

noninvasively with a high negative predictive value (86% and 91%, respectively). However, the positive predictive value was far lower (36% and 59%, respectively). This study concluded that these modalities should be used together with arteriography as they are better for screening.

## Treatment

Medical therapy for ICAS consists of antiplatelet therapy with aspirin or clopidogrel. Studies have evaluated the single and combination use of both agents. The Warfarin and Aspirin for Symptomatic Intracranial Arterial Stenosis (WASID) trial in 2005, a double-blind randomized trial, determined that there was no significant benefit from warfarin over aspirin for stroke or death prevention in ICAS. A high risk of recurrent stroke existed for patients on medical therapy alone.<sup>92</sup> The Clopidogrel plus Aspirin for Infarction Reduction (CLAIR) study found that the combination therapy of clopidogrel and aspirin was more effective than aspirin alone in reduction of microemboli formation (relative risk reduction of 42.4%).<sup>94</sup> The Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRISS) study compared medical treatment with endovascular treatment.<sup>95</sup> Medical management with aspirin and clopidogrel was better than medical management plus angioplasty and stenting using the Wingspan stent system. This study demonstrated lower stroke recurrence rates in those medically treated with dual antiplatelet therapy compared with aspirin alone.

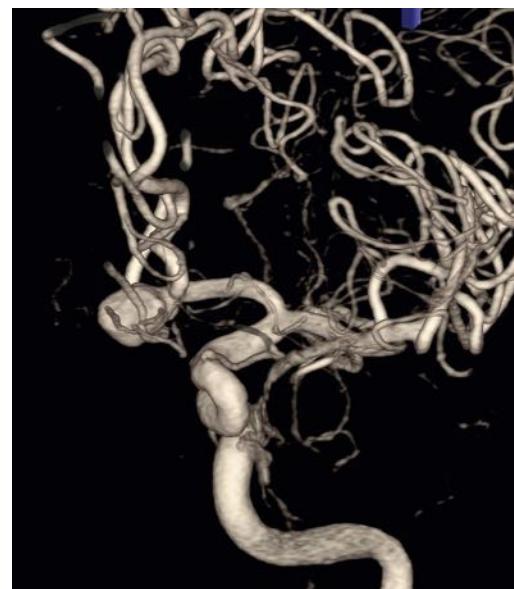
Despite the results of these studies, surgical and endovascular interventions have shown promise. Surgical treatment for ICAS was introduced in the 1960s. Initial studies demonstrated that EC-IC bypass was not effective in preventing stroke in carotid and middle cerebral arterial atherosclerotic disease as compared with aspirin therapy,<sup>96</sup> despite patency rates of 96%.

Endovascular intervention has evolved into a viable treatment modality for ICAS. In 2005, the US Food and Drug Administration (FDA) approved the Wingspan self-expanding nitinol stent for use in the cerebral vasculature. Initially it was limited to patients with greater than 50% ICAS but by 2012, it was restricted to 70% to 99% stenosis with recurrent stroke despite medical management. This was prompted by a US multicenter study demonstrating that while endovascular therapy for symptomatic ICAS had high technical success rates, peri-procedural neurologic complications were 6.1%, 80% of these resulting in death within 30 days.<sup>97</sup> These findings were the catalyst for the SAMMPRISS trial which concluded that aggressive medical management was still more effective than stenting in reducing 30-day rates of stroke or death.

## INTRACRANIAL ANEURYSM

### Background

Intracranial aneurysms are dilations of vessel segments at branch points and involve all vessel layers. Unlike aneurysms in other vascular beds, intracranial aneurysms are typically saccular or



**Figure 99.5** CTA reconstruction of an intracranial aneurysm of the anterior communicating artery (ACOM) from the LICA.

berry aneurysms. Other types of aneurysms included fusiform, mycotic, dissecting or microaneurysms seen in small perforator vessels in hypertensive patients (Fig. 99.5).

