeons are considered the local wound care experts and are expected to manage cases that do not respond to conservative treatments recommended by primary care clinicians. This chapter focuses on the diagnosis and management of chronic wounds of the extremities that are often sent to vascular surgeons for definitive management.

The most common etiologic factors in **nonhealing limb ulcers** are **chronic venous insufficiency**, **arterial occlusive disease**, and **diabetic neuropathy**. Although venous insufficiency is prevalent, patients with arterial insufficiency and diabetic neuropathy are at the highest risk of limb loss.³ Accurate identification and treatment of these underlying disorders is the most important determinant of ulcer healing.

In many communities, specialized wound clinics have been developed, promising major benefits in wound healing, limb

salvage, and quality of life.^{4,5} These centers, in optimal situations, are able to effectively coordinate the efforts of diverse specialists to improve the treatment of difficult patients with chronic wounds. It is clear that a vascular specialist is a critical component of the team that can provide the comprehensive management of arterial and venous insufficiency required by a high percentage of patients treated in wound centers. Similarly, a vascular surgeon participating in a multispecialty wound center can coordinate with specialists, including endocrinologists, plastic or orthopedic surgeons, podiatrists, orthotists, and physical therapists, to maximize positive outcomes for their patients.

NORMAL WOUND HEALING

Healing of acute wounds normally proceeds through well-defined phases of hemostasis, inflammation, proliferation, and remodeling. Although these phases are typically described separately, the process is actually a gradual progression guided and regulated by the complex interaction of platelets, neutrophils, macrophages, and other cells that respond to and produce growth factors, cytokines, proteases, and inhibitors.⁶⁻⁸ Although the effects of many of these proteins have been described, the deficiencies that lead to the failure of timely healing are not well described. It is clear that all of the common causes of nonhealing wounds, including venous hypertension, arterial insufficiency, chronic pressure, and chronic inflammation, inhibit this orderly healing process, usually creating stasis in the inflammatory stage, with little meaningful tissue proliferation demonstrated.


Inflammatory Phase 24hr → 2/52 ::

The inflammatory phase of wound healing is critical to the normal healing process. Mediated by mast cells, neutrophils, and macrophages, inflammation develops within 24 hours of acute wounding and continues for up to 2 weeks. The involved cells produce chemokines, cytokines, and growth factors that mediate the inflammatory process.⁹ Cytokines such as tumor necrosis factor- α (TNF- α), interferon- δ (IFN- δ), and the interleukins (ILs) are released by activated lymphocytes and macrophages into the tissue, resulting in further recruitment and activation of fibroblasts and epithelial cells in the wound. Neutrophils following chemoattractant signals migrate into the wound, releasing concentrated matrix metalloproteinases (MMPs). The MMPs are responsible for clearing damaged tissue from the wound area by breaking down collagen (MMP-1 and -8), gelatin (MMP-2 and -9), and elastin (elastase). The activity of MMPs is closely controlled by tissue inhibitors of MMPs (TIMPs), which are produced principally by macrophages.⁹

Proliferative Phase

In the proliferative phase, growth factors, including platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), and vascular endothelial growth factor (VEGF), are secreted by multiple cell types but primarily by macrophages. They are responsible for the recruitment of fibroblasts to

commence the proliferative phase and for the initiation of angiogenesis required to support tissue generation and epithelial growth.^{10,11} Fibroblasts responding to signaling growth factors and cytokines migrate into the extracellular matrix, synthesizing collagen and proteoglycans and developing granulation tissue to fill the wound. Orderly capillary growth and networking must occur to support the developing granulation tissue; this requires a complex interplay of growth factors, including multiple isoforms of VEGF, TGF- β , and hypoxia-inducible factor-1 (HIF-1).^{12,13} MMPs are also required for the normal progression of angiogenesis and must be secreted at the correct time by budding capillary loops to allow them to degrade the existing capillary basement membrane as they sprout to establish a new capillary channel.

Epithelialization and Remodeling

Epithelialization occurs most rapidly on a well-granulated, confluent tissue bed, in response to signals from growth factors, such as epithelial growth factor and keratinocyte growth factor. Epithelial cells migrate into the wound from the periphery by secreting MMPs to degrade the nonviable tissue at the wound edge, allowing migration into the wound. Normally epithelial migration should continue until other epithelial cells are contacted.¹⁴

Remodeling is a long-term process in which type III collagen is largely replaced by mature type I collagen. This process also requires the presence of MMPs to degrade the type III collagen in a controlled fashion mediated by TIMPs, facilitating its replacement with maturing type I collagen.¹⁵

MECHANISMS OF ABNORMAL WOUND HEALING IN CHRONIC WOUNDS

Chronic nonhealing wounds occur when the normal healing process is disrupted. This is most frequently the result of an underlying disorder that causes a prolonged, unchecked proinflammatory state. These disorders include venous hypertension, chronic pressure, bacterial colonization, inadequate tissue perfusion, and cellular senescence.

Inflammation

Recurrent or prolonged inflammatory stimuli result in chronic wounds that are characterized by persistent upregulation of proinflammatory cytokines and MMPs. Although this environment is necessary for a brief period for acute wound healing, persistence of this environment has detrimental effects. Wound fluid collected from chronic nonhealing ulcers has been reported to inhibit DNA synthesis and mitotic activity of normal skin fibroblasts and keratinocytes.¹⁶ In contrast, fluid collected from acute wounds stimulate these measures of cellular activity. Chronic wound fluid may contain high levels of MMP-2 and MMP-9 and abnormally low levels of TIMPs.¹⁷ In venous ulcers, MMP levels decrease after compression treatment. In a study of 56 patients with pressure ulcers, Ladwig

et al. found that the ratio of MMP-9 to TIMP-1 was associated with wound healing outcomes: an elevated concentration of MMP-9 in relation to TIMP-1 was predictive of poor healing.¹⁵ Although this upregulation of protease levels might be expected to degrade endogenous growth factors, Drinkwater et al.¹⁶ reported that the level of VEGFs in venous ulcer tissue was not decreased and was persistently high compared with normal tissue, and was equivalent to levels in tissue from acute wounds. In a separate study, these researchers found that fluid from venous ulcers inhibited angiogenesis, postulating that this effect must be caused by the presence of inhibitors or a lack of available receptors rather than an absence of stimulatory growth factors.¹⁷ Patients with critical limb ischemia (CLI) also demonstrate deficits of growth factor function. Palmer-Kazen et al.¹⁸ found that distal limb tissue in patients with CLI had lower levels of VEGF compared with nonischemic proximal tissue in the same limb.

Cytokines

Upregulation of proinflammatory cytokines, including TNF- α , IL-1, and IL-6, has also been described in chronic venous wound fluid.¹⁹ These levels were found to improve when ulcers began to heal, with a decrease in size and improvement in granulation. Diabetic foot ulcers may also display proinflammatory upregulation and low expression of angiogenic factors.¹⁹

Cell Senescence

Cellular senescence has been reported in fibroblasts collected from chronic nonhealing ulcers. Lal and colleagues²⁰ found that fibroblasts from patients with increasing levels of venous disease by clinical class, etiologic, anatomic, and pathophysiologic (CEAP) criteria displayed a progressively diminishing response to agonist-induced proliferation. Fibroblasts from CEAP class 6 patients displayed severe inhibition of the proliferative response to TGF- β 1. Mendez and colleagues²¹ reported a series of studies of cultured fibroblasts from venous ulcers, indicating that these typically display phenotypic characteristics of cellular senescence, including slow growth and altered morphology. Stimulation of senescent fibroblasts may be a key target of therapy for improving the healing potential of chronic leg ulcers.

Therapeutic Targets

The development of therapeutic targets based on the known mechanisms of poor healing has been difficult, given its overall complexity. Initial strategies at modulating protease expression have not yielded major improvements in healing. A dressing composed of a combination of collagen and regenerated cellulose (Promogran, Systagenix, North Yorkshire, United Kingdom) has been developed, based on its ability to bind MMPs in wound fluid *in vitro*.²² However, in a prospective randomized study of 276 patients with diabetic foot ulcers, treatment with this dressing for 12 weeks failed to result in a significantly higher incidence of complete healing (37%) compared with ulcers treated with saline-moistened gauze (28%).²³

General treatments for the reduction of inflammation such as doxycycline and nonsteroidal anti-inflammatory drugs have been studied in animal models and considered for clinical use.²⁴

However, a literature review of pharmacological agents for venous leg ulcer healing did not find evidence to recommend routine use of these agents.²⁵ Some researchers believe that the simple inhibition of upregulated proteases or cytokines is unlikely to yield significant gains in healing. As evidenced by the importance of MMPs in multiple aspects of the normal healing process, gross inhibition of their function impairs capillary development, epithelial migration, and collagen maturation. Beidler et al.,²⁶ in an analysis of cytokine levels and venous ulcer healing, found that untreated ulcers with higher levels of proinflammatory cytokines, including IL-1, IL-12p40, and IFN- δ , healed significantly better than those with lower levels of these cytokines before compression. It is clear that strategies to address the abnormal progression of healing in chronic ulcers must consider that inflammation is necessary at various points in the process and must be suppressed at other stages. Currently no diagnostic modalities are available to rapidly test the MMP or cytokine levels in wound fluid or tissue in a laboratory setting, but clinically relevant testing strategies are under development.

Etiology of Ulceration

The successful treatment of patients with nonhealing leg ulcers requires that the underlying cause of ulceration be correctly diagnosed. Common differential diagnoses of leg ulceration are provided in Table 118.1. It has been reported that multiple causes are involved in more than 20% of leg ulcers, so it is clear that each potential diagnosis must be considered in every patient.²⁷ Based on the history and physical examination, the proper cause or causes of chronic ulcers can be defined in the majority of patients, but if doubt remains, confirmatory noninvasive testing should be performed.

Venous Leg Ulcers

The epidemiology and pathophysiology of venous leg ulcers are described in Chapter 156 (Chronic Venous Disorders: Post-Phlebitic Syndrome, Natural History, Pathophysiology, and Etiology). Risk factors related to the development of venous ulcers are the same as those for the development of venous disease in general. It is important to understand that venous disease in any combination of anatomic sites may result in limb ulceration, including superficial venous insufficiency alone. The anatomic sites of venous reflux defined by duplex ultrasound examination in a series of 138 patients with venous leg ulcers are listed in Table 118.2.²⁸

The pathway between chronic venous hypertension and limb ulceration has been debated for years. In some patients, persistent venous hypertension with chronic limb edema leads to the gradual development of skin changes. Chronic upregulation of pro-inflammatory cytokines appears to mediate the development of tissue fibrosis and the clinical appearance of lipodermatosclerosis (Fig. 118.1). This is believed to be a preulcerative condition that should stimulate treatment to correct the underlying venous pathology or eliminate edema to reduce the risk of future ulceration. Ulceration eventually occurs either spontaneously or due to minor limb trauma in the lower calf or ankle that then does not heal.

TABLE 118.1 Differential Diagnosis of Causes of Chronic Nonhealing Leg Ulcers

Etiology of Wound	Differential Diagnosis	Method of Investigation
Infectious conditions	Mycobacterial Fungal Bacterial Treponemal/spirochetal	Wound biopsy with special stains and cultures, VDRL, PPD, CBC, ESR, C-reactive protein, chest X-ray, wound X-ray
Malignancy	Basal cell carcinoma Squamous cell carcinoma Kaposi sarcoma Lymphoma Mycosis fungoides	Wound biopsy for pathologic evaluation
Macrovascular arterial insufficiency	<u>Arteriosclerosis</u> <u>Posttraumatic</u> <u>Embolic</u> <u>Acute or chronic thrombosis</u>	Noninvasive vascular studies Bidirectional color Doppler, tcPO ₂ Contrast arteriography Computed tomography arteriography Magnetic resonance arteriography
Vasculitis/vasculopathy (microvascular arterial insufficiency)	<u>Diabetic microangiopathy</u> <u>Hypertensive microangiopathy</u> <u>Thromboangiitis obliterans</u> <u>Raynaud disorder</u>	tcPO ₂ Laser Doppler Possible biopsy
Venous insufficiency (deep and superficial)	Deep venous thrombosis Extrinsic compression (tumors) Deep valve insufficiency Perforator valve insufficiency Superficial venous insufficiency	Strain gauge plethysmography (maximum venous outflow) Venasus photoplethysmography Bidirectional color Doppler Air plethysmography
Lymphatic obstruction/lymphedema	Venolymphatic disease (secondary to congestive heart failure, hepatic failure, renal failure, other overload states) Primary or secondary lymphatic insufficiency Lymphangiosarcoma	Clinical diagnosis, history, physical examination, chest X-ray, liver function tests, chemistries, lymphangiography
Hematologic abnormalities	Anemia (sickle cell) Polycythemia Dysproteinemia	CBC, iron studies (Fe, TIBC, folate, B ₁₂) Sickle cell prep
Collagen vascular disorders	<u>Systemic lupus erythematosus</u> <u>Scleroderma</u> <u>Polyarteritis nodosa</u> <u>Wegener granulomatosis</u>	FANA Rheumatoid arthritis prep Serum complement Rheumatologic workup
Excessive pressure	Diabetic neuropathy Alcoholic neuropathy Decubitus ulcer Postoperative deformity Bone spurs	Monofilament (10 g) Vibratory sensation (>25 mV) X-rays

CBC, complete blood count; ESR, erythrocyte sedimentation rate; FANA, fluorescent antinuclear antibody test; PPD, purified protein derivative; tcPO₂, transcutaneous oxygen tension; TIBC, total iron-binding capacity; VDRL, Venereal Disease Research Laboratory.

TABLE 118.2 Anatomic Distribution of Venous Reflux in 138 Patients²⁸

Venous System	Limbs (%)
Deep alone	43.5
Deep and superficial	21.0
Deep, perforator, and superficial	6.5
Superficial alone	18.1
Superficial and perforator	10.9

Diabetic Foot Ulcers

The epidemiology and pathophysiology of diabetic foot ulcers are reviewed in detail in Chapter 119 (Podiatric and Vascular

Teams). For management purposes, it is critical to remember that the underlying causes of ulcers, such as polyneuropathy, vascular insufficiency, and infection, must be addressed before specific wound treatments can assist in healing. Inadequate pressure offloading is the most common cause of failure to heal, and no active wound therapy can overcome persistent pressure on a plantar ulcer. The assistance of an expert orthotist and consistent patient education to achieve compliance are far more important to the healing of diabetic foot ulcers than the specific dressing or agent selected.

Limb Ulcers Associated with Arterial Insufficiency

The treatment of patients with chronic nonhealing leg ulcers associated with arterial insufficiency involves a critical assessment



Figure 118.1 Limb with chronic venous insufficiency illustrating wound tissue scarring and lipodermatosclerosis.

of the patient's suitability for invasive procedures and the potential risk of limb loss based on ulcer characteristics. Data from several clinical trials studying CLI have identified a risk of major amputation in 25% to 40% of patients at 1 year if revascularization is not performed.^{29,30} However, the hemodynamic criteria for CLI are broad and further evaluation of the specific level of perfusion to the wound bed is needed to predict which patients have a good chance of healing without revascularization. It appears clear that the severity of the wound itself is important, such that a superficial partial-thickness wound (Fig. 118.2) may not require the same level of perfusion as a deep, complicated leg ulcer involving tendon or bone (Fig. 118.3) to achieve healing. The WIFL classification system (see the section on Wound Classification Systems later) was designed to capture the severity of wound tissue damage, arterial insufficiency, and infection as an aid to prediction of healing potential.³¹

The natural history of chronic wounds with arterial insufficiency that do not receive revascularization was reported in a study of 169 limbs.³² At 1-year follow-up, 52% of limb ulcers were healed, and 23% required amputation (Fig. 118.4). Risk factor analyses revealed that the ankle-brachial index (ABI) and wound grade were associated with amputation at 1 year. In another study of nonrevascularized patients with CLI and wounds, limbs were separated into groups based on the toe pressure in the affected limb.³³ If the toe pressure was 20 to 50 mm Hg, 85% of patients were able to achieve limb salvage with wound management using standard multispecialty wound protocols, compared with only 60% in those with a toe pressure less than 20 mm Hg. Unfortunately, survival in these patients is poor, particularly in the patients with the lowest toe pressures less than 10 mm Hg, in whom only 8% of patients achieved amputation-free survival at 3 years. This is due to severe medical comorbidities affecting these patients, including a high prevalence of renal failure and cardiac dysfunction, which also lead to higher risks for efforts at revascularization.³⁴ This information suggests that some patients with AI and wounds who are at high risk for a poor outcome with revascularization can be reasonably treated without revascularization, and many will experience limb salvage. Revascularization should be



Figure 118.2 Wagner grade 1 diabetic foot ulcer. The wound penetrates through the full thickness of the skin, involving the subcutaneous tissue but not the deeper tissue layers.



Figure 118.3 Complex heel ulcer with exposed tendon and infected bone.

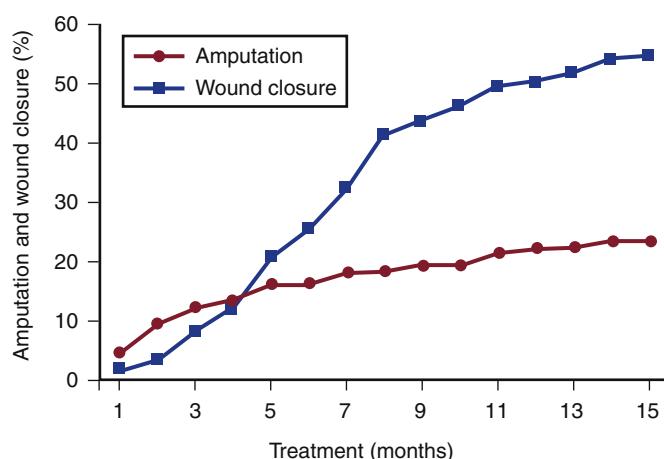


Figure 118.4 Incidence of major amputation and complete wound closure by life-table analysis in 169 limbs with tissue loss and nonrevascularized arterial insufficiency. (From Marston WA, et al. Natural history of limbs with arterial insufficiency and chronic ulceration treated without revascularization. *J Vasc Surg*. 2006;44:108–114.)

considered early in those who have rest pain, those with more severe wound grades, and those with pedal gangrene. Wounds treated initially with wound management without revascularization should be monitored closely for progress, and if this does not occur within 4 to 6 weeks, revascularization should be considered. Arterial insufficiency is a common complicating factor for limb ulcers associated primarily with other causes, including venous insufficiency, diabetes, and rheumatoid arthritis. It is important that the status of the arterial supply be determined in every patient at the initial evaluation.

Other Causes of Limb Ulceration

Although the preceding causes are important factors in more than 90% of nontraumatic limb ulcers, other causes, including vasculitis, sickle cell anemia, malignancy, and dermatologic disease, are routinely seen by vascular specialists. It is beyond the scope of this chapter to review these leg ulcers in detail. The key to diagnosing these atypical causes is ulcer biopsy. Many of these conditions may be confused with venous ulceration and may coexist in a patient with chronic venous insufficiency. The most important diagnosis to make is **Marjolin ulcer**, which may develop when squamous transformation occurs in a pre-existing benign chronic wound (Fig. 118.5). This neoplasm is often not detectable by observation, so the physician must maintain a high index of suspicion. Whenever a wound does not respond to a comprehensive treatment plan as expected or a wound that has been healing ceases to progress for no known reason, a biopsy should be performed to rule out malignancy. Further information on the diagnosis and management of atypical wounds is beyond the scope of this chapter.

CLINICAL PRESENTATION AND INITIAL EVALUATION

The primary cause of most wounds can be identified after the history and an attentive physical examination. **Figure 118.6** contrasts common types of lower extremity ulcerations.



Figure 118.5 Chronic wound with squamous cell malignancy (Marjolin ulcer).

Wound Classification Systems

Key factors in describing wounds include depth, infection and ischemia. The earliest recognized system for classification of diabetic foot ulcers was the **Meggitt–Wagner** grading system. This included depth, infection and ischemia, but did not allow for adequate concomitant description of these factors. It therefore lost some of its descriptive and predictive potential. It was replaced by the **University of Texas** Classification System. It included depth, infection and ischemia for each grade and stage and was more predictive of outcome. UT, however, only included a “yes/no” for both infection and ischemia (**Table 118.3**).^{21–23,35}

In an attempt to address the evolving interdisciplinary nature of limb preservation and to address some of the issues listed above, Mills and coworkers proposed a new classification of the threatened lower extremity that also includes the presence and extent of wound ischemia and infection.³¹ The **WIFl** classification (see Table 107.3) has been widely validated to correlate to the risk of amputation in several subsequent publications. Additional “add-ons” to the WIFl system have included ambulatory function to assist in decision-making.^{31,36,37}

Wound Size Measurement

At each visit, it is important to measure the wound size to document progress and alter the treatment plan if necessary. Subtle changes in the wound itself, including the development of inflammation or bacterial colonization, may manifest only as the suppression of healing. Routine wound measurement allows the consideration of alternative treatment methods as soon as progress in wound healing ceases.