### Epidemiology

Aneurysms are more prevalent in females with a ratio of 3:2, occurring most commonly in 35- to 60-year-olds. More than one aneurysm is present in 10%–30% of patients.<sup>98</sup> The overall prevalence in the population is between 1.8% and 2.8%. The incidence of rupture varies between 2 to 22.5 cases per 100,000 population worldwide, with an increase in incidence with each decade.<sup>98</sup> Prevalence may be higher in patients with aortic coarctation and aortic aneurysms. Risk factors include smoking and hypertension, inherited syndromes and genetic variants. There is a 4%–9% risk for aneurysm for first-degree family members in familial aneurysmal disease, with increased rupture risk at smaller sizes.<sup>99</sup> While widespread screening is not recommended, CTA or MRA are indicated in patients who have two or more family members with intracranial aneurysms or history of subarachnoid hemorrhage.

### Treatment

Intracranial aneurysms are often asymptomatic until rupture, with patients presenting acutely with subarachnoid hemorrhage (SAH). Other symptoms can include mass effect with headache, cranial neuropathy and seizures. Sudden increase in blood pressure may trigger rupture. This may be related to exercise, sexual activity, defecation and high anxiety or stressful situations.<sup>100</sup>

Most aneurysms are found incidentally during workup for associated symptoms. CT scans accurately diagnose the pathology, although MRI sequences can detect smaller amounts of subarachnoid blood. As with ICAS, DSA is the gold standard



**Figure 99.6** Angiogram of ACOM aneurysm from the LICA.

for imaging based on anatomic detail, morphology and adjacent proximity to branches and perforators (Fig. 99.6).

Treatment of unruptured aneurysms is by surgical aneurysm clipping or endovascular with coiling or intracranial stent placement. The International Study of Unruptured Intracranial Aneurysms or ISUIA<sup>100</sup> found risk of rupture related to larger aneurysm size (>10 mm) in the non-SAH patients, but not in SAH patients. In smaller aneurysms (<10 mm), the risk of rupture was 11 times higher in SAH than in the non-SAH. The trial concluded that posterior circulation location was a predictor of rupture in both groups, and clarified that familial intracranial aneurysms have nearly a 17 times higher risk of rupture compared to matched size and location.

Open surgery was performed in 83% and 94% of the retrospective and prospective arms while endovascular therapy was only performed in the prospective arm, accounting for 19% of aneurysm treatments. Morbidity and mortality at 1 year was 12.6% for clipping and 9.8% for coiling in the retrospective arm, and 10.1% for clipping and 7.1% for coiling in the prospective arm. Variables associated with worse outcomes included older age, large aneurysm size (>12 mm) and posterior circulation location. Small aneurysms (<10 mm) do still rupture. The Unruptured Cerebral Aneurysm Study (UCAS) showed that the presence of aneurysmal irregularity is a rupture risk factor.<sup>101</sup>

Treatment of ruptured intracranial aneurysms is urgent as the risk of rerupture is 4%–13.6% in the first 24 hours. This risk is up to 50% at 6 months without intervention. Recurrent hemorrhage has a mortality of 50%–85%. The International Subarachnoid Aneurysm Trial (ISAT) compared surgical clipping to endovascular coiling for ruptured aneurysms<sup>102</sup> and concluded that the endovascular treatments had better clinical outcomes at 10 years. The Cerebral Aneurysm Rerupture After Treatment (CARAT) and the Barrow Ruptured Aneurysm Trial (BRAT) both found no differences between surgery and coiling.<sup>103,104</sup> The BRAT trial did, however, demonstrate

improved outcomes for posterior circulation aneurysms with endovascular coiling.

Best current therapy is based on individual anatomic and physiologic risk along with the experience of the treating institution and providers.

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*This prospective randomized trial evaluated symptomatic patients undergoing either medical or surgical therapy including carotid artery elongation (straightening). The authors noted a lower stroke and transient ischemic attack rate in the surgical arm and thus concluded that there was a benefit to elongation.*

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*In this NIH-funded trial, the investigators found that for patients with symptomatic intracranial arterial stenosis, aggressive medical management combined with percutaneous angioplasty and stenting was associated with a higher risk of early stroke compared with medical management alone (14.7% vs. 5.8%, P = 0.002). In fact, enrollment was terminated early because of the differential stroke rates.*

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A risk–benefit analysis which found that intracranial aneurysms should be repaired when the benefit to life expectancy exceeds the risk of repair. Definitely no repair is indicated for aneurysms less than 7 mm in diameter and outcomes are worse for those located in the anterior circulation.