Numerous methods are available to document and follow wound size, including digital photography with computerized



Figure 118.6 (A) Leg ulcer associated with chronic venous insufficiency. (B) Diabetic neuropathic ulcer. (C) Plantar ulcer in a patient with diabetes and chronic Charcot neuropathy. (D) Leg ulcer in a patient with both arterial and venous insufficiency. (E) Leg ulcer in a patient with systemic lupus and venous insufficiency. (F) Squamous cell carcinoma arising in a chronic foot ulcer. (G) Leg ulcer associated with rheumatoid arthritis. (H) Bacterial biofilm covering the surface of a nonhealing venous leg ulcer. (I) Same ulcer depicted in (H) after elimination of the biofilm following debridement and 2 weeks of antibiotic therapy. (J) Chronic leg ulcer in a patient with sickle cell anemia.

planimetry, direct planimetry, and simple measurement of dimensions. Software systems are also available to allow the determination of wound size from calibrated digital photography.

Wound Bed Assessment and Preparation

Once the history and physical examination are completed and a general idea of the underlying cause of the wound is

determined, the wound itself must be assessed for local factors inhibiting healing. Numerous factors must be identified and corrected to optimize healing potential, a process termed “wound bed preparation.” The components of this process include debridement of nonviable tissue, identification and correction of bacterial involvement, control of chronic inflammation, elimination of limb edema, and control of wound exudate. The first two components are addressed here.

TABLE 118.3

Incidence of Limb Amputation in Patients Presenting with Limb Ischemia Based on Wagner Grade^a at Initial Presentation

Grade	Criterion	Amputation at 12 Months (%)
0	Preulcerative lesion	
1	Superficial ulcer	12
2	Ulcer extending deep to tendon, bone, or joint	19
3	Deep ulcer with abscess or osteomyelitis	31
4	Forefoot gangrene	49
5	Whole foot gangrene	100

^aGrades 1–4 (*n* = 169).

From Marston WA, et al. Natural history of limbs with arterial insufficiency and chronic ulceration treated without revascularization. *J Vasc Surg*. 2006;44:108–114.

Debridement

The majority of chronic limb ulcers are covered with nonviable tissue, including callus, eschar, fibrinous material, and slough. This tissue has no regenerative capability, harbors bacteria, and prevents the migration of healthy epithelium into the wound. Debridement is required to excise nonviable tissue and should be aggressive, particularly at the initial evaluation. Cellular senescence has been identified in wound tissue around diabetic foot ulcers and chronic venous ulcers of long duration, indicating the need for wound excision to remove all surrounding tissue in these cases (Fig. 118.7).³⁸ In a prospective multicenter study of becaplermin for the healing of diabetic foot ulcers, a secondary analysis suggested that centers employing more frequent wound debridement achieved better healing rates.³⁹

In a retrospective review of 676 patients enrolled in clinical trials of novel therapeutic agents for venous or diabetic ulcers, the incidence of wound debridement was studied and correlated with wound closure.⁴⁰ Thirty-three centers where limbs were debrided more frequently were associated with higher rates of wound closure for both types of wounds, but an increased frequency of wound debridement per patient did not statistically correlate with higher rates of wound closure. Using a large retrospective data set, Wilcox and colleagues (2013) documented faster healing with weekly debridement ($P < 0.001$) of a variety of chronic wounds.⁴¹ Based on this information, it appears that debridement for chronic wounds is important to eliminate nonviable tissue and may be required multiple times during the treatment course of the wound. However, the current body of evidence provides no definitive guidance on the question of how often chronic wounds should be debrided or the best timing.

Numerous alternatives to surgical debridement have evolved, including chemical debridement, ultrasound debridement, hydro-debridement, and larval therapy. In general, there are two situations in which alternatives to surgical debridement may be desirable: patients in long-term nursing facilities, and those who have difficulty traveling to wound or surgical clinics for surgical debridement when required. These patients may benefit from chemical debridement or some other method.

Chemical

Chemical debriding agents are typically composed of enzymatic agents, including collagenase (Santyl, Healthpoint Ltd., Fort Worth, TX). Collagenase may be used as a maintenance debriding agent to remove moderate amounts of fibrinous slough from the wound surface, but it is usually ineffective against thick tissue or eschar.

Larval

Larval therapy using medical maggots has been studied as an alternative to conventional therapy in several nonrandomized studies. Sherman reported that 80% of maggot-treated pressure wounds achieved complete debridement, compared with 48% of conventionally treated wounds.⁴² However, most of the studies evaluating maggot therapy have used autolytic or chemical debridement as comparators. A randomized study of larval therapy compared with hydrogel for the management of chronic leg ulcers was reported in 2009.⁴³ All other wound therapies were similar for each group. The study found that larval-treated wounds experienced significantly faster debridement than the hydrogel-treated group, but at the expense of significantly higher ulcer-related pain scores. No difference in ulcer healing or patient quality of life was demonstrated.

Ultrasound

Debridement using standard surgical techniques may be particularly painful, leading to interest in alternative methods that achieve wound debridement while increasing patient comfort. Several energy modalities, including ultrasound, have been investigated as adjuncts to debridement.⁴⁴ Ultrasound may be used in conjunction with a surgical or debridement instrument: the instrument directly contacts the wound and uses a fluid medium to deliver ultrasound energy to the tissue to loosen and remove nonviable tissue. Ultrasound energy delivered using a noncontact, mist technique does not provide debridement effects.

In summary, no other form of debridement has demonstrated superiority to standard surgical debridement, and most of these methods are less cost effective in the majority of cases. Alternative methods of debridement are generally recommended when surgical debridement is not possible or is not desirable.

Bacterial Colonization

Significant bacterial infection is a common complication in chronic wounds. In several prospective randomized clinical trials of therapies for diabetic foot ulcers, wound infection requiring systemic antibiotic therapy occurred in 20% to 25% of cases.^{45,46} However, the treatment of bacteria in wounds that do not appear to be clinically infected is controversial. This is even more problematic when one considers that clinical examination sensitivity is less than 15% and over 80% of wounds with elevated bacterial loads go undetected and therefore incompletely treated.^{47,48} Moreover, it is believed that uninfected healing wounds are colonized with bacterial flora. Treatment with antibiotics is not indicated, so routine culturing of wounds in these cases is not recommended. The

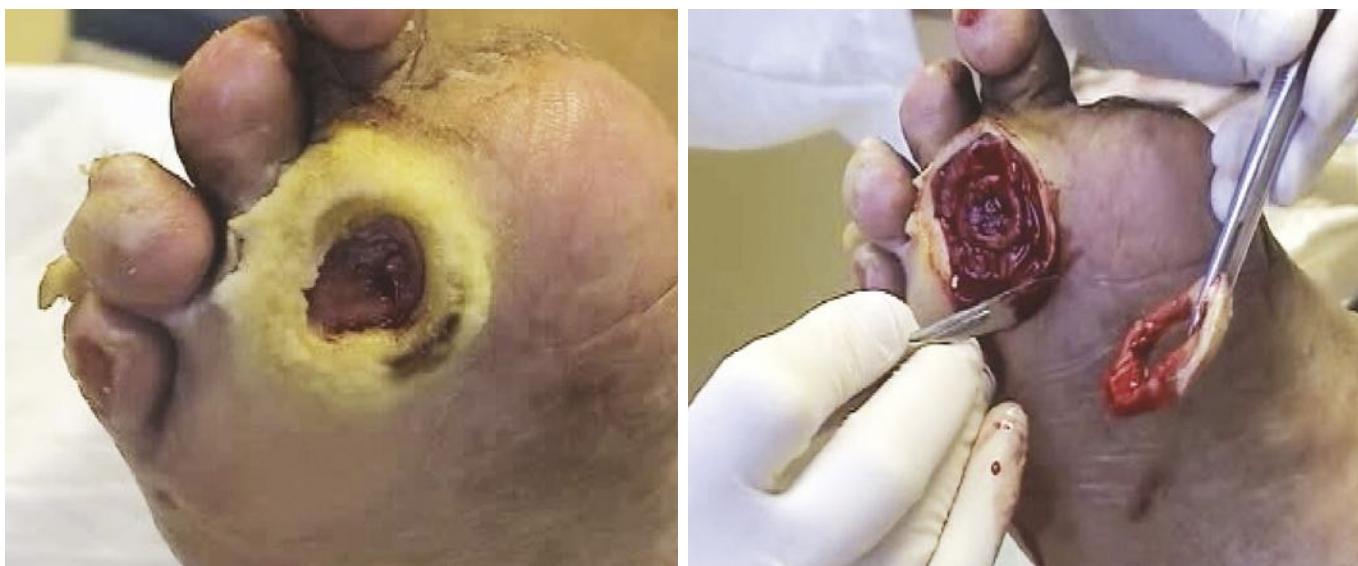


Figure 118.7 Example of aggressive debridement of senescent tissue in and around the wound bed to create an acute wound out of a chronic wound.

eradication of normal skin and nonvirulent wound bacteria is not desirable and may support the growth of more virulent and resistant bacterial strains. Of note, however, recent studies have identified an increase in the incidence of resistant organisms from cultures of chronic nonhealing ulcers that do not respond to standard treatment protocols.⁴⁹

Biofilms harboring bacteria are well known to cover indwelling catheters, industrial surfaces, and dental structures. Bacteria in these situations secrete a polysaccharide substance that covers the colonies, which grow and interact to inhibit host-generated control mechanisms. Mechanical methods of cleansing these surfaces can minimize biofilms, but they typically repopulate rapidly after cleansing. In chronic wounds, biofilms appear to multiply to the point at which they inhibit healing by stimulating chronic inflammation, inactivating growth factors critical to the healing process, and preventing orderly angiogenesis required for healing (Fig. 118.8).⁵⁰ If untreated, it is believed that biofilms will continue to inhibit wound healing or may lead to more significant systemic infection.

Several factors influence the effect of bacteria on wound healing. These include: bacterial load, species,⁵¹ virulence^{52,53} and biofilm.^{54–56} There is evidence to suggest that wound healing generally begins to decrease at 10⁴ colony forming units per gram of tissue (CFU/g).^{51,57,58}

The current “gold standard” for detecting high bacterial load in chronic wounds remains quantitative analysis of tissue biopsies. However, many wound care practitioners cannot take wound biopsies. Additionally, microbiological analysis and molecular diagnostics are expensive and time-consuming compared with semi-quantitative swab analysis, resulting in the latter being more widely used.^{59,60} A recent study comparing semi-quantitative and quantitative culture methods found semi-quantitative culture data to be highly variable and therefore an unreliable method of determining bacterial load in wounds.⁶¹

An emerging technology that may assist clinicians with this quandary is point-of-care fluorescence imaging (MolecuLight

i:XTM, MolecuLight Inc., Toronto, ON, Canada), which allows noninvasive, non-contact visualization of the presence and location of bacteria at loads greater than 10⁴ CFU/g. The violet light emitted from the imaging device elicits a red fluorescence signal from porphyrin-producing bacteria and a unique cyan fluorescence signal from *pseudomonas aeruginosa* (Fig. 118.9).⁶² Clinical trials are already establishing high diagnostic accuracy with fluorescence imaging. With quantitative tissue culture as a reference standard, a >95% positive predictive value was shown for red and cyan fluorescence detecting bacterial loads capable of delaying healing.^{47,63,64} Studies have also demonstrated a sensitivity 300%–400% greater than the current standard of care.^{47,48}

PROPERTIES AND CATEGORIES OF WOUND DRESSINGS

In general, the selection of a wound dressing should be based on wound characteristics, including location, inflammation, and amount of exudate. Moisture balance is important, and the dressing should maintain a moist environment conducive to tissue growth and epithelial migration. Based on the high concentration of inflammatory cytokines and proteases in chronic wound fluid, excessive fluid should be wicked away from the ulcer and the skin surface to prevent further tissue inflammation and damage from prolonged contact.

A multitude of agents with theoretical healing benefits have been added to wound dressings, including collagen, zinc, enzymes, copper, chlorophyll, honey, avocado oil, and others with little proof of benefit. Table 118.4 lists the common categories of wound dressings and their typical uses.

Diabetic foot ulcers are typically treated with dressings that donate moisture to the wound bed, such as hydrogels, because the wound usually produces little exudative drainage. More heavily draining wounds are better treated with alginates or



Figure 118.8 Examples of the appearance of biofilm covering chronic wounds.



Figure 118.9 Side-by-side comparisons of photographic images and point-of-care fluorescence images showing the unique cyan fluorescence of *Pseudomonas aeruginosa* on both open wound tissue and intact skin.

TABLE 118.4 Dressing Categories and Characteristics

Dressing Category	Characteristics	Examples
Alginate <i>Exudate</i>	Forms moist gel as it absorbs – requires a secondary dressing	Algisite
	Conformable/fills dead space	Kaltostat
	Manages moderate to heavy exudate	Maxorb
	Can be combined with antimicrobials	Melgisorb
Collagens	Bovine, equine, porcine or avian-derived products that assist in stimulating wound progression	Fibracol
	Multiple forms – gel, pad, paste, powder, sheets	Promogran
	Some dissolve completely and others will need to be removed (check manufacturer guidelines)	Biostep
	Usually require a secondary dressing	Triple Helix Collagen Dressing
Should not be used on infected wounds		
Composites	Combine different dressing functions into one product (i.e., antimicrobial, absorption, adhesion)	Covaderm Plus
		DermaDress
		Leukomed
		Mepore
Foams	Absorb moderate amounts of exudate	Biatain
	Can be used under compression	Optifoam
Gauze	Highly permeable	PolyMem
	Appropriate for wound cleansing, as a cover dressing and for dressing securement	Mepilex
	Not appropriate as a primary wound dressing	Curity
		Kerlix
Hydrocolloids	Impermeable to bacteria	Kling
	Facilitates autolytic debridement – do not use on infected wounds	Packing strips
	May tear fragile skin	Comfeel
		Duoderm
Hydrogels <i>DFU</i>	Glycerin and water-based products available as amorphous gels, sheets or impregnated dressings	Exuderm
	May be antimicrobial	Replicare
	Donates moisture to wounds	Duoderm gel
	Can assist in autolytic debridement	Elasto-gel
Super Absorbents <i>Exudates</i>	May reduce pain	Intrasite
	Requires secondary dressing	Solosite
	Absorb large amounts of exudate	ConvaMax
	Fluid lock technology similar to diapers	Drawtex
	Available in different dressing sizes and rolls	Drawtex edema wrap
	Some products may become bulky as they absorb more exudate	

hydrofibers with greater moisture removal capabilities. Venous leg ulcers are heavily exudative, with a high protease content to the fluid. This requires more absorbent dressings that actively wick exudate away from the wound and surrounding skin. Compression systems are placed on top of this primary dressing and should be changed as often as necessary to prevent saturation of the dressing, usually one to three times weekly.

As concern over resistant bacterial species has increased, a vast array of dressings containing antimicrobial agents has been

developed. Employing these agents generally requires a balance between the positive antimicrobial effect and the inhibition of normal tissue proliferation and wound healing. The long-term use of iodine-based topical antibiotics in chronic wound healing fell out of favor after *in vitro* studies suggested the suppression of fibroblast function. Slow-release dressings containing cadexomer iodine were developed, designed to reduce the concentration of iodine limiting negative effects on wound healing while inhibiting bacterial growth. In a small multicenter

randomized study comparing cadexomer iodine to wet-to-dry dressings in venous leg ulcers treated with compression, the cadexomer iodine–treated wounds were found to heal more than twice as rapidly as the control ($P = 0.0025$).⁶⁵

Silver and numerous other antimicrobial agents have been incorporated into dressing materials, many combined with other dressing characteristics that also permit moisture management in the wound bed. A Cochrane analysis of the benefit of silver-releasing dressings for the healing of chronic wounds found insufficient evidence to recommend their use for the treatment of infected or contaminated wounds.⁶⁶ In a randomized study of 129 patients with venous leg ulcers colonized with critical levels of bacteria and poor healing, a silver-containing foam dressing was compared with a non-silver-containing dressing; both groups received multilayer compression.⁶⁷ After 4 weeks, the silver-treated ulcers had closed an average of 45%, compared with 25% in the control group ($P < 0.05$). The wounds were not treated with the product to complete healing, so the rate of wound closure was not assessed. A prospective randomized trial performed in chronic venous leg ulcers evaluated the effect of routine use of silver-donating dressings compared with non-silver-donating dressings over a 12-week period.⁶⁸ All patients were treated with high-strength compression and primary dressings of similar absorptive capacity either with or without silver. No demonstrable effect on healing or quality of life was associated with the use of silver. Given the increased cost of these dressings, it was concluded that routine use is not indicated.

Based on this information, it may be concluded that topical antimicrobial agents should not be used routinely to treat wounds for extended periods, but targeted use in well-defined wounds with critical levels of bacterial involvement may yield a benefit.

VENOUS LEG ULCERS

All patients with venous leg ulcers (VLUs) who are candidates for corrective procedures should have diagnostic studies to determine their specific anatomy and physiology. Particular attention should be paid to correctable venous abnormalities, including saphenous reflux, perforator incompetence, and iliac outflow stenosis.

The American Venous Forum and Society for Vascular Surgery published treatment guidelines for venous leg ulcers in 2014. These comprehensive practice guidelines include recommendations on therapy to prevent ulceration, therapies to heal VLUs, and methods to prevent ulcer recurrence after healing.⁶⁹

Compression

Sustained high-strength compression of the limb remains the basis of treatment for venous leg ulcers. Discussed in detail in Chapter 157 (Treatment of Chronic Venous Disorders), compression must be initiated before other therapies and throughout the treatment course to attain healing. Adjuvant therapies will uniformly fail if limb compression is not maintained during treatment in an ambulatory patient.

Pharmacologic Treatment

Pentoxifylline

In a review of randomized controlled trials, Jull et al.⁷⁰ found five trials in which pentoxifylline and compression were compared with placebo and compression. Pooling these data resulted in the conclusion that more patients in the pentoxifylline group achieved healing. In one of the studies, Falanga et al.⁷¹ reported a median time to healing of 100 days for placebo, compared with 71 days for pentoxifylline at 800 mg three times daily.

Flavonoids

Flavonoids are a class of plant-derived compounds that display anti-inflammatory and antioxidant properties. Two randomized controlled trials studied the benefit of flavonoids in addition to compression for venous leg ulcer healing, and both found a significant benefit for flavonoid treatment.^{72,73}

Anticoagulants

In an RCT on 284 patients with VLUs treated with compression therapy and surgical intervention, daily subcutaneous injection of low-molecular-weight heparin (LMWH) for 12 months was found to accelerate wound healing.⁷⁴ Patients treated in the group randomized to receive LMWH experienced complete ulcer healing in 83.8% at 12 months compared with 60.6% at 12 months in those treated without LMWH. Although the cost and complications associated with daily LMWH use for a year may not warrant therapy for most patients with VLUs, this therapy may be considered for carefully selected recalcitrant ulcers not responding to other therapies.

Indications for Intervention

Gohel et al.⁷⁵ performed a randomized study comparing the efficacy of saphenous stripping plus compression with compression alone for the healing and prevention of venous leg ulcers in patients with superficial venous reflux. Significantly fewer patients in the surgery group experienced recurrent ulceration (15%) compared with the compression-only group (34%) at 1-year follow-up (Fig. 118.10). At 4 years of follow-up, 56% of patients treated with compression alone had developed recurrent ulceration compared with 31% of those in the surgery group ($P < 0.01$).

Based on the results of this trial, it is reasonable to recommend venous intervention to reduce the incidence of ulcer recurrence whenever superficial venous reflux is a prominent component of the abnormal venous function. This constitutes 30% to 50% of cases seen at most venous leg ulcers centers. However, intervention cannot be recommended for most patients to accelerate wound healing. The contribution of incompetent perforators to global venous insufficiency remains controversial and is discussed in detail in Chapter 158 (Chronic Venous Insufficiency: Treatment of Perforator Vein Incompetence), but it is clear that some leg ulcers are associated with large incompetent perforators that should be ligated or ablated.

There is also limited evidence supporting the removal of varicose channels extending into the ulcer bed to eliminate the final channel of venous hypertension extending into the area of

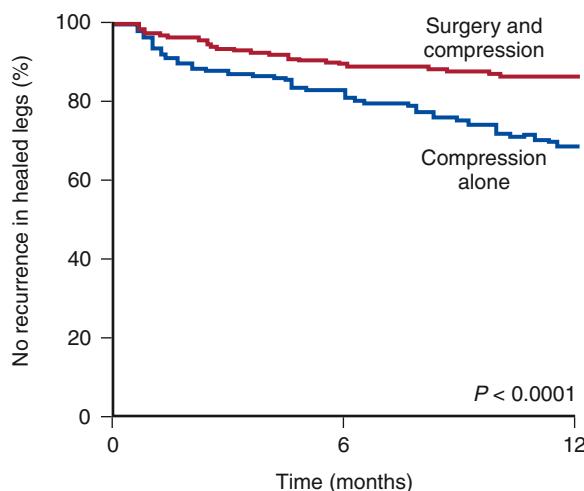


Figure 118.10 Incidence of ulcer recurrence in patients with chronic venous insufficiency due to superficial venous reflux treated with compression alone compared with compression plus surgical stripping of the saphenous vein. (Modified from Gohel MS, Barwell JR, Taylor M, et al. Long term results of compression therapy alone versus compression plus surgery in chronic venous ulceration (ESCHAR): randomized controlled trial. *BMJ*. 2007;335:83.)

ulceration.⁷⁶ This may be done surgically or with sclerotherapy. Deep venous reconstruction can be considered in some cases (see Ch. 159, Chronic Venous Insufficiency: Deep Vein Valve Reconstruction).

Adjunctive Therapies to Accelerate Healing

Treatment of venous leg ulcers with compression bandaging using any number of systems results in healing in approximately 60% to 70% of patients after 4 to 6 months of consistent therapy.^{26,77} Numerous adjunctive methods have been studied in an attempt to accelerate this healing process, including skin grafting, growth factors, living human skin equivalents, collagen matrices, platelets, topical therapies, ultrasound, electrical stimulation, and other modalities. The majority of these therapeutic strategies have limited data supporting their efficacy.

One additional adjunctive strategy to consider for patients with venous leg ulcers is referral to physical therapy for an exercise prescription. Evidence is still limited but suggests that appropriate patients would benefit from progressive resistance exercises and at least 30 minutes of walking at least three times per week. Completion of this regimen suggests that for every four patients treated with prescribed exercise plus compression, one more patient might heal than if using compression alone. Additionally, the risk of including exercise is low to most patients given the benefits of physical activity and the impact of prolonged inactivity on function.⁷⁸

Skin Grafting

Although split-thickness skin grafts have been employed for decades in an attempt to heal recalcitrant venous leg ulcers, there is little quality information supporting the benefit of this practice. There are no adequately powered randomized studies reporting the results of skin grafts versus compression

therapy alone. The Cochrane Database recently reviewed the available clinical studies and concluded that further research is needed to assess whether skin grafting increases ulcer healing.⁷⁹ Although definitive evidence is lacking, some clinicians consider skin grafting in slow responding wounds or for patients with large soft tissue deficits that are able to granulate well to provide a clean healthy bed to support graft take. In a nonrandomized study of 111 patients, Jankunas demonstrated improved healing and durability with skin grafting compared with conservative therapy for large venous wounds that were present longer than 6 months, but only 65% of cases were judged to have good take of the split-thickness skin graft.⁸⁰

For patients with large ulcers and extensive peri-ulcer lipodermatosclerosis, radical excision and free-flap tissue transfer have been described, with durable improvement in some cases.

Cellular and/or Tissue-Based Products

There are currently over 75 different cellular and/or tissue-based products available for use in wound care. These include animal and human tissue-based non-viable cell preparations; viable human cells, cultured *in vitro*, delivered via either an animal or synthetic substrate; and intact tissue from non-cultured viable human cells.⁸¹

DIABETIC FOOT ULCERS

See Chapter 117 (Diabetic Foot Abnormalities and their Management) for diagnostic modalities and a discussion of wound debridement, pressure offloading, and treatment of infection. The Society for Vascular Surgery also recently published comprehensive practice guidelines for the care of patients with diabetic foot ulcers in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. The reader is referred to these guidelines for additional information on optimal management of diabetic foot ulcers (DFUs).⁸²

Adjunctive Therapies to Accelerate Healing

Vitamin D

In a randomized clinical trial, 60 patients with Wagner grade 3 DFUs were randomized to standard wound therapy with or without supplementation of 50,000 IU of vitamin D every 2 weeks.⁸³ After 12 weeks of treatment, the authors reported that the vitamin D-treated patients had significantly greater reduction in wound size as well as significant reductions in HbA1c, LDL, high sensitivity C-reactive protein and erythrocyte sedimentation rate. Based on this study, many clinicians believe vitamin D supplementation to be reasonable in DFU patients.

Growth Factors

Although multiple growth factors have been studied in clinical trials, to date only PDGF has been approved by the FDA for the treatment of diabetic foot ulcers. Bevacizumab (Regranex, Ortho-McNeil, Raritan, NJ) is a recombinant human

BB isoform of PDGF suspended in a gel designed for topical application. Becaplermin is applied daily to the diabetic foot ulcer and covered with saline-moistened gauze. It has been studied clinically in four prospective, randomized, placebo-controlled trials. In a meta-analysis of these studies, Smiell et al.⁸⁴ aggregated the 922 patients studied for analysis. Fifty percent of ulcers treated with the higher dose of becaplermin (100 mcg/g) for 20 weeks healed, compared with 36% treated with placebo gel ($P = 0.007$). Adverse events were rare, and the only medication-related event was local tissue sensitivity in 2%.

Kantor and Margolis⁸⁵ studied 26,599 patients from a clinical wound treatment database and reported effective wound closure at 20 weeks in 31% of those treated with standard care, compared with 43% treated with becaplermin. The incremental cost of increasing the odds of healing by 1% over standard therapy was \$36.59 for becaplermin. In 2008 the FDA released a **black box warning** concerning the risk of fatal cancers in patients treated with becaplermin. Based on long-term follow-up studies of patients enrolled in randomized studies, there was no increased risk of malignancy in patients treated with becaplermin, but those who developed malignancies had a greater risk of dying from them.⁸⁶ This information is based on a small number of observations, so it should be interpreted with caution. It does emphasize, however, that the drug should be considered only in refractory diabetic foot ulcers failing to respond to standard therapy.

ULCERS ASSOCIATED WITH ARTERIAL INSUFFICIENCY

Patients with limb ulcers and associated arterial insufficiency should undergo diagnostic evaluation to attempt prediction of whether the ulcer can heal without revascularization. Potential studies include ABIs, toe pressures, transcutaneous oxygen/tension pressure (tcPO₂), and laser Doppler. These are reviewed in detail elsewhere in this text.

Local Wound Management

The basic tenet of managing wounds due to arterial insufficiency is to keep them infection-free and as stable as possible until revascularization occurs. In the case of open arterial wounds, this may mean use of moisture-retentive dressings with or without an antimicrobial component. In arterial wounds presenting as **dry eschar**, the focus is on maintaining that dry environment and protecting the area from any trauma. The use of alcohol or iodine over dry eschar and cotton and/or gauze padding can be beneficial in achieving these goals.

The need for revascularization is assessed using several variables. If the patient has severe pain at rest and is a good candidate for revascularization, this should be performed as soon as possible on an elective basis. Patients with diabetes and arterial insufficiency rarely have significant pain at rest, probably due to neuropathy. Wound size, depth, and character are all important measures. A small grade 1 ulcer on the dorsum of the foot is

much more likely to heal without revascularization than is a large, complicated, deep wound on the plantar surface of the foot. The potential for healing based on noninvasive tests must be balanced with the risk of complications associated with the intervention required for revascularization. In patients in whom the risk–benefit assessment does not favor revascularization, the potential for healing should be optimized with standard wound care along with consideration of the modalities discussed next.

Pharmacologic Treatment

Pentoxifylline and Cilostazol

There is no high-quality evidence suggesting that either pentoxifylline or cilostazol is able to accelerate wound healing in patients with ulcers associated with arterial insufficiency.

Prostaglandins

Prostaglandins, particularly prostaglandin E₂ and prostacyclin, in addition to their potent vasodilatory effects, can prevent leukocyte activation and platelet aggregation. In some studies, treatment has resulted in significant improvement in patients with CLI.^{87,88} However, a number of problems with prostaglandins have hindered their widespread use. Most are intravenous medications with short half-lives, requiring intravenous infusion for administration. Also, troubling side effects at clinically relevant doses, including headaches and dizziness, are frequent. Although available in other countries, no prostaglandin therapeutic agents have been approved by the FDA for the treatment of ischemic wounds.

Angiogenesis for Critical Limb Ischemia and Ischemic Wounds

Since the discovery of VEGF and techniques that allow it to be delivered to target tissue, there has been great enthusiasm for therapeutic strategies promising the development of new capillary beds to support blood supply. In numerous animal models, the transfer of VEGF to localized target tissues has resulted in angiogenesis, with the proliferation of blood vessels and increased tissue perfusion.⁸⁹ The application of this powerful technology to humans has been a long, arduous process because of concern over unintended adverse effects, such as tumor induction and the promotion of occult malignancies, resulting in accelerated growth and metastatic potential.

Local gene transfer to facilitate therapeutic angiogenesis has the theoretical advantage of producing protracted growth factor expression compared with single doses or direct applications of growth factors to wounds. Unfortunately, no angiogenic growth factor therapies have yet achieved FDA approval for use in patients with CLI and leg ulceration. Although several early phase clinical studies appeared promising, larger studies did not confirm that these therapies healed more wounds or prevented amputation. Similarly, investigations of progenitor cell therapies have also failed to demonstrate significant reduction in the incidence of amputation or improved wound healing in CLI patients. Clinical trials continue with various progenitor cell preparations in this patient population.^{90,91}

Intermittent Pneumatic Compression

Numerous studies have documented the ability of various forms of intermittent pneumatic compression (IPC) to increase blood flow in ischemic limbs, suggesting that this modality may have a place in the treatment of CLI. Two general types of IPC have been described. In synchronized IPC, compression and deflation are gated to the cardiac cycle, with 55 to 80 mm Hg applied at end-diastole to maximize venous emptying. Pump decompression occurs before systole to reduce afterload and limit compression-related competition with systolic inflow to the limb.⁹² Nonsynchronized IPC has been described in numerous protocols using various pressures, inflation durations, and deflation durations. Typical protocols involve an inflation pressure of 120 to 180 mm Hg, an inflation duration of 3 to 5 seconds, and a deflation time of 15 to 20 seconds. IPC of affected limbs is recommended for 2 to 4 hours daily.

There have been no direct comparisons of the beneficial effects of synchronized versus nonsynchronized IPC. Nonsynchronized IPC is generally less expensive and is more amenable to home use; this makes it attractive, given the length of therapy required in patients with CLI.

IPC reduces the edema that often occurs in patients with CLI. This, combined with improved venous emptying during IPC, may result in an increase in the arteriovenous pressure gradient in the limb. With less resistance to inflow, blood flow may increase, resulting in increased tissue perfusion, relief of rest pain, and improved ulcer healing. IPC also has been reported to increase the concentration of prostacyclin and nitric oxide in the treated limb.⁹³ These peripheral vasodilators in theory may stimulate improved tissue perfusion, despite the presence of large-vessel occlusive disease.

Several investigators have evaluated the hemodynamic effects of IPC on lower extremity blood flow. The velocity of blood flow in the popliteal artery increased after the initiation of IPC.^{94,95} This increase was also noted in patients with significant arterial insufficiency.⁹⁶ Delis et al.⁹⁷ reported marked increases in popliteal artery blood flow during foot or calf compression, depending on the segments compressed (Fig. 118.11).

Delis et al.⁹⁸ studied 25 patients with claudication treated with nonsynchronized IPC of the foot and calf and 12 claudicants treated with an unsupervised exercise program. After 3 months of treatment, the IPC group had significant improvements in claudication distance, ABI, and mean popliteal artery blood flow. Control patients demonstrated no significant improvement. Of interest, 12 months after the cessation of IPC, the IPC group continued to demonstrate significant improvements over baseline in walking distance and ABI.

Using synchronized IPC, Vella et al.⁹² reported on the treatment of 98 limbs with ulcers related to arterial insufficiency. These patients were not candidates for revascularization because of either inadequate outflow vessels or medical comorbidities. In limbs with an initial $\text{tcPO}_2 < 20 \text{ mm Hg}$, ulcer improvement or healing was obtained in 19 of 29 limbs (65%); if the initial tcPO_2 was $> 20 \text{ mm Hg}$, 54 of 62 limbs (87%) healed or improved. From these data, the authors concluded

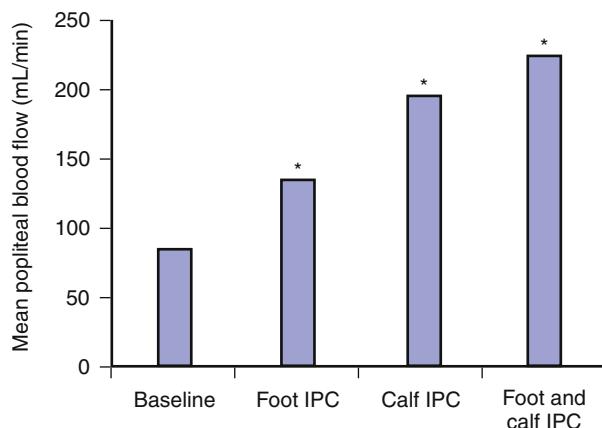


Figure 118.11 Mean popliteal artery blood flow in claudicants at baseline compared with claudicants using intermittent pneumatic compression (IPC) of various types. Each type of IPC resulted in significantly higher flows than baseline (* $P < 0.001$). (From Mansbridge J, Liu K, Patch R, Symons K, Pinney E. Three-dimensional fibroblast culture implant for the treatment of diabetic foot ulcers: metabolic activity and therapeutic range. *Tissue Eng*. 1998;4:403–414.)

that synchronized IPC is useful in a subset of patients with arterial insufficiency and nonhealing ulcers.

Case series of the clinical use of nonsynchronized IPC have also been published. Louridas et al.⁹⁹ reported on the use of IPC in 33 limbs with CLI, including 23 with nonhealing ulcers. Limb salvage was attained in 58%, and complete healing occurred in 26%. Chronic renal failure was a significant negative risk factor, with limb salvage attained in 86% of patients without chronic renal failure. Kavros and colleagues retrospectively compared the outcome in 24 patients with CLI and tissue loss treated with IPC compared with 24 patients treated without IPC.¹⁰⁰ All patients had no options for revascularization and were treated with standard wound care protocols. In the IPC treated group, 42% required amputation compared with 83% in the control group ($P < 0.01$).

The foregoing information is encouraging, providing a physiologic basis for IPC's positive effects in patients with arterial insufficiency and nonhealing ulcers. The question remains, however, whether the improvement in blood supply generated by this technique is sufficient to make a difference in the patient's wound-healing ability. No prospective randomized studies of IPC for ulcer healing have been performed.

Wound Management After Intervention

Management of the ischemic limb ulcer after revascularization is critical, because of the changes in the local environment that occur with a new blood supply. Limb edema after surgical bypass is common and may be severe, resulting in a breakdown of surgical incisions and worsening of ulcerated areas. The application of short-stretch compression bandaging immediately postoperatively can assist in edema control and is an intervention that can be easily taught to family members/caregivers. Developing a strategy to combat limb edema is important in each patient, particularly at the time of hospital discharge, and may include a combination of limb elevation and appropriate compression.

IPC devices are very useful for limiting limb edema in the early postoperative period. For patients with bypass grafts

ending at the popliteal level, below-knee IPC for several hours a day reduces edema significantly. When the distal anastomosis extends to the lower leg or ankle, a pedal compression boot can be used, with reasonably good results.

Patients with dry gangrene of the digits or eschar over the heel or other ulcerated areas must be followed closely after revascularization. When the blood supply is successfully restored, these areas tend to heal under the eschar, and the eschar begins to separate at the interface between healing and necrotic tissue. Unfortunately, this is a favorable environment for infection, and it is common for these wounds to develop an increased bacterial load and frank infection if frequent debridement and careful wound management are not continued. After debridement, the remaining healthy tissue should be able to granulate, responding to standard wound-healing techniques.

BIOPHYSICAL TECHNOLOGIES

Negative-Pressure Wound Therapy

Negative-pressure wound therapy (NPWT) devices are designed to apply controlled suction to a wound bed at continuous or intermittent pressure settings to stimulate wound closure. Negative pressure can result in numerous alterations in the wound environment, including removal of excess exudate, stimulation of senescent cells, mobilization of macrophages, and stimulation of angiogenesis. NPWT has been used over uncovered bone, tendon, and other deep tissues, resulting in the clinical impression of a favorable response.

There are numerous reports in the literature concerning the use of NPWT for a wide variety of wound-related conditions, including dehisced abdominal wounds, open infected sternotomy wounds, lymphorrhea, pilonidal cysts, and complex traumatic injuries. Little systematic study was available until 2005, when Armstrong and Lavery¹⁰¹ published results of a prospective randomized study trial of NPWT for a specific indication. In this protocol, 162 patients with diabetic foot problems requiring partial foot amputation were randomized to standard moist wound care or NPWT after their surgical procedure. The primary outcome was complete healing after 16 weeks of treatment. In the NPWT group, 56% of wounds closed at 16 weeks, compared with 39% in the control group ($P = 0.04$). There was no difference in the incidence of adverse events between the two groups.

In another randomized multicenter trial, 342 patients with non-ischemic Wagner grade 2 or 3 diabetic foot ulcers were randomized to NPWT or moist wound therapy using hydrogels or alginates.¹⁰² All patients were offloaded with devices specific to the wound location. At 16 weeks, 43% of wounds in NPWT patients were completely healed, compared with 29% in the moist therapy group ($P = 0.007$). No difference was noted in the incidence of infection or osteomyelitis in the two groups, but fewer secondary amputations (mostly digital) were required in NPWT-treated feet ($P = 0.035$).

NPWT has become a fixture in most hospitals and wound centers and is a useful solution to some complex wound problems. However, the modality must be used carefully and with frequent evaluation to avoid complications. There are



Figure 118.12 Monoplace Hyperbaric Oxygen Chamber.

prospective randomized studies that support its use in diabetic foot ulcers and postsurgical diabetic foot wounds.^{101,102} There is also emerging evidence for use of NPWT following vascular surgery.^{103,104} It must be remembered that this modality is not a cure-all, and it must be used with a specific goal in mind rather than routinely for every wound.

Oxygen Therapy

Hyperbaric oxygen (HBO) therapy involves treating the patient with 100% oxygen at elevated atmospheric pressures in a specially designed chamber (Fig. 118.12). The benefits of increasing the partial pressure of oxygen in the tissues may include improved oxygen supply, reduction of inflammation and edema, and inhibition of infection. HBO is reportedly useful in the treatment of a number of wound problems, including complex diabetic foot ulcers, osteomyelitis, necrotizing fasciitis, and the healing of tissue flaps. Typical treatment protocols for leg ulcers involve one or two treatments daily for a total of 20 to 40 treatments.¹⁰⁵

HBO has long been considered a potential treatment modality for ischemic ulcers. Oxygen can stimulate angiogenesis, enhance fibroblast and leukocyte function, and normalize cutaneous microvascular reflexes.^{106,107} Clinically HBO has been demonstrated to improve tcPO_2 in the limbs of some patients with ischemic ulcers. Significant side effects of treatment are uncommon but may be severe, including barotraumatic otitis, hyperoxic seizures, and pneumothorax.

The use of HBO is covered as an adjunctive therapy in the United States under a National Coverage Determination for specific conditions following 30 days of treatment with standard wound care first.⁸¹

Faglia and colleagues randomized 68 patients with ischemic diabetic foot ulcers to standard foot ulcer treatment with or without HBO therapy.¹⁰⁸ Amputation was required in 33% of the control group, compared with 8.6% of the HBO treated group ($P = 0.016$).

Abidia et al.¹⁰⁹ randomly assigned 18 patients with non-healing ischemic diabetic limb ulcers to 100% oxygen or air at

2.4 atmospheres for 90 minutes in a hyperbaric chamber daily. In this double-blinded study, both groups received 30 sessions, after which the outcome was measured. In the oxygen group, five of eight ulcers were closed completely, compared with one of eight in the control group ($P = 0.027$).

In 2004, the Cochrane Collaborative reviewed HBO therapy for chronic wounds and concluded that HBO reduces the risk of amputation for patients with diabetic foot ulcers and increases the chance of healing at 1 year.¹¹⁰ However, it noted that these findings were based on small, underpowered studies, and that further randomized studies are greatly needed to clarify the benefits of this costly therapy.

Since the publication of the aforementioned Cochrane review, several studies have focused on the use of tcPO₂ to select patients for HBO treatment. Grolman et al.¹¹¹ measured tcPO₂ in the ischemic limb of 36 patients breathing room air, followed by 100% oxygen. They found that a greater than 10 mm Hg increase in tcPO₂ in the ischemic foot was associated with a healing rate of 70%, compared with a healing rate of 11% in those with an increase of less than 10 mm Hg. Others have reported that the improvement in foot tcPO₂ obtained during a trial session of HBO is also predictive of wound healing.¹¹²

Another study randomized 107 patients with Wagner grade 2–4 diabetic foot ulcers to comprehensive wound care with or without HBO therapy.¹¹³ After 30 treatment sessions, the incidence of wound healing and freedom from criteria requiring amputation were assessed by a blinded vascular surgeon. Criteria for major amputation were met in 13 of 54 patients in the sham group and 11 of 49 in the HBOT group ($P = 0.846$). Twelve (22%) patients in the sham group and 10 (20%) in the HBOT group were healed ($P = 0.823$). All other indices of wound healing were also not statistically significantly different between groups.

Considerations of cost efficacy are important, given the effort and cost required to deliver HBO therapy. Patients often travel long distances for daily treatments at great cost to themselves and their families. Although protocols for the treatment of ischemic limb ulcers vary significantly, most involve a total cost of \$15,000 to \$40,000. In an assessment for the Canadian government, Chuck et al.¹¹⁴ from the University of Alberta compared HBO and standard care for diabetic foot ulcers using a decision model and available outcome data. They found that the average yearly cost (in Canadian dollars) for HBO-treated ulcers was \$40,695 compared with \$49,786 for standard care. They concluded that adjunctive HBO was cost-effective compared with standard care alone.