A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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# Vertebral Artery Dissection and Other Conditions

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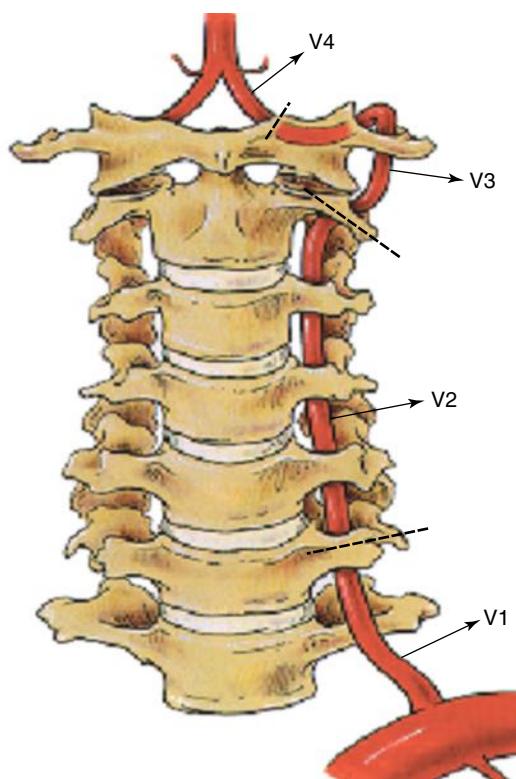
The vertebobasilar system supplies blood to the brain stem, cerebellum, and occipital lobes via paired vertebral arteries. Posterior circulation ischemia is most often related to atherosclerosis involving the vertebobasilar arteries, but may also be related to other vasculitides. Although vertebobasilar ischemia (VBI) is less common than ischemic episodes related to internal carotid artery disease, approximately 25% of all ischemic strokes do occur in the posterior brain circulation; these events should be diagnosed appropriately as they may be the result of a treatable vasculopathy. For patients who experience posterior circulation transient ischemic attacks, disease in the vertebral

If posterior circ TIA's

arteries portends a 22% to 35% risk of stroke over 5 years.<sup>1–4</sup> The mortality is 20%–30%, higher than for anterior circulation events.<sup>5–7</sup>

## PATHOGENESIS AND ANATOMY

The surgical anatomy of the paired vertebral arteries is divided into four segments: segment V1 includes the origin of the vertebral artery as it arises from the subclavian artery to where it enters the C6 transverse process; segment V2 includes the segment of the artery buried within the intertransversarium muscle



**Figure 100.1** The four segments of the vertebral (V) artery. (From Berguer R. Surgical management of the vertebral artery. In: Moore WS, ed. *Surgery for Cerebrovascular Disease*, New York: Churchill Livingstone; 1986.)

and the cervical transverse processes of C6 to C2; segment V<sub>3</sub> includes the segment of the vertebral artery that extends from the top of the transverse process of C2 to the atlanto-occipital membrane at the base of the skull; and segment V<sub>4</sub> includes the intracranial, intradural portion of the vertebral artery beginning at the atlanto-occipital membrane and terminating as the paired vertebral arteries converge to form the basilar artery (Fig. 100.1).

Ischemia affecting the temporo-occipital cerebral hemispheres or brain stem and cerebellum characteristically produces **bilateral symptoms**. Classic VBI symptoms are **dizziness, vertigo, drop attacks, diplopia, perioral numbness, alternating paresthesia, tinnitus, dysphasia, dysarthria, and ataxia**. When two or more symptoms are present, likelihood of VBI is high (Box 100.1).