Additional Considerations: Topical Oxygen

Recent clinical trials of topical oxygen therapy (TOT) for DFUs have been encouraging. Topical oxygen appear to supplement wound tissue PO₂, which has been shown to increase collagen deposition and decrease wound infection. TOT also appears to generate a sustained increase in wound tissue angiogenesis, and in chronic human wounds it can induce a progressively increasing and sustained elevation of VEGF expression.^{115,116}

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Podiatric and Vascular Teams

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A podiatrist is a clinician who practices medicine and/or surgery of the human foot and ankle. The scope of practice for podiatrists varies by country and even province (in Canada) or state (in the United States). When paired with vascular surgeons, podiatrists are particularly well-suited to augment the long-term medical, surgical, and functional care of the patient with diabetes and an at-risk limb.

THE PROFESSION AND SPECIALTY OF PODIATRIC MEDICINE

Podiatry is both a profession and a specialty of medicine with a rich history. While podiatrist, podiatric physician, or podiatric surgeon are the common monikers in the US, around the world, podiatrists are known by different names, including chiropodists, podologue, podologo. The depiction of specialized foot care dates back to the Egyptians c.2400 BCE. Lewis Durlacher, the surgeon-chiropodist to the royal household who served under George IV, William IV, and Queen Victoria, was one of the first to call for a protected profession. Both Napoleon and Abraham Lincoln relied on the services of foot specialists. New York was the first state to license podiatrists in the US in 1895. The *Journal of the American Podiatric Medical Association* was first published in 1907. Shortly thereafter, the first British journal, *The Chiropodist*, was published in 1914. One of the profession's early advocates, William M. Scholl, graduated from Illinois Medical College (now Loyola University) with an MD in 1904. His grandfather was a shoemaker in Germany,

and Scholl was appalled by the lack of foot care in the United States. He invented several foot care products, resulting in the creation of a global company that was worth \$77 million at the time of his death in 1968.

Education and Training

In the United States, a candidate for podiatric medical school must first complete 4 years of undergraduate training. There are nine colleges of podiatric medicine in the United States, located in New York City, Philadelphia, Miami, Cleveland, Chicago, Des Moines, Phoenix, Oakland, and Los Angeles. Candidates must sit for the Medical College Admission Test (MCAT) to be considered for admission. Podiatric medical school consists of a 4-year program and includes course work in the basic sciences and clinical medicine. Graduates receive the Doctor of Podiatric Medicine (DPM) degree. All states require graduates to complete a residency in order to practice. Podiatric residencies are 3 years long with standardized curriculum and are accredited by the Council on Podiatric Medical Education (CPME). Some podiatrists complete additional fellowship training in diabetic limb salvage, trauma and reconstruction, pediatrics, infectious disease, or research. There are two boards recognized by the CPME to provide certification in podiatry, the American Board of Podiatric Medicine (ABPM) and the American Board of Foot and Ankle Surgery. The ABPM now provides certificates of added qualification for podiatrists who meet certain criteria and pass an examination in amputation prevention and wound care (Fig. 119.1).

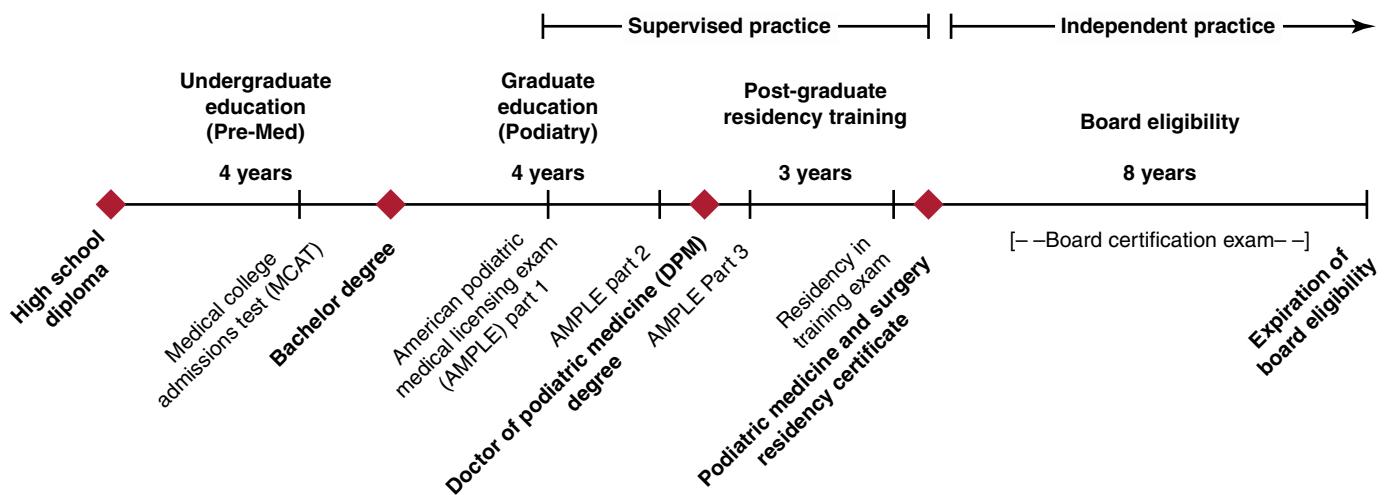


Figure 119.1 The Education and Training Pathway Leading to Practice for Podiatrists in the United States.

The British model of podiatric education predominates in the Commonwealth and Ireland. The minimum education requirement to practice is a Bachelor of Podiatry degree with options to subsequently obtain advanced degrees for specialization. In the United Kingdom the minimum education requirement to practice Podiatric Medicine is a Bachelor of Science degree (BSc). There are 13 universities that offer the degree program. If the applicant already holds an undergraduate degree in health sciences this allows the student to enter into a postgraduate degree Master of Science in Podiatry (MSc) or Doctorate level studies (Doctor of Podiatric Medicine; DPM). Degrees take approximately 3–4 years respectively, except the DPM requires 6 years as the MSc is a prerequisite for the level of study (Fig. 119.2).

Once qualified the newly trained clinician undertakes a 1-year preceptorship which entitles the graduate to undertake minor surgical techniques, administer local anaesthetic, and supply prescription-only medicines. Specialization typically fall into the broad categories of Musculoskeletal, Diabetes & Vascular, Rheumatology & Dermatology.

Practice in the Commonwealth roughly mirrors that of the UK; the British model of podiatric education predominates, requiring a minimum Bachelor of Science degree and professional registration. Australia has recently developed a program more aligned to the United States model, requiring students to have already obtained an undergraduate degree in a scientific or healthcare discipline, culminating in a Doctor of Podiatric Medicine degree. However, this model currently exists in tandem with the British model and the British Podiatric Surgical Pathway training pathway. Canada similarly has two training models, one following a diploma-based model, and one following the United States DPM model. In Canada, considerable differences exist between the two training pathways, with diploma-trained clinicians being restricted to the title, “Chiropodist,” and title Podiatrist being reserved for DPM-trained individuals.

Scope of Practice

In the United States, the scope of practice for podiatric medicine is determined by state law, which accounts for geographic

variations in practice. In most states a podiatrist can complete a history and physical examination, order laboratory work or imaging, and deal with a broad range of medical conditions and their treatment, including prescribing medication, admission to the hospital, and performing surgery. Podiatrists perform partial foot amputations; in a few states they can perform below-the-knee amputations. In many states, podiatrists can harvest their own autologous grafts from areas proximal to the ankle if the graft is to be applied to the foot or ankle, and they can supervise the delivery of systemic hyperbaric oxygen treatments. Privileges to perform what is within a podiatrist's scope of practice is determined by the facility and its medical staff.

Podiatry practice in the United Kingdom is regulated centrally by the Health and Care Professions Council (HCPC). Practice is standardized across the four devolved nations (England, Scotland, Wales and Northern Ireland) and follows a two tier system, whereby clinicians may be registered as a Podiatrist or a Podiatrist Practicing Podiatric Surgery, depending on level of training and qualification. Podiatric surgeons, being podiatrists who have undergone further training, naturally share a significant portion of the same skills as Podiatrists. However, the UK podiatric surgeon skillset extends to include a wide range of surgical techniques, afforded to them by their extensive training and annotation with the HCPC. Those with a surgical annotation may undertake surgical care encompassing the lower limb. Podiatric surgeons may perform extensive limb salvage work involving the forefoot, rearfoot, and ankle and minor or major amputations, as well as advanced reconstructive approaches in cases of Charcot foot deformities. Podiatrists and podiatric surgeons often work closely with vascular colleagues in the UK, usually side by side in multidisciplinary teams. This symbiotic relationship has led to reciprocal learning, improved patient care and aided in shaping the scope of practice of UK podiatry.

In a fashion analogous to the profession of dentistry, UK podiatrists undertaking surgical practice require rigorous training, which takes a minimum of 10 years in total to complete (Fig. 119.2). Prospective podiatric surgical trainees require a minimum of 1 year clinical experience in general podiatric

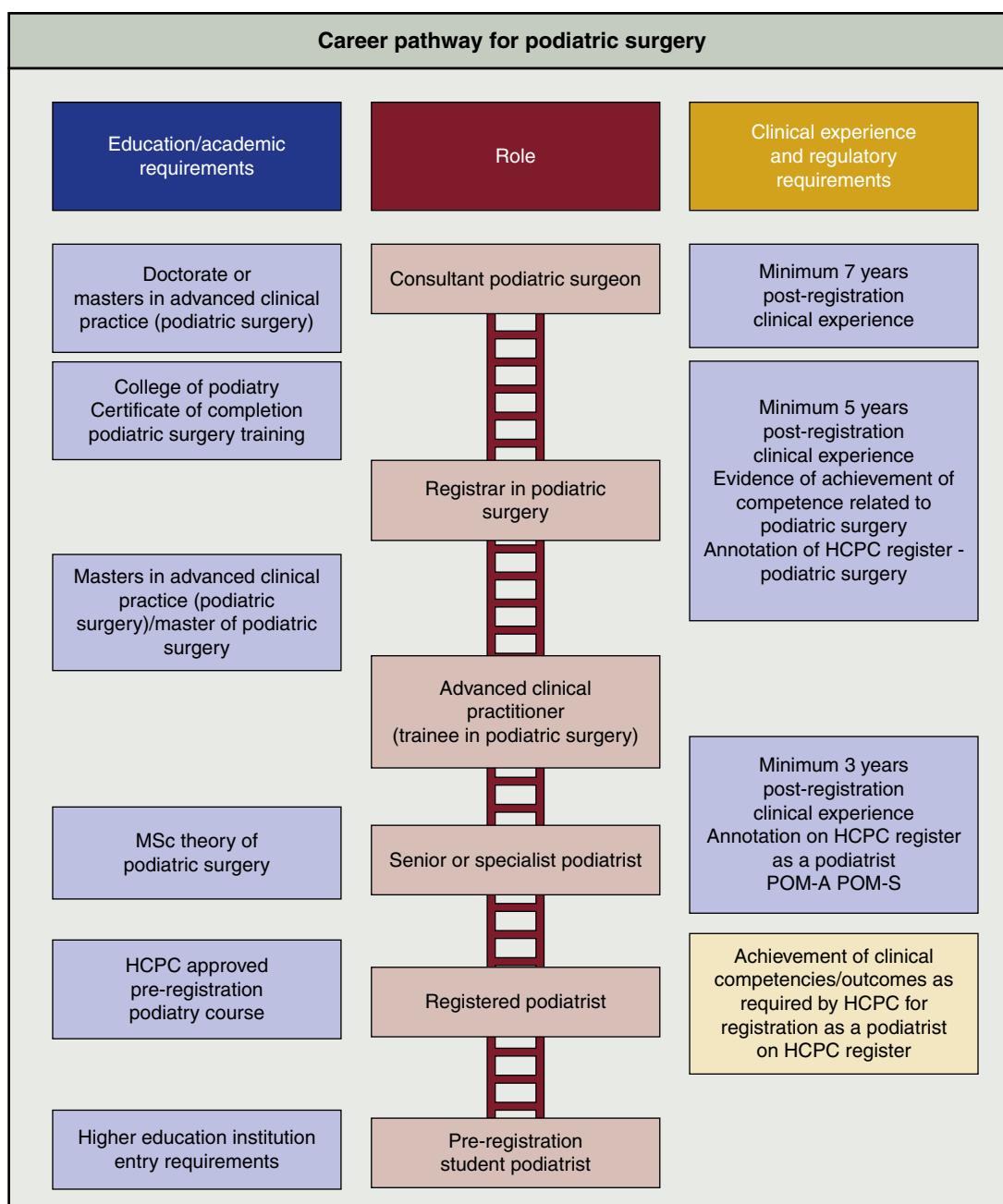


Figure 119.2 The Education and Training Pathway Leading to Practice for Podiatrists in the United Kingdom.
(From the Royal College of Podiatry.)

practice. The completion of a Master's degree in the theory of podiatric surgery allows the student to apply for a surgical training position within an approved training center. Training positions last a minimum of 3 years and must be accompanied by a Master's level training in Advanced Clinical Practice. A training post allows podiatrists to apply for a Registrar in Podiatric Surgery; further training and postgraduate education at doctoral level is offered culminating in a DPM degree. Once the student has completed the Registrar period, entitlement for Compulsory Completion of Podiatric Surgical Training (CCPST) can be sought. After a minimum of 10 years' training, podiatrists may then qualify for the position of Consultant Podiatric Surgeon.

Regardless of location, in practice, the podiatrist and the vascular surgeon often share patients. Podiatrists are trained to perform a clinical peripheral vascular examination and often order and interpret noninvasive vascular studies, which commonly result in referrals to the vascular specialist. They rely on the vascular surgeon for the treatment of impaired wound healing due to ischemic disease or when a patient as a candidate for surgery has marginal or poor perfusion – a frequent occurrence in the care of the diabetic foot.

Research and Contributions by Podiatrists

In the 1990s the podiatry group at the University of Texas Health Science Center in San Antonio was particularly productive in

TABLE 119.1 The University of Texas Foot Ulcer Classification and Risk of Amputation by Grade and Stage

	0 (Pre- or postulcerative lesion)	1 (Superficial ulcer)	2 (Ulcer extending to tendon, capsule, fascia, or muscle)	3 (Ulcer extending to bone)
A (No infection or ischemia)	0%	0%	0%	0%
B (Infected)	12.5%	8.5%	28.5%	92%
C (Ischemic)	25%	28%	25%	100%
D (Infection and ischemia)	50%	50%	100%	100%

research and publishing manuscripts on the diabetic foot as the prevalence of diabetes had been steadily increasing in the US for two decades. The University of Texas ulcer classification was described and validated and is still in use both clinically and in research today. The UT Ulcer classification was a novel two-axis system which graded ulcers by depth and staged them by the complications of infection and ischemia and correlates to risk of amputation (Table 119.1).¹ The University of Texas Foot Risk Categories² were the predicate to the American Diabetes Association and International Working Group on the Diabetic Foot (IWGDF) systems (Table 119.2). The WiFi classification of threatened limbs is another approach to the threatened limb and was a collaboration of podiatrists and vascular surgeons.^{3,4} Charcot foot classifications have also been proposed by podiatrists. The Sanders–Frykberg classification is anatomic.⁵ The Rogers & Bevilacqua classification⁶ mirrors the 2-axis grading and staging of the UT ulcer classification and is prognostic for amputation⁷ (Table 119.3).

Epidemiological studies published by podiatrists have characterized the racial and ethnic disparities in diabetic foot ulcerations and amputations.⁸

Emphasis in podiatric graduate education and training have given podiatrists a foundational understanding of biomechanics and they have applied this knowledge to the etiology of diabetic foot complications.⁹ Minor trauma from repetitive cycles of stress (walking) in patients with neuropathy and abnormal foot pressures has become accepted major etiopathogenesis of diabetic foot ulceration.¹⁰

Podiatrists have published on the diabetic foot in the *Journal of the American Medical Association*,¹¹ the *New England Journal of Medicine*,¹² and *The Lancet*,¹³ among others. Podiatrists have co-authored the Global Vascular Guidelines¹⁴ which were later endorsed by the American Podiatric Medical Association.

TEAM-BASED CARE FOR THE DIABETIC FOOT

Care for the patient with chronic limb-threatening ischemia (CLTI) is particularly complex and previous lack of specialty training and consensus definitions were cited as major obstacles in achieving the best possible outcomes.¹⁵ Public need combined with technological advances have brought podiatric and vascular surgeons together to develop interdisciplinary

TABLE 119.2 The University of Texas Diabetic Foot Risk Category with Description and Risk of Ulceration and Amputation by Category

Category	Characteristics	Ulceration Rate	Amputation Rate
0	No neuropathy	5.1%	0%
1	Neuropathy	14.3%	0%
2	Neuropathy with vascular disease and/or deformity	7%	2%
3	Previous history of an ulcer	64.5%	25.8%

TABLE 119.3 The Two-Axis Charcot Foot Classification Proposed by Rogers and Bevilacqua with Risk of Amputation by Location and Stage

Location and Stage	1 Forefoot	2 Midfoot	3 Rearfoot/Ankle
A (Acute Charcot foot without deformity)	0%	0%	0%
B (Charcot foot with deformity)	0%	0%	0%
C (Charcot foot with deformity and ulceration)	0%	3.6%	0%
D (Charcot foot with osteomyelitis)	0%	0%	5.4%

teams. They began not only sharing clinic and operating time, but also sharing ideas about patient care and clinical research.¹⁶

Professional Collaborations

In the United States, the American Podiatric Medical Association and the Society for Vascular Surgery established an alliance in 2009¹⁷ with the objectives of writing a joint statement on the multidisciplinary team approach in the diabetic foot, producing a supplement on diabetic foot care in both professions' journals, establishing joint postgraduate courses at the annual

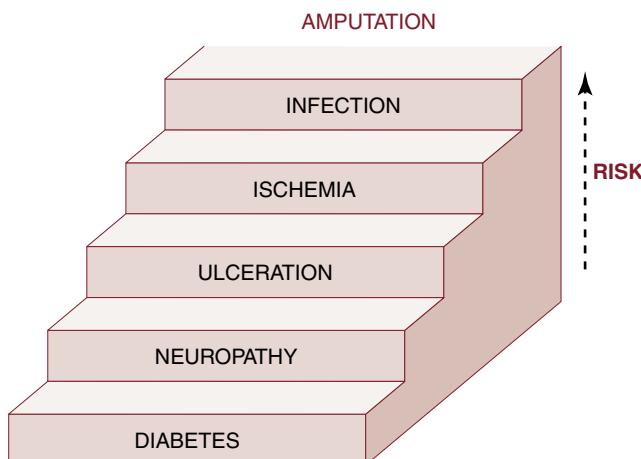


Figure 119.3 The elevating risk of the “stairway to an amputation” or the natural history of diabetes-related amputations.

scientific meetings of both organizations, collaborating on best practice guidelines and advocacy and awareness on the care of the diabetic foot. The alliance was successful in accomplishing all objectives including jointly publishing 14 manuscripts from more than 20 collaborating centers around the world. Podiatry and vascular surgery seemed like natural allies in the struggle against amputation. A decade later, the fragmentation of medical care to the CLTI patient is improving, but efforts are still ongoing in the integration of programs.¹⁸ In 2020, this ultimately led to the formation of the American Limb Preservation Society (ALPS) to serve as an interdisciplinary bridge to marry podiatric and vascular surgery together with other members of the limb preservation team.¹⁹

Structure and Function of CLTI Teams

Optimal diabetic foot management requires a multidisciplinary approach including wound care, vascular surgery, podiatry, infectious disease, as well as holistic patient care.²⁰ In 1925, Elliott P. Joslin, MD perhaps first described the role of podiatrists working in collaboration with other physicians to prevent foot ulcers, infections and gangrene.²¹ The teams focus on de-escalating risk in the components of the natural history of diabetes-related amputations is illustrated by the “stairway to an amputation” (Fig. 119.3).

The Toe and Flow (podiatry and vascular) model is a popular and effective structure for an amputation prevention team.²² The model utilizes podiatric and vascular surgeons at the core, with other disciplines as necessary. The patient is placed on a virtual continuum and vascular surgery is primary with poor limb perfusion, whereas podiatry is primary with infection and well-perfused tissue defects or deformities. The model describes three tiers of care based on the setting and resources available (Table 119.4). In 2019, we wrote about creating centers of excellence for CLTI in the Global Vascular Guidelines.¹⁴ We focused on the fact it was not sufficient to simply have a designated team, but the team must function in an effective manner. We recommended a structured manner to create the team and measure the outcomes (Fig. 119.4). The

TABLE 119.4

The Three Tiers of Specialized Centers that Care for the Diabetic Limb at Risk

A – Basic Model of Care

Aim	Prevention and basic curative care
Patients	Own population
Setting	General practitioners' office, health center, or small regional hospital
Potential clinicians	<ul style="list-style-type: none"> • General practitioner • Podiatrist • Diabetic nurse
Facilitating elements	Close collaboration with a referral center

B – Intermediate Model

Aim	Prevention and curative care for all types of patients; more advanced assessment and diagnosis
Patients	From the regional catchment area of the hospital, possibly with additional referrals from outside the region
Setting	Hospital
Potential clinicians	<ul style="list-style-type: none"> • Diabetologist • Vascular surgeon • Podiatrist • Diabetic nurse
Facilitating elements	<ul style="list-style-type: none"> • Motivated coordinator to inspire team • Exchange of experience with other centers • Staff meetings to discuss diabetic foot patients • Active collaboration with other departments within the hospital • Active collaboration with extramural facilities (general practitioners, nursing homes, etc.)

C – Center of Excellence

Aims	<ul style="list-style-type: none"> • Prevention and specialized curative care for complex cases • To advance the knowledge base and to teach other centers
Patients	National, regional, or even international referral center
Potential clinicians	<ul style="list-style-type: none"> • Diabetologist • Vascular surgeon • Podiatrist • Orthopedist • Orthotist • Educator • Plaster technician • Rehabilitation specialist • Diabetic nurse • Psychiatrist
Setting	Usually a large teaching or university hospital
Facilitating elements	<ul style="list-style-type: none"> • Organize regional, national, or international meetings • Allow providers to visit to improve knowledge and practical skills • Active collaboration with other reference centers • Active participation in the development of guidelines

Reprinted from Rogers LC et al. Toe and Flow: Essential components and structure of the amputation prevention team. *J Vasc Surg*. 2010;52:23S.

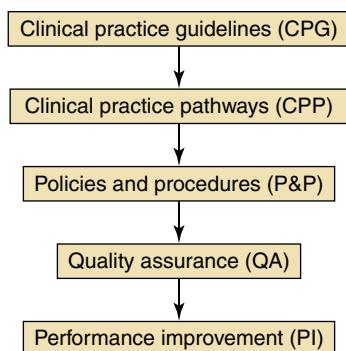


Figure 119.4 A schematic on how to organize diabetic foot care within a multidisciplinary team. (Reprinted from Conte MS, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *J Vasc Surg*. 2019;69:S.)

team should establish goals from clinical practice guidelines (CPG). Many CPGs exist for various aspects of the diabetic foot, including those authored by the International Working Group on the Diabetic Foot (IWDGF). CPGs are used to create local practice pathways. Policies and procedures should be specific to maintain adherence of the pathway. Quality assurance measures are used to determine the effect of the intervention and outcomes.

Effect of Team-Based Care

An effective means of amputation prevention is the formation of a multidisciplinary diabetic footcare team. The International Diabetes Federation has decreed that more than 85% of diabetes-related amputations are preventable and that this measure is attainable when podiatrists and vascular surgeons are partnered in cohesive teams.²³ A large population-based observational study reported a 69% reduction in the diabetes-related amputation rate over 5 years after implementation of better organized foot care.²⁴ Our group was able to reduce amputations by 72% over 2 years by implementing a team concept for limb salvage that included both podiatrists and vascular surgeons.²⁵ Another study found that a multidisciplinary team consisting of physicians, podiatrists, and nurses led to a 51% reduction in ulceration in a high-risk population (previous history of a DFU) over a 2-year period.²⁶ Perhaps even more impressive, a meta-analysis of 25 studies evaluating the effect of team-based care on amputations rates found all but 1 study favoring the team.²⁷

Some 77% of the foot-related costs of a patient with diabetes are attributable to inpatient stays. Cohesive teams that follow guidelines can have an impact on the inpatient management of the patient with a complicated lower extremity. Wukich led a team of experts from the American Diabetes Association to create inpatient management guidelines²⁸ based on an outline developed by Fitzgerald and coworkers who identified seven essential skills for limb salvage to be used by a “diabetic rapid response acute foot team.”²⁹

A Duke University study of over 230,000 Medicare beneficiaries found that a patient visiting a podiatrist in addition to another health professional had a sustained reduction in risk of

foot complications.³⁰ Patients were 31% less likely to develop a foot ulcer and 77% less likely to develop cellulitis or Charcot foot. Another study found that patients who were under the care of a podiatrist had a 29% reduced risk of amputation and a 24% reduced risk of hospitalization, saving the insurer an average of \$19,686.³¹ The Toe and Flow model was studied by Basiri and colleagues comparing two provincial health districts in Alberta, Canada.³² In Calgary, a vascular podiatry team cared for patients with CLTI and in Edmonton the care was not team-based. The Calgary zone had significantly fewer major limb amputations and an improvement in the high-low amputation ratio.

It is worth noting that during the COVID-19 pandemic, which is ongoing at the time of the writing of this chapter, the disruption in the multidisciplinary care of the diabetic foot led to worsened outcomes, including a higher rate of amputations.³³ Not only have previous studies referenced above proved the positive effect of adding a team to care for the diabetic foot, but impediments in the team caused by the pandemic proved that removal of a team had negative effects. Specifically in regard to vascular outcomes, patients presented with more severe vascular disease during the pandemic since regular surveillance and care was disrupted.^{34,35} Our proposed Pandemic Diabetic Foot Triage System was a response to help determine the site and urgency of care for the patient with CLTI.³⁶

PREVENTATIVE CARE

The team can function in three broad categories of amputation prevention: primary prevention, secondary prevention, and post-secondary prevention (Fig. 119.5). Primary amputation prevention is performed in those with diabetes with or without neuropathy or mild PAD but no open lesions or major lower extremity complications. These patients require neuropathy screening, PAD screening, special footwear, education, diabetes control, and annual visits for comprehensive diabetic foot exams. The primary focus in this category is to prevent lower extremity complications such as DFU. Secondary amputation prevention is performed once a patient develops a major complication such as a DFU, Charcot foot, gangrene, or infection. An algorithmic, multidisciplinary approach to the complicated lower extremity is most effective and is covered in this and other chapters of the textbook.

Post-secondary amputation prevention is performed after resolution of an acute lower extremity complication. The authors prefer the term “remission” when referring to these patients as it more correctly reflects the ongoing risk in recurrence and mortality, similar to cancer. Five-year mortality associated with diabetes-related lower extremity conditions continues to rival all but the most aggressive forms of cancer.¹⁸ Patients who heal from a DFU have a 50% recurrence within 12 months.³⁷ After an amputation, there is also a 50% likelihood of a contralateral amputation within 2 years.³⁸

The focus in the post-secondary prevention group is to prevent the recurrence of a diabetic foot complication or the onset of a new one. The target should be functional restoration

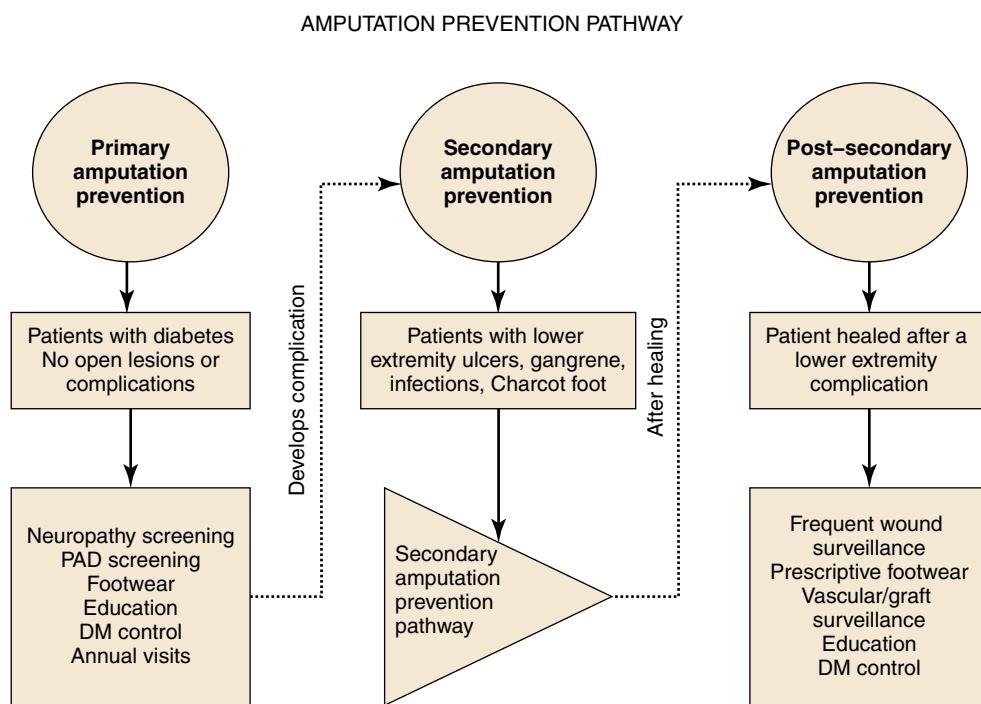


Figure 119.5 Amputation Prevention Pathway and Progression.

and an increase in ulcer-free, activity-rich days. Strategies to achieve this include regular podiatric surveillance,^{30,31} prophylactic surgery,^{39–41} prescriptive footwear,⁴² and thermometric analysis.⁴³

SUMMARY

Certainly, the multidisciplinary team, and more specifically one with collaborating podiatrists and vascular specialists, has been shown to be highly effective at improving the outcomes of limbs at risk for amputation.⁴⁴ Podiatry's role on that team cannot be overstated. Podiatric and vascular surgeons must frequently cooperate in the care of the complicated lower extremity due to diabetes. Understanding each provider's role will streamline care. Pathway-driven teams can improve patient outcomes and reduce costs to the healthcare system. To truly care for the threatened limb, one must create a team of those with the passion and necessary skills. The podiatrist on this team is paramount to the success of the mission.

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Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367–2375.

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

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Upper Extremity Arterial Disease: Epidemiology, Etiology, and Diagnostic Evaluation

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Upper extremity ischemia accounts for less than 5% of patients presenting for evaluation of limb ischemia, with a vast majority of cases being caused by autoimmune/connective tissue diseases. In contrast to the lower extremity, atherosclerosis is not a major etiology of upper extremity ischemia. According to a Dutch study, only 2.3% of diabetic patients and no nondiabetic patients were found to have abnormal Doppler waveforms in either of the upper extremities.¹ This chapter provides an overview of upper extremity arterial diseases, with emphasis on the epidemiology, diagnosis, and natural history.

EPIDEMIOLOGY

A number of pathologic conditions may contribute to upper extremity arterial disease and, as a result, little comprehensive epidemiologic data are available. One exception is Raynaud syndrome, which is characterized by intermittent digital ischemia, caused by vasoconstriction, in response to cold, caffeine, or emotional stress (see Ch. 142, Raynaud Phenomenon). The prevalence of Raynaud phenomenon, from population-based surveys is estimated to be 3%–5% of the general population.² This increases among people living in cold climates, with up to

20% to 30% of those surveyed complaining of cold-induced digital pain.³ Most patients with Raynaud syndrome have primary (idiopathic) Raynaud's, formerly known as Raynaud disease. Patients who have an identifiable arterial pathology or associated disease contributing to their condition are classified as having secondary Raynaud's, formerly known as Raynaud phenomenon. This distinction has prognostic implications as secondary Raynaud's is more likely to progress to severe occlusive disease leading to digital rest pain, and ulceration. Diseases associated with secondary Raynaud's include scleroderma, mixed connective tissue disease (MCTD), systemic lupus erythematosus (SLE), and rheumatoid arthritis. Of these, scleroderma accounts for the majority of secondary Raynaud's patients diagnosed.³ It is important to remember a patient may present with Raynaud's symptoms years before the diagnosis of an underlying systemic disease.

ETIOLOGY AND PATHOGENESIS

Upper extremity arterial disease can be broadly categorized based on anatomic location (large vs. small vessel) and etiology (vasospastic vs. occlusive). In general, vasospastic etiologies affect smaller vessels and occlusive affect larger vessels. The clinical appearance of occlusive and vasospastic disease may be similar, but delineating between them is essential for appropriate treatment. Processes leading to upper extremity arterial disease are vast. In addition, there can be both vasospasm of larger vessels, as occurs with ergot-containing medications, and concurrent atherosclerotic disease in patients who also have Raynaud's. Patients with Raynaud syndrome have normal digital artery pressure at baseline. In response to certain triggers (cold, stress, caffeine), they experience digital artery smooth muscle contraction leading to profound, albeit temporary, digital hypoperfusion. Upon relief of the trigger, the vasoconstriction ceases and normal flow is restored.

The pathophysiological mechanisms underlying Raynaud syndrome remain poorly understood despite the fact that it has been more than a century since it was first described by Maurice Raynaud.⁴ Multiple abnormalities including those of the sympathetic nervous system,^{5,6} digital blood vessels, altered sensitivities, numbers of α -adrenoceptors,^{7,8} and β -adrenoceptors,⁹ and vasoactive peptides, including calcitonin gene-related peptide,^{10,11} and endothelin¹² have been hypothesized. It is being increasingly recognized that the pathophysiology of Raynaud syndrome, whether primary or secondary, is complex and multifactorial.

The etiology for occlusive disease is primarily atherosclerotic but can include additional more acute entities, such as thromboembolic events and iatrogenic or traumatic related injuries and vasculitides. Atrial fibrillation and proximal atherosclerosis are common etiologies for thromboembolism. Iatrogenic causes include dialysis access resulting in steal phenomenon as well as radial, brachial, or axillary artery access for monitoring lines, endovascular procedures, or conduits. Symptomatic atherosclerotic lesions in the upper extremity are less common than in the lower extremity with the majority of these lesions being in the brachiocephalic trunk and subclavian artery. When found, atherosclerotic lesions in this distribution are

significant for overall patient management, even when asymptomatic. For example, in asymptomatic patients a difference in systolic blood pressure of 15 mm Hg or more between arms, indicative of subclavian stenosis, was found to be associated with a 1.7 \times increased risk of cardiovascular mortality and 2.5 \times risk of peripheral vascular disease.¹³ The same risk factors that apply to lower extremity PAD apply to the upper extremity, such as smoking, hypertension, dyslipidemia, and diabetes.¹⁴

SMALL VESSEL ARTERIOPATHIES

Numerous small vessel arteriopathies in the upper extremity, defined as those distal to the wrist, may lead to hand ischemia. The diseases leading to the most severe upper extremity arterial ischemia are autoimmune or connective tissue diseases such as scleroderma, rheumatoid arthritis, systemic lupus, and others.

Scleroderma

Scleroderma (systemic sclerosis) is the most common connective tissue disorder in patients with secondary Raynaud's. It is a generalized disorder of connective tissue, the microvasculature, and the small arteries. Early findings include microvasculature damage, mononuclear-cell infiltrates, and fibrosis with later disease showing dense collagen and loss of cells.¹⁵ There is a female-to-male ratio of at least 3:1, and an incidence of approximately 50 per 1 million people in the United States. Cutaneous involvement is almost universal, and the clinical course is characterized by progressive scarring and small vessel occlusions in the skin, gastrointestinal tract, kidneys, lungs, and heart. Serology often reveals anti-centromere or anti-topoisomerase (anti-Scl-70) antibodies. It is postulated that damage seen in scleroderma is mediated through these cytotoxic antibodies to endothelium. Vascular injury, primarily in arterioles, precedes fibrosis.

Systemic Lupus Erythematosus

SLE occurs most often in young females, and damage to affected organs appears to be caused primarily by immune complex deposition from a proinflammatory state.¹⁶ The prevalence is 20–150 cases per 100,000 population with a higher proportion of African, Hispanic, or Asian ancestry affected compared to other groups.¹⁷ The diagnosis is made clinically since the available laboratory tests, while quite sensitive, are not specific.¹⁸ Clinical criteria include fevers, arthralgias, skin rash, Raynaud syndrome, and nephritis. Raynaud syndrome (secondary) is present in as many as 80% of these patients.

Rheumatoid Arthritis

While rheumatoid arthritis is primarily a chronic inflammatory joint disease, there is a subgroup of patients with extra-articular involvement of the skin, eyes, lungs, spleen, and blood vessels. Several types of vasculitis have been described in rheumatoid arthritis, the most severe of which is termed rheumatoid vasculitis, a systemic process that involves both arteries and veins. As treatment for RA has improved, the incidence of rheumatoid

vasculitis has dropped from 9.1 to 3.9 cases per million population. The etiology of rheumatoid arthritis is unknown, but it likely results from immune-mediated damage. There is a strong association between rheumatoid vasculitis and specific genotypes of the epitope HLA-DRB1. It has been hypothesized that these genotypes mark a predisposition that in response to an unknown stimulus, such as infection, leads to immune complex deposition and inflammation. Additional risk factors include male sex, current smoking, and longstanding seropositive nodular erosive disease.¹⁹ Hydroxychloroquine and low-dose aspirin have been shown to be protective in preventing development of vasculitis in RA patients.²⁰

Sjögren Syndrome

Sjögren syndrome is characterized by dry eyes and mouth and may be primary or secondary to another connective tissue disease. The female to male ratio is 9:1 with an estimated incidence of 7 cases per 100,000 population, although this varies across continents.²¹ It may be associated with small vessel arteriopathy, which can then be subdivided into acute necrotizing, leukocytoclastic, and lymphocytic vasculitis. Vasculitis in Sjögren's is common and usually presents as a rash or peripheral neuropathy. Some patients develop a systemic vasculitis that affects medium-sized vessels and can resemble polyarteritis nodosa.

Mixed Connective Tissue Disease

MCTD is a group of autoimmune disease states that do not fall into a named disease category. Patients characteristically have high titers of antibodies to an extractable nuclear antigen, which consists of ribonucleic acid and protein. MCTD clinically presents as an overlap syndrome with features of two or more connective tissue diseases, such as SLE, rheumatoid arthritis, or scleroderma.¹⁴ There is a high frequency of Raynaud syndrome, arthritis, polymyositis, and interstitial lung disease within this group of patients.

Buerger Disease

Buerger disease (thromboangiitis obliterans) is characterized by segmental thrombotic occlusions of the small- and medium-sized arteries (see Ch. 139, Thromboangiitis Obliterans).²² The disease most commonly affects the lower extremities but the upper extremities are involved in as many as 50% of these patients. It classically occurs in young male smokers and is often associated with both migratory thrombophlebitis and secondary Raynaud syndrome. Diagnostic criteria include age less than 45 years, tobacco abuse, exclusion of other diseases with similar clinical findings, normal arteries proximal to the popliteal or brachial arteries, and documentation by objective means of digital arterial occlusion.²³

Hand–Arm Vibration Syndrome

Hand–arm vibration syndrome (HAVS) refers to the finding of Raynaud syndrome after long-term use of vibrating tools.²⁴

The initial group of patients were stonecutters, but the disease has been described in various occupations, including welders or grinders in shipyards, timber fellers, and windshield replacement technicians in the auto-glass industry.²⁵ The exact pathophysiology of this condition is not known, but it is postulated that kinetic energy imparted to the small vessels and nerves of the hand by vibrating tools with power in certain frequency bands is harmful. The damage appears to accumulate over time. Early on, patients have vasospastic Raynaud syndrome, which over a period of time, progresses to digital artery occlusive disease²⁶ (see Ch. 184, Conditions Arising from Repetitive Trauma and Occupational Vascular Problems).

Fibromuscular Disease

Fibromuscular disease involving the forearm, palmar, and digital arteries is rare.²⁷ Patients often present with finger ischemia because of arterial embolization and occlusion. It has been postulated that the condition known as hypotenar hammer syndrome, in which patients have the acute onset of hand ischemia after using the heel of their hand as a hammer, is actually due to trauma to a preexisting fibromuscular disease lesion.²⁸

Hypersensitivity Angiitis

The term hypersensitivity angiitis describes a group of patients who present with acute onset of significant digital ischemia, usually with ulceration, but have no demonstrable underlying abnormality, such as connective tissue disease or embolic source.²⁹ An immune-mediated arterial wall injury has been hypothesized as the underlying etiology, although strong evidence is lacking in that regard. It is a benign condition that follows a course of progressive improvement.

Malignancy

Raynaud syndrome has been reported in association with several malignancies.^{30–32} The exact mechanism is unknown, but it appears related to tumor-based immunologic processes, including both small vessel arteritis and immune complex deposition, possibly including cryoglobulins.

Frostbite

Freeze injury of the small vessels of the digits results in Raynaud syndrome. Mild frostbite usually results in vasospastic Raynaud syndrome, while significant freezing injury may result in occlusive disease of the digital arteries.

LARGE VESSEL ARTERIOPATHIES

The most common large vessel arteriopathy in the upper extremity is atherosclerosis. Risk factors are the same as those for occlusive disease elsewhere in the body. These include tobacco use, hyperlipidemia, hypertension, diabetes, male gender, and age. The most common mechanism via which atherosclerosis may cause upper extremity ischemia is occlusive disease, with

involvement of the origin of the left subclavian artery being the most common location. It is estimated that 6%–10% of people with lower extremity peripheral arterial disease will have concurrent left subclavian stenosis.³³ Aneurysms are rare in the upper extremity but can occur in the subclavian or axillary arteries. Chronic trauma from arterial thoracic outlet syndrome can lead to subclavian artery stenosis, which is accompanied by digital ischemia due to embolic phenomenon (see Ch. 125, Thoracic Outlet Syndrome: Arterial).

Takayasu arteritis is a common large vessel vasculitis involving the aorta and its branches. It is a panarteritis, affecting all layers of the arterial wall, and results in chronic granulomatous inflammation that primarily manifests as diffuse and/or nodular lesions in the arterial wall.³⁴ Upper extremity ischemia may occur with disease within the subclavian arteries.³⁵ Giant cell arteritis (GCA) mainly involves the walls of medium and large arteries. In GCA the temporal artery is most commonly involved; however, upper extremity arteries are occasionally affected.³⁶ Embolic occlusion from atrial fibrillation or other sources is classically seen in the brachial artery before the bifurcation of radial and ulnar arteries.

Another well-described presentation of upper extremity ischemia occurs after placement of dialysis access. Access-related hand ischemia (ARHI) refers to a distal hypoperfusion ischemic syndrome after dialysis access placement. It occurs in 5% to 10% of cases when the brachial artery is used.³⁷

Iatrogenic injury to the radial and brachial arteries has increased in conjunction with increased use of the upper extremity for access in coronary and peripheral catheterization procedures. Early reports of brachial artery access revealed a complication rate as high as 17%, but this has since declined to

1% to 5%.^{38–40} The median nerve lies in close proximity to the brachial artery within the covering fascia, and is at high risk for compression if a hematoma occurs. Therefore, development of a brachial access site hematoma should be addressed immediately to prevent long-term nerve injury. Occlusion of the radial artery is seen in 1% to 10% of interventions using radial access, however recanalization is common.^{41,42} In addition, an intact ulnar artery and palmer arch can maintain collateral flow to the hand in cases of radial artery occlusion. An Allen test should be performed before any radial access procedure to confirm adequate collateral flow. Additionally, patients with shock physiology requiring multiple vasopressor agents can have resultant upper extremity digit ischemia in addition to lower extremity ischemia.

Box 120.1 below lists the causes of hand ischemia, and Table 120.1 details the portion of the arterial system affected by these etiologies.

CLINICAL FINDINGS

Acute Ischemia

Patients with acute ischemia of the upper extremity are more likely to be females and tend to be older than those with lower extremity ischemia.⁴³ Compared to the lower extremity, acute ischemia of the upper extremity is more often from thromboembolic (cardiac source most common), traumatic, or iatrogenic causes. However, symptomatology remains the same: pain, paresthesias, and paralysis. Physical examination reveals diminished or absent pulses (brachial, radial, or ulnar), pallor, dependent rubor, and reduced temperature. As mentioned earlier, classic Raynaud syndrome is characterized by pain, color,

BOX 120.1 Causes of Hand Ischemia

Arterial Vasospasm

- Ergotism
- Idiopathic vasospastic Raynaud syndrome
- Vinyl chloride exposure

Arterial Obstruction

Large-Artery Causes

- Atherosclerosis
- Thoracic outlet compression
- Arteritis
- Takayasu
- Giant cell
- Fibromuscular disease
- Iatrogenic injury
- Access-related hand ischemia (ARHI)

Small Artery Causes

- Connective tissue diseases
- Scleroderma
- Rheumatoid arthritis
- Sjögren syndrome
- Systemic lupus erythematosus
- Myeloproliferative disorders

- Thrombocytosis
- Leukemia
- Polycythemia
- Buerger disease
- Hypersensitivity angiitis
- Cold injury
- Vibration injury
- Henoch–Schönlein purpura
- Cytotoxic drugs
- Hypercoagulable states
- Arterial drug injection

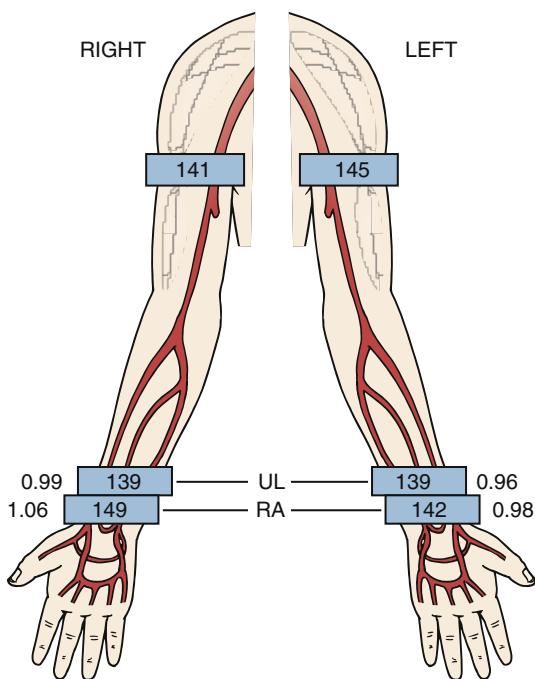
Proximal Large Artery Sources of Embolism to Distal Small Arteries

- Ulcerated or stenotic atherosclerotic plaque
- Aortic arch
- Innominate artery
- Subclavian artery
- Aneurysms
- Innominate artery
- Subclavian artery
- Axillary or brachial artery
- Ulnar artery

From Landry GL, et al. Severe hand ischemia. In: Pearce WH, Matsumura JS, Yao JST, eds. *Trends in Vascular Surgery* 2003. Chicago: Precept Press; 2004:280.

TABLE 120.1 Arterial Diseases and Artery Affected

	Subclavian	Axillary	Brachial	Forearm	Hand
Atherosclerosis	•				
Giant cell arteritis	•				
Takayasu disease	•	•			
Fibromuscular dysplasia		•			•
Embolic		•	•		•
Connective tissue disease				•	•
Diabetes mellitus				•	•
Repetitive trauma					•
Hypercoagulation					•
Cryoglobulins					•
Pressors/polyvinyl chloride					•

**Figure 120.1** A Normal Wrist to Brachial Index Study.

and temperature changes often in response to cold or emotional stress. Tissue loss is rare in cases of acute occlusion due to the abundant network of collateral circulation in the upper extremity. The reported limb salvage rate is 98% in patients with acute ischemia of the upper extremity.⁴⁴

Chronic Ischemia

Chronic ischemia of the upper extremity may manifest as muscle pain with use, ulcers, or gangrene in the upper extremity. Findings on physical exam may be normal at rest, but the hand and digits are cool and brachial and wrist pulses are diminished or absent. ARHI symptoms may range from only occurring in

conjunction with dialysis to gangrene (see Ch. 178, Hemodialysis Access: Nonthrombotic Complications).³⁷ Fistula compression usually is associated with an increase in wrist pulses, Doppler signals, or both.

DIAGNOSTIC EVALUATION

Clinical Evaluation

The initial evaluation of patients with upper extremity ischemia starts with a detailed history and physical examination with specific attention to signs and symptoms of an underlying connective tissue disease. Pertinent historical information includes temperature sensitivity, dry mouth, dry eyes, arthritis, history of trauma or instrumentation, history of repetitive activities such as sports, as well as occupational history to evaluate for vibration arterial injury.

A complete arterial examination should be performed in a warm room and patients should be allowed to rewarm before their examination during cold weather. Brachial and forearm blood pressures are measured. In cases of suspected claudication, they should be measured at rest and after 2 to 5 minutes of exercise. A gradient of 20 mm Hg or more is considered significant when comparing sides. All pulses are palpated, and Doppler insonation of the radial, ulnar, palmar, and digital arteries is performed to evaluate the quality of Doppler waveforms. Auscultation of the supraclavicular and infraclavicular fossa may reveal a bruit, indicating possible subclavian artery stenosis.

The hands and digits should be examined carefully, with temperature, capillary refill, and ulcers noted. Fingers should be examined for clubbing, sclerodactyly, and telangiectasia; nail beds should be checked for splinter hemorrhages. Clubbing is seen in chronic pulmonary disease. Telangiectasia and sclerodactyly are seen in scleroderma, in addition to other connective tissue diseases. Splinter hemorrhages in nail beds are seen in embolic disease. Finally, a complete upper extremity neurologic examination may give clues to external compression of a neurovascular bundle suggestive of TOS.

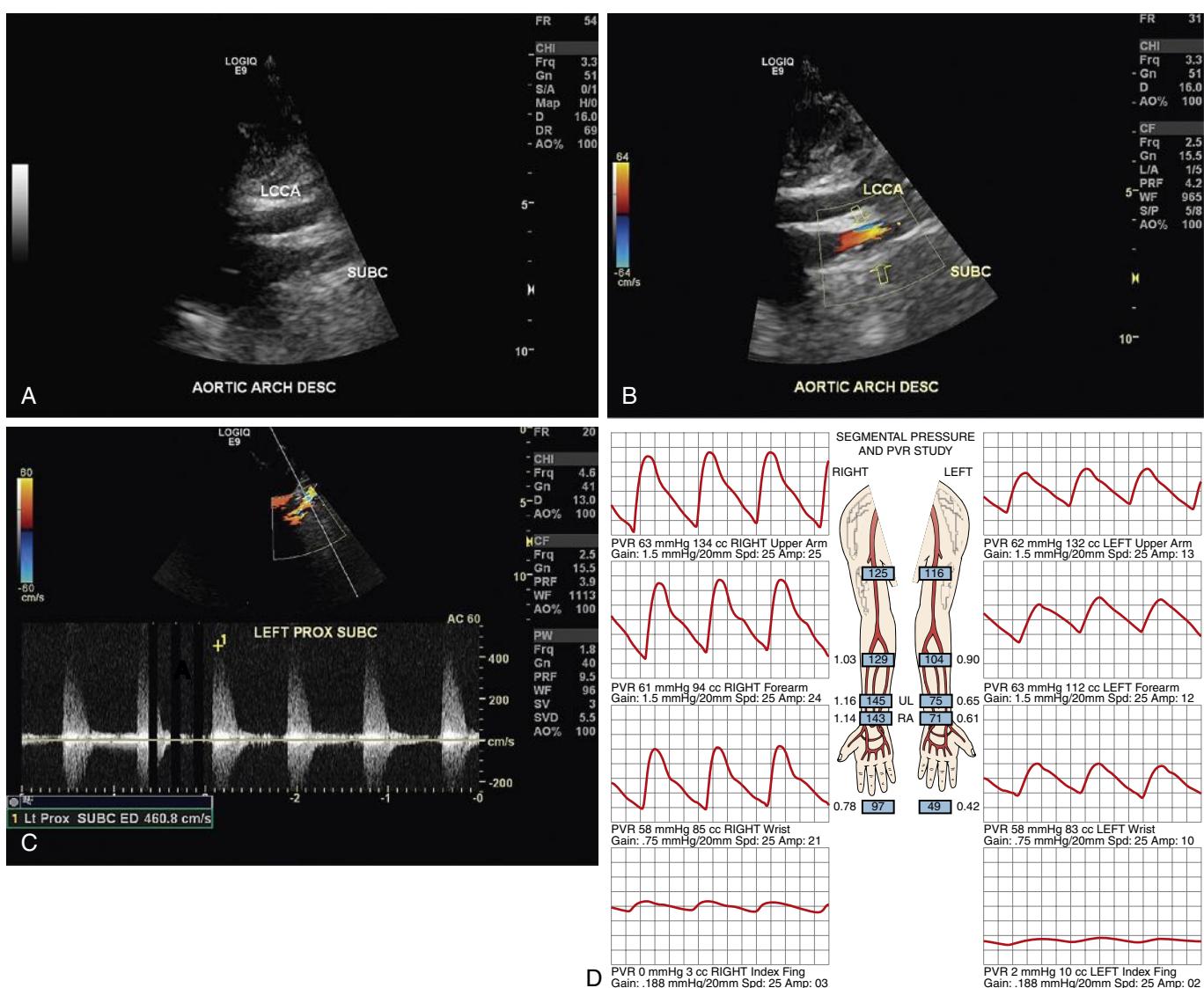


Figure 120.2 Left Subclavian Artery Stenosis Demonstrated on Ultrasound. (A) B-mode ultrasound image of the descending aortic arch with the left common carotid artery and left subclavian artery origins clearly visible. A bulky atherosclerotic plaque is narrowing the origin of the left subclavian artery. (B) Color Doppler image demonstrating arterial flow through the stenosis at the origin of the left subclavian artery (yellow arrows). (C) Color duplex image with the velocity through the left subclavian artery stenosis dramatically elevated at 460.8 cm/s. (D) Segmental pressures and pulse volume recordings of the same patient identifying reduction in PVR amplitude and latency and reduced wrist and finger to brachial index.

Vascular Laboratory Evaluation

Basic vascular laboratory evaluation consists of segmental pressure measurements of the upper extremity and finger pressure measurements and waveforms (Fig. 120.1). This allows differentiation of large artery disease (reduced wrist arterial pressure with no further reduction at the finger level) from small artery disease (normal upper extremity examination, abnormal finger pressures). Duplex ultrasonography is also particularly useful in large vessel occlusive diseases, such as subclavian artery stenosis (Fig. 120.2).

The diagnosis of secondary Raynaud's is made clinically. However, qualitative testing for the severity of cold sensitivity in Raynaud syndrome can be useful. The most basic test for cold sensitivity is finger temperature recovery after ice-water

immersion. Nailfold capillary microscopy can help distinguish between primary and secondary Raynaud's, as those with an underlying autoimmune rheumatic disease, or at risk of developing one, will have enlarged or distorted capillary loops and/or sparsity of these capillary loops in the periumgual region. If the initial battery of tests is nondiagnostic and the patient has significant obstructive disease (by vascular laboratory criteria) or digital ulceration, further testing to determine the presence of a hypercoagulable state is conducted. This consists of antithrombin III, protein C, and protein S levels, anticardiolipin and antiphospholipid (lupus inhibitor) antibodies, Lp(a) levels in patients with hyperlipidemia, and tests for familial hypercoagulable states such as factor V Leiden (see Table 120.2) (see Ch. 40, Disorders of Coagulation: Hypercoagulable States).

Other Imaging

Imaging can be extremely useful when the diagnosis cannot be established by clinical assessment and basic vascular laboratory studies alone. For embolic disease, both duplex ultrasound and echocardiography are recommended. If these do not reveal an embolic source, the aortic arch and intrathoracic upper extremity arteries should be imaged. Both computed tomographic

arteriography (CTA) and magnetic resonance arteriography (MRA) provide excellent resolution and are less invasive than catheter-based arteriography.⁴⁵

Finally, invasive arteriography is generally reserved for patients with unexplained digital artery occlusion in an asymmetrical distribution to rule out a surgically correctable proximal lesion where a CTA or MRA fails to reveal an etiology (Fig. 120.3). The entire upper extremity vasculature should be visualized. In addition, both upper extremities should be imaged, with hands in the anatomic position. The presence of significant bilateral disease, even with unilateral symptoms, is an indication of a systemic disease.

TABLE 120.2

Most Commonly Used Vascular and Basic Clinical Laboratory Tests Used to Diagnose Upper Extremity Arterial Disease

Vascular Laboratory
Finger pressures
Finger photoplethysmographic waveforms
Cold challenge test
Basic Clinical Laboratory
Complete blood count
Erythrocyte sedimentation rate
Antinuclear antibodies
Rheumatoid factor
Additional Tests in Select Cases
Hypercoagulable screening
Protein C
Protein S
Antithrombin III
Lupus anticoagulant
Anticardiolipin and antiphospholipid antibodies
Lipoprotein A
Factor V Leiden
Thyroid panel

TREATMENT

The medical, surgical, and endovascular treatment of upper extremity arterial disease is covered in Chapter 121 (Upper Extremity Arterial Disease: Medical, Endovascular, and Open Surgical Management). Therefore, this chapter provides an overview of treatment as it relates to the natural history of the disease process.

Medical

Most patients with primary Raynaud syndrome are best treated with cold, caffeine, and tobacco avoidance, with medication reserved for more severe cases. The most effective drug to date has been the calcium channel blocker nifedipine, although amiodipine can also be used.⁴⁶ Losartan has also been demonstrated to be effective in patients with Raynaud syndrome in randomized trials.⁴⁷ Many patients may take the medication from late fall to late spring or when they anticipate facing cold exposure. Fluoxetine, a selective serotonin uptake inhibitor, has also been shown to be effective in a double-blind, randomized, controlled trial.⁴⁸ Other drugs that have a modest clinical effect include prazosin,⁴⁹ sildenafil,⁵⁰ reserpine, cilostazol,⁵¹ and captopril.⁵² Bosentan, an endothelin receptor blocker, appears to

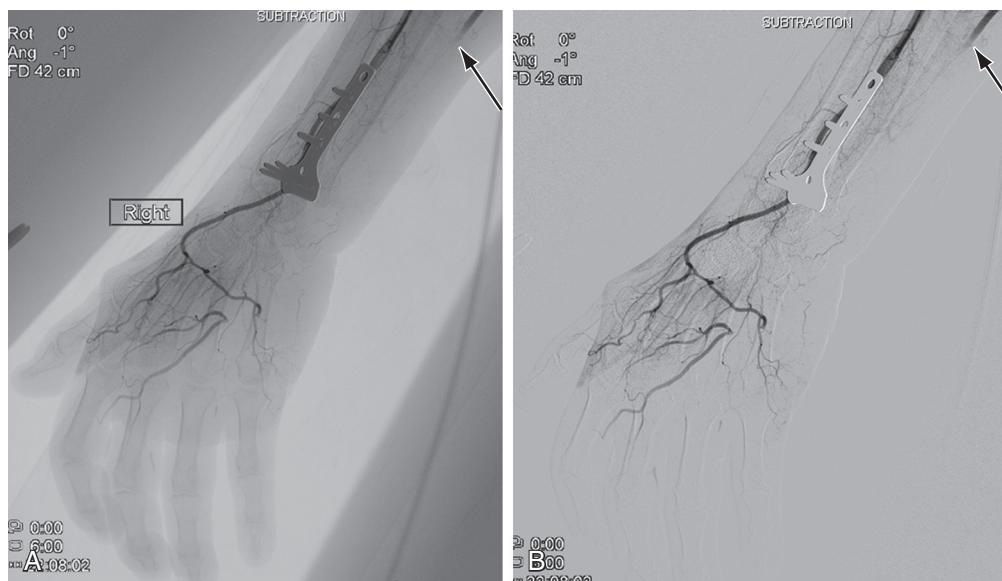


Figure 120.3 A sample of an abnormal hand and forearm arteriogram (**A**, unsubtracted; **B**, subtracted) where the ulnar artery (arrow) is occluded from an embolus (arrow).

particularly benefit patients with scleroderma.⁵³ The results of medical treatment in patients with occlusive secondary Raynaud syndrome have been less effective in these patients. About 20% to 30% of patients do not tolerate nifedipine because of ankle swelling, headache, or fatigue. This group has an intermediate risk for progression that is dependent on the natural history of the underlying cause of the occlusive disease.⁵⁴ Patients with both arterial obstruction and an underlying disease have the worst prognosis and the highest risk for ulceration and tissue loss. Of note, if ulceration is not present at the initial consultation, it is unlikely to develop in the future, and those with ulceration have only 50% chance of further ulceration developing.⁵⁴

Surgical

Thoracic sympathectomy has been used both for treatment of digital artery vasospasm and as an adjunct for healing of digital ischemic ulceration. For vasospasm, although initially successful, symptoms invariably return, often within 3 to 6 months,⁵⁵ possibly related to the rich network of collateral nerve pathways in the upper extremity. Alternatively, periarterial digital sympathectomy performed in the common digital arteries has been suggested as a superior strategy, and a number of small series claim long-lasting benefit from such a procedure.⁵⁶ In a study of 100 patients with digital ulceration, patient outcomes were independent of whether they underwent thoracic sympathectomy or not.⁵⁷ Patients with digital ulceration have obstructed digital arteries and are most likely already maximally vasodilated; thus, sympathectomy is unlikely to improve blood flow, and remains unproven at this time. Other treatments that have been reported include spinal cord simulation and biofeedback.^{58,59}

Thoracic outlet syndrome requires cervical or first rib resection with or without repair of the artery depending on presence of aneurysmal degeneration (see Ch. 125, Thoracic Outlet Syndrome: Arterial). Large artery occlusion, arterial aneurysm, thoracic outlet syndrome with arterial damage or occlusion, fibromuscular disease, and upper extremity arterial trauma with symptoms are best treated by revascularization (see Ch. 121, Upper Extremity Arterial Disease: Medical, Endovascular, and Open Surgical Management).

Results for upper extremity bypass are excellent and even superior to those reported for lower extremity ischemia. In our institution, 20 upper extremity bypasses were performed for chronic upper extremity ischemia over a 13-year period with

patency and limb salvage rates of 85% and 100%, respectively, at 3 years.⁶⁰ Excellent 1-year patency (90%–96%) and limb salvage rates (100%) of upper extremity bypass have been reported by other groups as well.^{61,62}

SUMMARY

Upper extremity ischemia is less common than lower extremity ischemia. Etiologies include vasospastic and occlusive disorders. Occlusive disease is associated with a worse prognosis for developing tissue loss. Most patients appear to have their most severe symptoms at the time of presentation. Vasospastic etiologies are more responsive to pharmacologic intervention, with nifedipine and losartan as the best studied medications. Sympathectomy does not confer a durable response in vasospasm and is of little to no use in occlusive disease. Finally, bypass is a viable option in patients with occlusive disease with excellent early to mid-term outcomes.

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

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Upper Extremity Arterial Disease: Medical, Endovascular, and Open Surgical Management

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Based on a previous edition chapter by Courtney J. Warner, Sean P. Roddy, and R. Clement Darling

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INTRODUCTION

Upper extremity disease and its management are amongst some of the most complex topics in vascular surgery. Unlike lower extremity disease, which is due to atherosclerosis most of the time, upper extremity arterial disease encompasses a wide variety of etiologies. These disease processes ranges from various autoimmune diseases, such as Takayasu and giant cell arteritis, to thoracic outlet disease, embolic disease, hypothenar syndrome, and atherosclerosis. Depending on the cause of

upper extremity ischemia, treatment varies from strictly medical management to strictly surgical management, but most often a combination of both is required.

Upper extremity arterial occlusive disease is responsible for less than 5% of all cases of limb ischemia.¹ Even in high-volume centers, arm reconstructions account for only 3% of elective limb revascularizations. Palmar and digital artery occlusive disease is the most common cause of upper extremity arterial occlusive disease, whereas large-vessel disease, including arteries proximal to the wrist, accounts for less than 10%. The majority

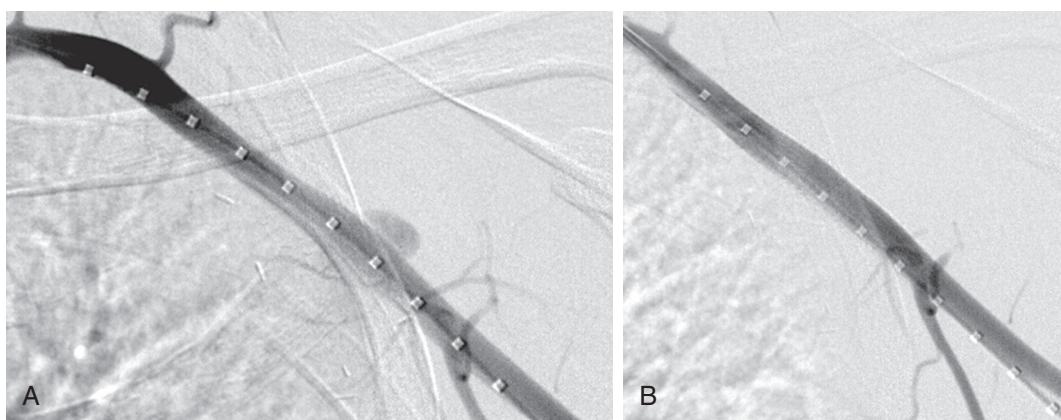


Figure 121.1 (A) Angiography of the left arm after penetrating trauma reveals a pseudo-aneurysm off the axillary artery. (B) After deployment of a covered stent graft in the axillary artery, no further extravasation is seen.

of arm emboli are cardiac in origin (75%). The most common site for emboli is the brachial artery (60%), followed by the axillary artery (26%). *In situ* thrombosis accounts for only 5% of episodes of arm ischemia.² This chapter deals with revascularization for both acute and chronic ischemia involving the intrinsic arteries of the upper extremities, including the axillary, brachial, radial, ulnar, and palmar arteries. Raynaud syndrome (see Ch. 142, Raynaud Phenomenon), thoracic outlet obstruction (see Ch. 125, Thoracic Outlet Syndrome: Arterial), occlusive disease of the great vessels (see Ch. 101, Brachiocephalic Artery Disease: Surgical Treatment), Takayasu arteritis (see Ch. 140, Takayasu Arteritis), and giant cell arteritis (see Ch. 138, Vasculitis and Other Arteriopathies) are described elsewhere.

TREATMENT

Conservative Therapy

Between 9% and 30% of patients seen by vascular surgeons with upper extremity arterial occlusive disease are managed conservatively because of significant comorbid conditions or minimal symptomatology. Conservative therapy classically includes anticoagulation for acute or subacute ischemia. Adjunct therapies like calcium channel blockers, topical nitrates, and phosphodiesterase inhibitors have also been used with variable success. Smoking cessation, optimizing cardiac output, avoiding vasoconstrictors, avoidance of caffeine and cold, and warming the upper extremity are also useful to obtain the best possible outcome.

Acute ischemia, typically embolic in nature, is best managed with operative embolectomy; however, postoperative mortality rates are as high as 12%, related to comorbid conditions.³ After successful brachial embolectomy, 95% of patients will remain free of symptoms.⁴ Patients managed conservatively are underreported in the literature. In the few reported series, assessment of symptoms and disability is inconsistent. However, in a series of 95 patients described by Baird and Lajos in 1964 with arm ischemia managed without surgery, 32% were left with permanent disability in the arm.⁵ In 1977, Savelyev and coauthors reported that 75% of patients managed conservatively had a poor functional outcome.⁶ In 1985, Galbraith and associates confirmed that 50% of their conservatively managed patients had persistent exercise-induced forearm pain (a claudication equivalent).⁷

Therefore, although conservative management is appropriate for some patients with acute ischemia, for those with a reasonable life expectancy, all efforts should be made to restore blood flow.

Endovascular Treatment

Endovascular therapies for the treatment of arterial occlusive disease have been increasingly performed during the last decade with advancement in catheter, balloon, and stent technology. The majority of lower extremity revascularizations in contemporary vascular surgery practices are now performed percutaneously. However, the upper extremity has not experienced the same paradigm shift, possibly due to the relative infrequency of interventions or the underlying causes of the arterial disease, as well as the simplicity of the open surgical procedures. A recent Japanese multicenter study reviewed 553 patients undergoing primary endovascular therapy with angioplasty and/or stenting for subclavian artery occlusive disease, with a primary patency of 90% at 1 year and 81% at 5 years, although it is unclear what aspect of the subclavian artery was involved.⁸ Most institutional reviews that describe treatment of occlusions in the axillary, brachial, radial, and ulnar arteries still involve surgical bypass or embolectomy.^{9,10} There are scattered reports of emergency placement of covered stents in the axillary artery in trauma patients.¹¹ An example of such therapy is illustrated in Figure 121.1. There are also reports of small series of patients treated by axillary artery angioplasty for radiation-induced occlusion, by brachial artery atherectomy, and by radial artery stenting for digital gangrene, but their numbers are low and follow-up is minimal.^{12–15} Therefore, dissection and exposure of the arterial anatomy for revascularization will be described at the most common levels of intervention (Fig. 121.2).

SURGICAL TREATMENT

Arterial Exposure

See Chapter 59 (Upper Extremity Vascular Exposure).

Axillary Artery

The patient is positioned supine and the arm is usually placed at the patient's side if an infraclavicular incision is being made.

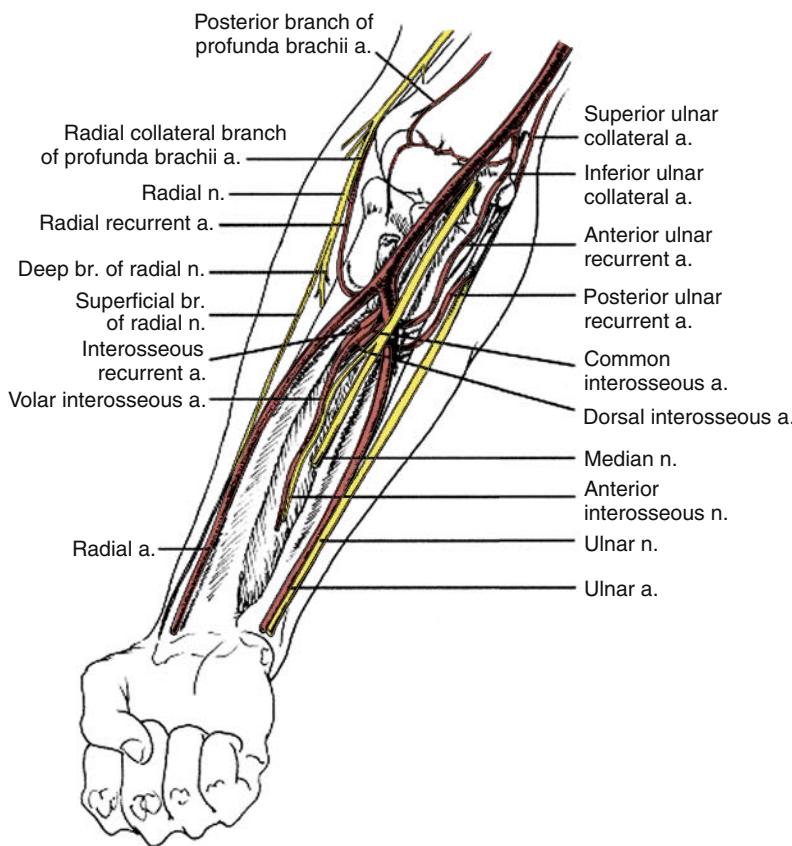


Figure 121.2 Forearm Nerve and Vessel Anatomy. The brachial artery typically bifurcates just below the elbow. (From Valentine RJ, Wind CG. *Anatomic Exposures in Vascular Surgery*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2003.)

This allows the surgeon to have better access to the operative field without hindrance. However, if the distal target is in the arm, circumferential prepping and draping may be needed. The axillary artery is exposed with a transverse incision 2 cm below the middle third of the clavicle (Fig. 121.3). The underlying pectoralis major muscle is divided, when possible, in the decussation between the sternal and clavicular portions. Division of the pectoralis major exposes the clavipectoral fascia, which is divided. The axillary artery is located cephalad to the vein. It is dissected carefully to avoid injury to the surrounding cords of the brachial plexus. The second portion of the axillary artery can be exposed by dividing the pectoralis minor muscle. If needed, the distal third of the axillary artery may also be exposed. An oblique incision is made along the lateral margin of the pectoralis major muscle with the arm abducted 90 degrees relative to the thorax. Once the subcutaneous tissue is divided, the axillary sheath is located near the posterior and inferior border of the coracobrachialis. Careful dissection avoids injury to the medial and lateral cords of the brachial plexus medially and the median and ulnar nerves laterally.

Brachial Artery

The mid or distal brachial artery is exposed through a medial incision over the bicipital groove, allowing access to the proximal or middle third of the brachial artery. The basilic vein and cutaneous branches of the median nerve are located within the subcutaneous tissue and should be avoided during dissection. Traction or transection of the median antebrachial cutaneous nerve may lead to hyperesthesia or anesthesia along the medial dorsal surface of the forearm and can be quite debilitating to

the patient. The brachial sheath is then incised longitudinally. The median nerve is the most superficial structure encountered. The nerve is gently mobilized and retracted to allow access to the brachial artery. Crossing vein branches should be divided to minimize the risk of injury to the posteriorly located ulnar nerve.

The distal third of the brachial artery and its bifurcation, in contrast, are exposed in the antecubital fossa (Fig. 121.4). A lazy S-shaped incision is recommended to expose the origins of the ulnar and radial arteries and to decrease the risk of contracture over the antecubital fossa. For the distal most brachial artery, a vertical incision can be used beginning just below the fossa. The skin and subcutaneous tissues are divided. Care is taken to preserve the superficial veins, especially the median antecubital vein, because it may be required for autogenous patch angioplasty closure. The bicipital fascia is incised and the brachial artery is seen coursing between the biceps tendon laterally and the median nerve medially. Dissection is continued distally until the ulnar and radial arteries are encountered. The radial artery is really a continuation of the brachial artery. The ulnar artery, on the other hand, comes off the brachial artery medially and, within 2 to 3 cm, dives beneath the pronator and epitrochlear muscles.

Radial Artery

The course of the radial artery in the forearm follows an oblique line from the brachial artery pulse medial to the biceps tendon to the styloid process of the radius. In the midforearm, the radial artery is medial to the brachioradialis and lateral to the flexor carpi radialis. A lateral longitudinal incision is made. The muscles are separated to reveal the radial artery as needed (Fig. 121.5). At the wrist the radial artery is exposed by a

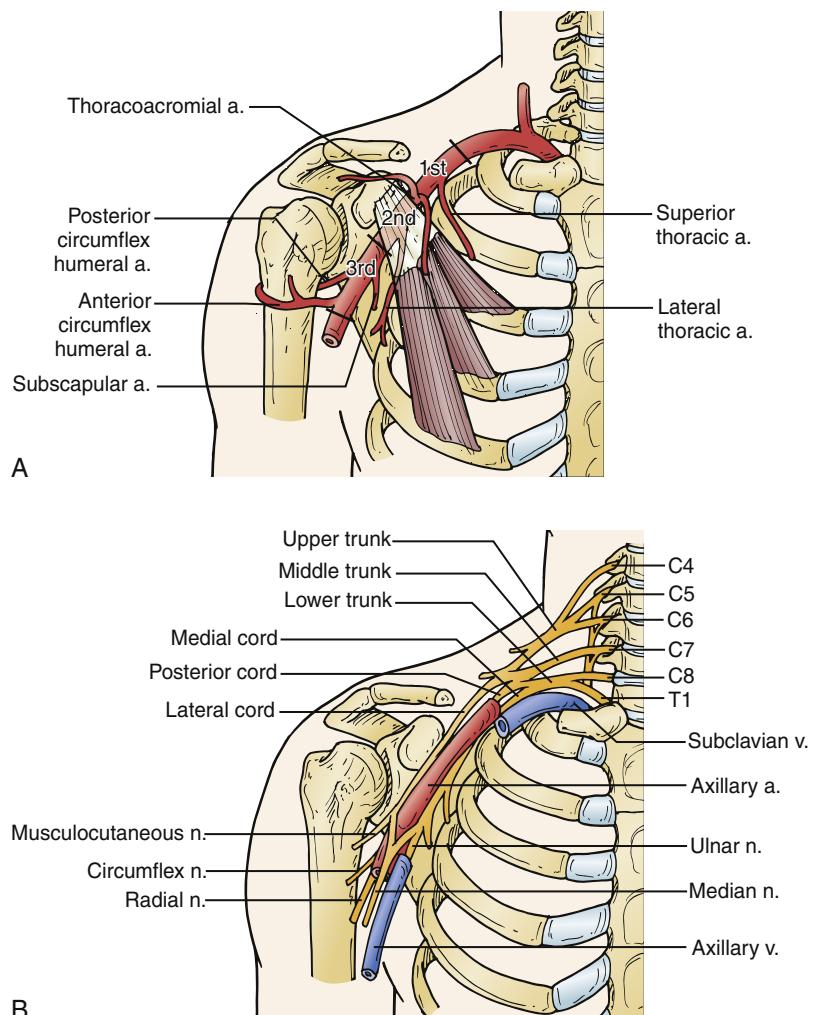


Figure 121.3 Exposure of the First Portion of the Axillary Artery. (A and B) illustrate the anatomy pertinent to exposure of the first portion of the axillary artery. The clavipectoral fascia is opened to expose the axillary sheath. The pectoral nerves and vessels, as well as the cephalic vein, should then be seen in the operative field.

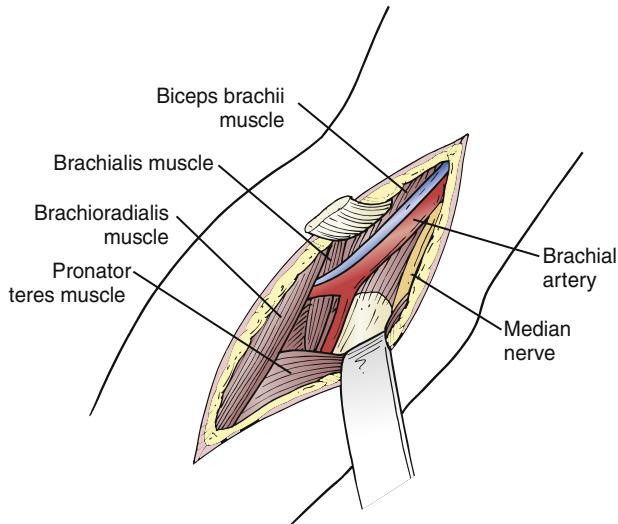


Figure 121.4 Exposure of the Brachial Artery at the Elbow. The bifurcation of the brachial artery can be exposed by retracting the pronator teres and flexor muscle mass. The radial artery can be followed the length of the incision, but the larger ulnar artery dives between the heads of the flexor digitorum superficialis.

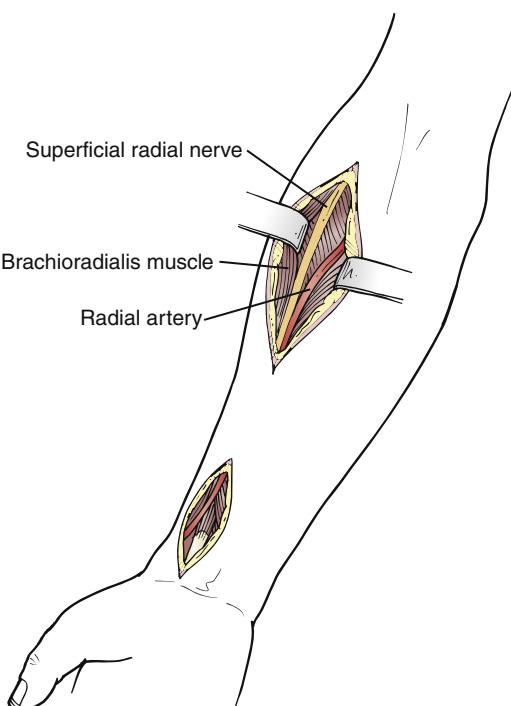


Figure 121.5 The radial artery in the midforearm can easily be exposed beneath the brachioradialis.

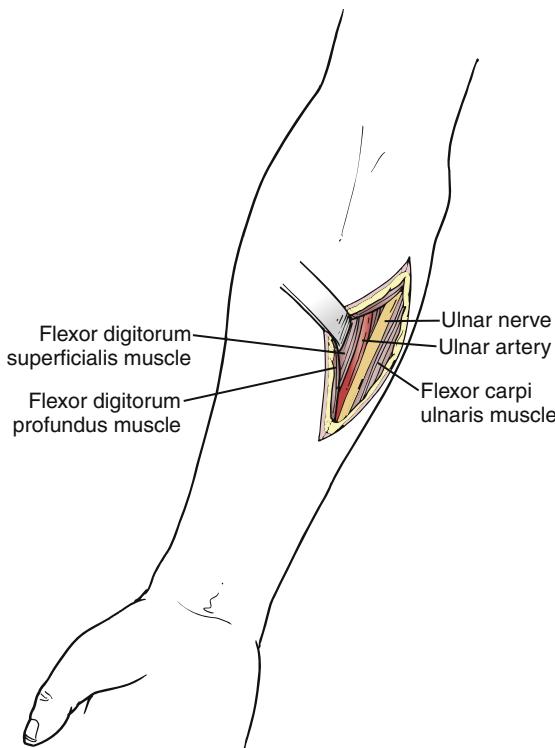


Figure 121.6 Exposure of the Forearm Ulnar Artery. The ulnar artery in the midforearm is reached between the flexor carpi ulnaris and flexor digitorum superficialis.

longitudinal incision between the tendons of the flexor carpi radialis and the brachioradialis muscles. This is the traditional site of the radial artery pulse in normal subjects. The artery is superficial and exposure is relatively straightforward. The superficial branch of the radial nerve is often located near the lateral aspect of the artery. Injury can result in troublesome paresthesias along the lateral aspect of the thumb.

Ulnar Artery

The ulnar artery extends from the medial epicondyle of the humerus to the pisiform bone. In the midforearm, the ulnar artery lies beneath the deep fascia between the bellies of the flexor digitorum laterally and the flexor carpi ulnaris medially (Fig. 121.6). The ulnar nerve joins the artery on its lateral aspect for its distal two-thirds. It may be injured if not carefully identified and preserved. At the wrist, the ulnar artery is lateral to the flexor carpi ulnaris (it is the most medial tendon palpable at the wrist). For exposure, this tendon is identified and a vertical skin incision is made lateral to it. The ulnar artery is relatively deeper than the radial artery at the wrist but just as easily exposed. The palmar cutaneous branches of the ulnar nerve are superficial to the artery here and should be preserved.

Interosseous Artery

The interosseous arteries of the forearm are naturally the smallest and most deeply situated of the forearm vessels. They are the embryologic analogue to the peroneal artery in the lower extremity, an artery of supply to the distal extremity musculature. The

initial few millimeters of the common interosseous artery can be accessed by following the ulnar artery down from the brachial artery, dividing some of the fibers of the superficial flexor digitorum, and looking for the large branch going lateral and deep from the ulnar artery. The common interosseous bifurcates into an anterior (or volar) interosseous and a posterior (or dorsal) interosseous just proximal to the forearm interosseous membrane. Exposure of the length of the anterior interosseous artery is best done through the same incision used to expose the mid-portion of the ulnar artery and then to separate the flexor carpi ulnaris from the superficial flexor digitorum. After an incision long enough to release the fascia is made, the superficial flexor digitorum is elevated along with the median nerve and dissection is carried along the volar surface of the flexor digitorum profundus. Next, the flexor pollicis longus is elevated toward the radius to expose the anterior interosseous neurovascular bundle; some fibers of the flexor pollicis longus may partially cover the anterior interosseous artery and need to be divided. The posterior interosseous artery is best approached through a dorsal forearm skin incision along the medial aspect of the radius. This artery is usually smaller and less often used for revascularization.

Palmar Arteries

Exposure of the palmar arteries is relatively simple. The blood supply of the hand is supplied by the superficial and deep palmar arches. The superficial palmar arch is supplied by a branch of the radial artery and ulnar artery. The deep palmar arch is supplied by the radial artery and a deep branch of the ulnar artery. The arteries in the arm and hand are analogous to those of the leg and foot. Exposure of the superficial palmar branch is straightforward, whereas the deep palmar arch is deeply located and requires retraction of the digital nerve. In our institution, we have bypassed to the deep palmar arch only rarely.

Exposure of the distal radial artery can be performed as described earlier. Alternatively, a vertical incision over the anatomic snuff-box can expose the distal radial artery in the hand. The snuff-box lies between the extensor pollicis longus tendon posteriorly and the tendons of the extensor pollicis brevis and abductor pollicis longus anteriorly. After deepening the incision through the subcutaneous tissue, the radial artery can be exposed in the floor of the snuff-box. (Fig. 121.7) The radial artery will then traverse around the top of the thumb to become the superficial palmar arch. Therefore, the radial artery can be dissected out even more distally on the dorsum of the hand beyond the snuff-box as well. Distal ulnar artery and the more proximal portion of the superficial palmar arch can be accomplished via a curved incision along the lateral border of the hypothenar eminence (Fig. 121.8). The aponeurotic layer is divided and the artery is then exposed in the upper part of the palm at the origin of the superficial palmar arch. No major nerves pass in this vicinity. Alternatively, the superficial palmar arch can be exposed in the palm by making an incision along the larger vertical or oblique skin creases in the mid-portion of the palm. After division of the skin, there is a superficial fascial layer that can also be divided. The arterial tree should be underneath this fascial layer.

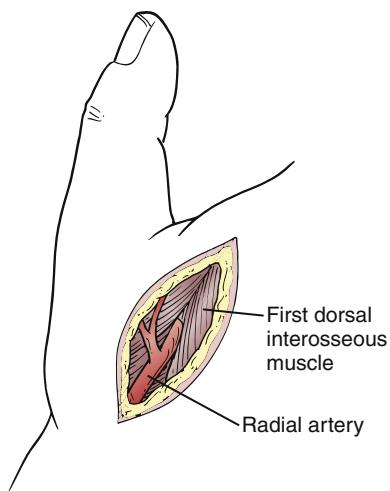


Figure 121.7 The segment of radial artery beyond the extensor pollicis longus tendon is exposed.

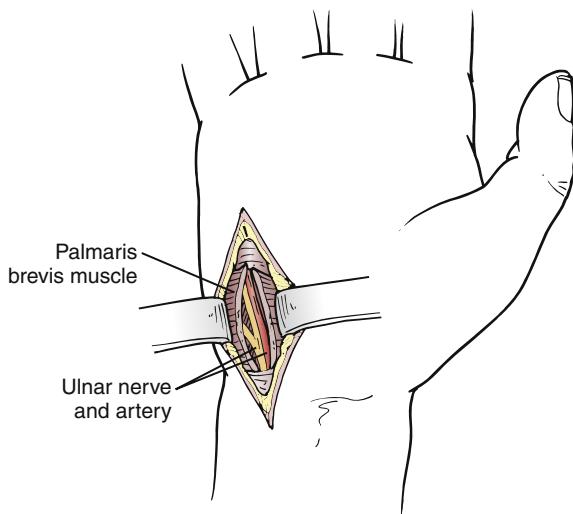


Figure 121.8 The ulnar artery and nerve beyond the tunnel of Guyon are exposed beneath the palmaris brevis muscle and hypotenar fascia.

Bypass Conduit and Tunneling

Autogenous vein is the conduit of choice for upper extremity reconstructions. The great saphenous vein is preferable, although use of *in situ* cephalic vein has been described.¹⁶ The more joints that the bypass crosses, the lower the patency rate.¹⁷ After systemic heparinization, the venous conduit is excised and its side branches ligated with fine polypropylene suture or silk ties. The vein is distended with a solution of dextran, heparin, and papaverine (500-mL bag of dextran 40 + 120 mg papaverine + 1000 units heparin). The excised conduit may be used in either reversed or orthograde (nonreversed) orientation, depending on the taper of the conduit. If orthograde orientation is used, the proximal anastomosis is performed, the conduit is distended, and the valves are rendered incompetent by passage of a retrograde Mills valvulotome. Prosthetic reconstructions in this setting have lower patency rates than do venous bypasses and should be avoided.⁹

Bypasses originating from the axillary artery are preferably tunneled anatomically along the axis of the axillary and brachial arteries because they are then less prone to movement or distortion. They may also be positioned anteriorly in the subcutaneous plane. However, superficial bypasses are more prone to distraction injuries from forcible abduction of the shoulder. Therefore, redundancy is paramount to avoid harming the conduit. Another alternative is the retrohumeral approach for tunneling.¹⁸ This involves a more proximal reconstruction which originates in the suprACLAVICULAR fossa and then traverses the subcutaneous plane inferior to the acromion process. The conduit continues from the posterior aspect of the upper arm around both medial and anterior where it descends through the fascia to the brachial artery.

Bypasses based on brachial artery inflow are most often tunneled in the subcutaneous plane. This facilitates physical examination for appropriate evaluation of bypass patency, ensures surveillance of the bypass with duplex, and avoids manipulation of the rich forearm nerve network. If good-quality basilic or cephalic veins are present, an *in situ* bypass may be performed.

In the case of distal radial-sided reconstructions, the graft is tunneled subcutaneously over the extensor pollicis tendons toward the anatomic snuff-box onto the dorsum of the hand. The bypass ends between the thumb and index finger, where the deep palmar arch (Fig. 121.9) or even a digital vessel in the absence of a complete arch (Fig. 121.10) is exposed. In the case of ulnar-sided reconstructions, the course of the vein graft is more direct and it passes superficial to the flexor retinaculum in the subcutaneous plane at the wrist lateral to the pisiform bone to join the superficial palmar arch.

INTERVENTIONS

Transbrachial Embolectomy

When an embolectomy is planned, several considerations are essential. If preoperative imaging (usually duplex ultrasound) has demonstrated occlusion of the distal brachial artery, it is important to expose the origins of both forearm arteries because the embolectomy catheter must be passed down each artery. If the catheter is passed blindly down the brachial artery, it will most likely travel down the radial artery. This will probably re-establish flow to the hand in the majority of patients. However, it may fail to restore adequate flow if the ulnar is the dominant arterial blood supply or if the catheter passes down the common interosseous artery, which does not provide any direct flow to the hand. We usually make a transverse arteriotomy in the brachial artery. Clot, frequently encountered at the bifurcation, can readily be removed. The majority of brachial embolectomies are performed under local anesthesia with monitored anesthesia care. The brachial artery may be pulseless, indicative of an embolus lodged more proximally. Caution should be exercised with proximal passage of an embolectomy catheter due to risk of dislodgment of debris that may embolize the vertebral artery near the origin of the subclavian artery. If there is any concern, contrast-enhanced angiography is



Figure 121.9 Palmar Artery Bypass Completion Arteriogram.



Figure 121.10 Digital Artery Bypass Completion Arteriogram.

warranted to define the anatomy. Once inflow is established, a size 2- or 3-F embolectomy catheter is passed distally down each forearm vessel. The arteriotomy can be closed primarily with running fine polypropylene suture if the artery is sufficiently large. If there is any doubt, the artery should be closed with a vein patch. Usually, a segment of vein can be harvested from the antecubital fossa.

After closure, an intraoperative continuous wave Doppler probe should be applied to each artery to ensure the presence of adequate flow. Immediate completion angiography is at the discretion of the surgeon but should be performed if the hand still appears ischemic, especially if extensive thrombus has been extracted from forearm arteries. Occasionally, embolization may have been a chronic process and resulted in distal arterial occlusion that cannot be completely resolved with embolectomy, but arteriography can be used to detect residual fresh thromboembolic material. If there is any suspicion of an inflow lesion, intraoperative arteriography can be performed by either the femoral or brachial route to diagnose and treat such lesions. A report by Zaraca et al. demonstrated a significant reduction in 2-year reocclusion rate in patients undergoing angiography after embolectomy (12% versus 2% without angiography).

After embolectomy, the rate of extension of the procedure was 26% in the angiography group versus 4% in the group without intraoperative angiography, suggesting that routine intraoperative angiography impacts outcomes and may be associated with a more thorough embolectomy.¹⁹

POSTOPERATIVE MANAGEMENT AND FOLLOW-UP

Postoperatively, surveillance with pulse volume recordings or Doppler segmental pressure measurements can be used to document the adequacy of the bypass. Duplex ultrasonography is used to determine the patency of the reconstruction and allow early detection of stenoses during surveillance of the venous conduit. The number of series reporting long-term patency is limited. Roddy et al. identified a 90% primary patency and 100% limb salvage rate at one year in their cohort of 61 bypasses.⁹ More recently, Spinelli and colleagues identified 23 patients with chronic ischemia that underwent upper extremity bypass.²⁰ At a mean of 34 months, primary patency was 83% with a limb salvage rate of 100%. Anticoagulation is essential after embolectomy. However, anticoagulation is not routinely indicated for bypasses unless the patient has known or suspected hypercoagulable state, or if there is a cardiac indication. Recurrent embolization occurs in one third of patients after successful embolectomy if systemic anticoagulation is not instituted. Even in patients started on warfarin after embolectomy, 11% sustained a further embolus if they had ongoing atrial fibrillation in an Edinburgh study.²¹ In those patients without atrial fibrillation as the source of embolus and in whom no preoperative, intraoperative or immediate postoperative angiography has been performed, formal diagnostic arteriography, CTA, or MRA should be considered to rule out alternate etiologies for thromboembolism. Intracardiac assessment with echocardiography is indicated if no arterial source is identified.

ALTERNATIVE THERAPY

Sympathectomy has been used with isolated reports of success,^{22,23} but the experience in most centers has been less than optimal (see Ch. 193, Current Role of Sympathectomy (Upper and Lower)). Thrombolysis of acutely occluded axillary or brachial arteries has been described with reasonable outcomes.²² However, in one large series, success was reported in just over half of the limbs treated, and 8 of 55 patients required surgical thrombectomy.²³ Thrombolysis has also been described as a treatment option for acute finger ischemia with disease distal to the wrist. In a small series, half of patients (8 of 16) experienced anatomic improvement on repeat angiography, but functional outcomes are less clear²⁴ (see Ch. 43, Thrombolytic Agents).

TRAUMA

Upper extremity trauma is relatively frequent and can be iatrogenic or noniatrogenic (see Ch. 181, Thoracic Vascular Trauma and Ch. 183, Vascular Trauma: Extremity).

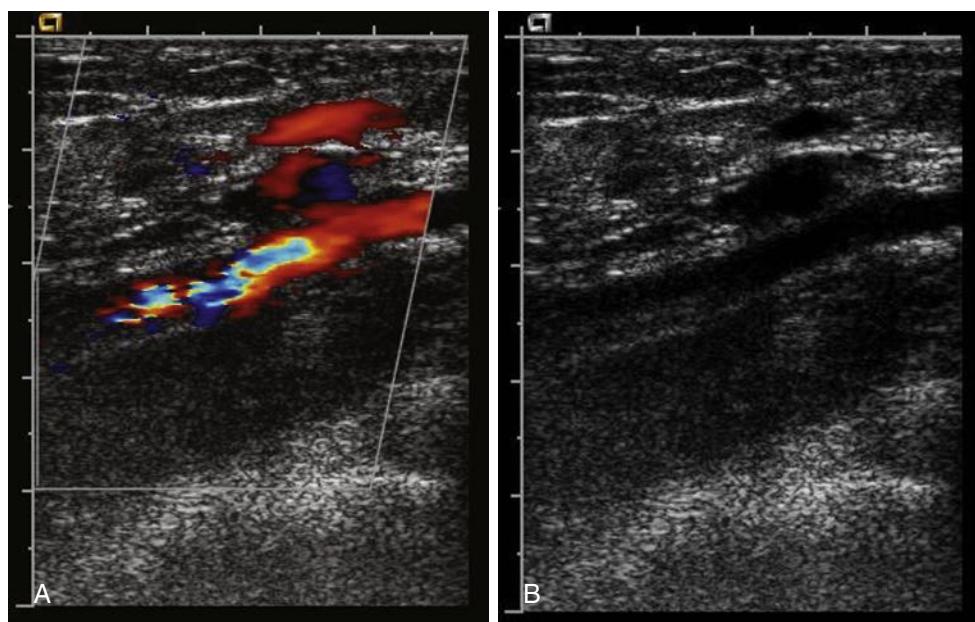


Figure 121.11 Brachial artery pseudoaneurysm after cardiac catheterization as seen through color duplex (A) and B-mode (B) ultrasound imaging.

Iatrogenic Trauma

Brachial Artery

Brachial artery pseudoaneurysm or occlusion related to cardiac catheterization is one of the most common indications for arterial surgery in the upper extremity.²⁵ The presence of a pseudoaneurysm may be suggested by a mass at the puncture site, evidence of distal occlusion or embolization, or neurologic complications related to median nerve compression within the sheath, usually manifesting as paresthesias. The diagnosis can generally be made with duplex ultrasonography (Fig. 121.11) (see Ch. 22, Vascular Laboratory: Arterial Duplex Scanning), and direct repair with evacuation of the hematoma compressing the median nerve can be performed under local anesthesia. Percutaneous thrombin injection is another therapeutic option. In a report of 14 patients successfully treated with ultrasound-guided thrombin injection for iatrogenic upper extremity pseudoaneurysms, there was a low complication rate with no recurrences at 8 months.²⁶ However, thrombin injection would not be appropriate if the patient has neurological deficits due to nerve compression from hematoma in the brachial sheath.

Occlusion of the brachial artery as a result of catheter insertion often requires more extensive reconstruction that usually involves a segmental bypass with either saphenous vein or cephalic vein from the ipsilateral arm. If recognized promptly, any propagated thrombus proximal or distal to the puncture site can be extracted with a balloon embolectomy catheter. Delayed recognition of this problem will often necessitate a longer-segment interposition graft with autogenous vein.

Radial Artery

The radial artery is the second most common site of upper extremity iatrogenic arterial injury as a result of catheterization.

Partial or complete occlusion of the radial artery after cannulation for monitoring purposes was apparent in 25% of 1699 patients undergoing cardiovascular surgery in a series by Slogoff and colleagues. None of these patients had hand ischemia.²⁷ Although the involved hand may be clinically pale, the fingers usually remain viable with intact neurological function due to collateral filling from the ulnar artery. Unless there is some obvious evidence of severe cyanosis, demarcation, neuropathy, or sensorimotor deficit, we generally recommend a period of observation after removal of the arterial catheter. Heparinization is desirable but not mandatory. Many will improve with conservative treatment. In the rare case in which the hand appears to be severely ischemic, repair with a short autogenous bypass of the radial artery above and below the puncture site is usually sufficient to effect improvement. Radial and ulnar artery vascular access for cardiac catheterization using up to 6-F sheath systems is increasing. Occlusion rates have been reported to be approximately 5% in either vessel,²⁸ and the overwhelming majority are asymptomatic and do not require reconstruction.

Noniatrogenic Trauma

Trauma related to blunt or penetrating trauma is unfortunately a common source of upper extremity arterial injury.²⁹ In civilian centers, these injuries are predominantly blunt or involve low velocity penetration. Military-associated upper extremity vascular injuries are complex because of the combined nature of the mechanism and significant multi-system injury.

Penetrating Trauma

Penetrating trauma is generally evident on evaluation in the emergency department. Repair of the injury is not usually complex, but obtaining proximal arterial control can be challenging. Injury to the subclavian arteries may require anterior

thoracotomy or a trapdoor-type incision, or both, or endovascular control with balloons. Injury to the axillary arteries is often best managed by initial proximal exposure of the subclavian artery from a supraclavicular approach. Proximal control of the brachial artery can usually be managed with a more proximal medial upper arm incision. Radial and ulnar artery injuries can often be managed with relatively local control, although exposure of the brachial artery at the elbow is always an option. Alternatively, application of a tourniquet may allow direct wound exploration. Patients with isolated radial or ulnar artery injuries and clinical evidence of satisfactory hand perfusion in all five digits can be managed by ligation of the affected artery. However, it is often not much more difficult to simply repair the involved artery with local vein. Whether to ligate or bypass an isolated forearm arterial injury in a pink viable hand is still debated.

Delayed Recognition

Delayed recognition of arterial injury related to penetrating trauma may occasionally result in pseudoaneurysm formation, and sometimes arteriovenous fistulae are also formed by this mechanism. Consequently, there should be a relatively low threshold for obtaining arterial imaging for any penetrating trauma that may produce an arterial injury. In the case of gunshot wounds with a trajectory passing near an artery, the initial imaging may suggest no injury. However, the artery may have suffered thermal injury, and repeat imaging is therefore recommended to evaluate for the formation of a pseudoaneurysm or arteriovenous fistula. Likewise, many forearm injuries related to broken glass may produce an occult radial or ulnar artery injury that is not identified at the initial inspection but may result in further hemorrhage and even the development of compartment syndrome days later. Given the potential difficulty with follow-up of these patients, imaging at the time of initial evaluation is recommended to avoid delayed recognition of these injuries. Once identified, arterial pathology such as pseudoaneurysm, arteriovenous fistula, and compartment syndrome should be addressed promptly. Alternatively, asymptomatic upper extremity arterial occlusions may be observed or reconstructed based on clinical condition paralleling treatment algorithms with the lower extremity. In the situation of possible occult injury, CTA or duplex of upper extremity arteries can be used to detect delayed pseudoaneurysm or arteriovenous fistula formation.

Blunt Trauma

Management of blunt trauma producing arterial injury is somewhat more complicated because of the difficulty in diagnosing and localizing the injury. The force of an impact strong enough to injure the artery may result in associated neurologic compromise and long-bone fracture. Because of this, it is important to assess and document a thorough neurologic exam, as missed injuries may result in long term sequelae. Frequently, these patients benefit from preoperative arteriography. Ongoing hemorrhage is generally not the problem, and exposure can be directed at the injured site. However, it is also more likely that there will be associated extensive venous injury and

the development of venous hypertension after reconstruction of the arterial lesion. In these cases, either direct repair of the vein or a short autogenous bypass of the injured venous segment is useful to decompress the venous hypertension in the affected arm and thereby decrease swelling and continued hemorrhage from the wound, although this remains controversial.³⁰

Pediatric Supracondylar Fractures

One area of controversy is the treatment of type III supracondylar fractures of the humerus in children who lack a palpable radial pulse after the injury. Long-term ischemia from arterial occlusion in a child may lead to Volkmann contracture, which results in permanent flexion and a clawlike deformity of the hand and fingers. The brachial artery may be pinched, avulsed, or thrombosed as it wraps around the fracture site. Orthopedic reduction is the accepted first treatment, with neurovascular re-evaluation after stabilization. If the pulse returns, no further treatment is necessary besides observation. If it does not and the hand appears white, pale, and ischemic, operative exploration is preferred. Debate exists in the literature regarding the optimal treatment when the pulse is not palpable but the hand is pink and viable. Some describe a conservative approach with serial examination.³¹ Others favor aggressive operative reconstruction whenever possible,³² either direct arterial repair with patch angioplasty or bypass using the great saphenous vein around the area of injury. Care must be taken with arterial manipulation in children to avoid spasm whenever possible. Fortunately, the incidence of this type of upper extremity ischemia is low. Multiple authors have found additional imaging such as contrast angiography or duplex ultrasonography does not alter the course of treatment.^{33,34}

COMPLICATIONS

Major complications that may occur after upper extremity arterial surgery include brachial plexus and median or ulnar nerve injury. Such injury is usually a result of traction and should be avoided by careful dissection during operative exposure. The use of electrocautery should be minimized to reduce the chance of direct thermal injury to the underlying nerves at all levels.

As with any arterial bypass, graft thrombosis can also occur. Some series found female smokers and patients with longer bypasses crossing multiple joints to have the lowest patency.^{2,9} An inflow lesion in the subclavian artery can also cause acute arm ischemia, if not appreciated as the etiology of an embolus to the arm (e.g., ulcerated plaque, thrombosed subclavian artery aneurysm, or arterial thoracic outlet syndrome). In such situations, even a technically perfect brachial embolectomy will fail to restore normal hand perfusion. Moreover, if the arteries are relatively free of atherosclerotic disease, embolectomy of the distal radial and ulnar vessels may result in arterial spasm. This problem is more commonly seen in women and children. However, it is a diagnosis of exclusion, and the first priority must be removal of retained embolic debris. If spasm is identified intraoperatively, topical or intra-arterial vasodilators such as papaverine, warm saline irrigation, and time should relieve

the constriction and result in an adequately perfused hand. Anticoagulation should be considered if the source of emboli remains a potential source, such as a cardiac etiology. However, if the source is treated, long-term anticoagulation is not usually needed.

COMPARTMENT SYNDROME

As in the lower extremity, reperfusion of the arm may result in a significant inflammatory response and swelling. This response is more common with treatment of acute ischemia in an individual without long-standing collateralization but overall is a rare event. Decompressive fasciotomy is the mainstay of treatment. This involves incising the fascia on both the volar and dorsal aspects of the arm. In severe cases, extension of the fasciotomy into the hand itself, through the carpal tunnel, may be required.

CONCLUSIONS

Upper extremity arterial disease is a challenging and often complex problem with a multitude of etiologies that can affect treatment plans and surgical reconstructions. However, careful work-up and examination can help delineate which underlying causes are creating the patient's symptoms. Often, patients with arterial upper extremity disease will need bypass reconstructions, sometimes to the hand. Bypasses to the hand are relatively straightforward and can be accomplished in the same way as one might do a bypass to the foot. Small series of patients have also been treated with endovascular means in the forearm. In our institution, that option is usually reserved for

patients whose medical comorbidities may be too serious for them to undergo bypass surgery. Typically, such interventions are done for patients with limited life expectancy and for palliative reasons, such as pain control.

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