Posterior circulation ischemia and strokes occur most commonly in relation to large-artery diseases (Table 100.1), with the **vertebral artery (VA)** being the most common vessel, and **atherosclerosis** the most common pathology leading to stroke in this distribution (Table 100.2). Less common processes include dissection, trauma, fibromuscular dysplasia, Takayasu disease, osteophyte compression, aneurysms, and other arteritides.

### Ischemic Mechanisms

In general, VBI ischemic symptoms are due either to **hemodynamic** or **embolic etiologies**. In contrast to ischemia due to

#### BOX 100.1

#### Symptoms Associated With Vertebrobasilar Ischemia

- Disequilibrium
- Vertigo
- Diplopia
- Cortical blindness
- Alternating paresthesia
- Tinnitus
- Dysphasia
- Dysarthria
- Quadriplegia
- Drop attacks
- Ataxia
- Perioral numbness

#### TABLE 100.1

#### Mechanisms of Posterior Circulation Stroke or Transient Ischemic Attack in 407 Patients

Mechanism	Number (%)
Large-artery occlusive disease	132 (32)
Embolism – cardiac source	99 (24)
Embolism – arterial source	74 (18)
Penetrating artery disease	58 (14)
Vasospasm/migraine	10 (2)
Other causes	34 (8)

Modified from Caplan LR, Wityk RJ, Glass TA, et al. New England Medical Center Posterior Circulation registry. *Ann Neurol*. 2004;56:389.

#### TABLE 100.2

#### Frequency of Symptomatic Vascular Occlusive Lesions in 417 Patients of posterior circulation

Lesion	Number
Innominate artery	2
Subclavian artery	5
Extracranial vertebral artery	131
Intracranial vertebral artery	132
Basilar artery	109
Posterior cerebral artery	38

Modified from Caplan LR, Wityk RJ, Glass TA, et al. New England Medical Center Posterior Circulation registry. *Ann Neurol*. 2004;56:389.

carotid artery occlusive disease, the low-flow mechanism of ischemia is better recognized and more frequent than in VA disease.

### Low Flow

Patients with **low-flow ischemia** have **transient symptoms** in the cerebral territories supplied by the basilar artery because they lack appropriate inflow from the vertebral arteries and have **inadequate collateral compensation**. Hemodynamic symptoms occur as a result of transient end-organ (brain

stem, cerebellum, occipital lobes) hypoperfusion, and can be precipitated by postural changes or transient reduction in cardiac output. Ischemia from hemodynamic mechanisms rarely results in tissue infarction. Rather, symptoms are short-lived and repetitive. Some patients may be prone to traumatic injuries from loss of balance or consciousness, resulting in falls. For hemodynamic symptoms to occur in direct relation to the VA, significant occlusive disease must be present in both paired vertebral vessels, in the dominant VA, or in the basilar artery itself. In addition, compensatory contribution from the carotid circulation via the circle of Willis must be incomplete. Alternatively, hemodynamic ischemic symptoms may result from proximal subclavian artery occlusion and subclavian/vertebral artery steal.

### Embolic

Embolic causes of VBI are generally from the heart, aortic arch, subclavian, vertebral, or the basilar arteries. Approximately one-third of VBI episodes are caused by distal embolization from plaque or mural lesions from subclavian or more distal vessels.<sup>8</sup> Emboli arise from atherosclerotic lesions, intimal defects from extrinsic compression or repetitive trauma, and rarely fibromuscular dysplasia, aneurysms, or dissections. While fewer patients suffer from embolic phenomena than from hemodynamic ischemia, tissue infarction is more common with embolic events. Emboli are much more likely to cause fatal events or debilitating strokes. The importance of the embolic mechanism as a cause of vertebrobasilar symptoms has been emphasized in clinical and anatomicopathologic studies. This information has been derived from autopsy and magnetic resonance imaging (MRI) studies, which have identified small infarcts in the brain stem and cerebellum and shown their source, via arteriography, to be lesions in the subclavian or

vertebral arteries. As opposed to patients with hemodynamic symptomatology, multiple and multifocal infarcts in the brain stem, cerebellum, and occasionally the posterior cerebral artery territory more often develop in patients with embolic ischemia.<sup>9,10</sup>

## DISEASE DISTRIBUTION

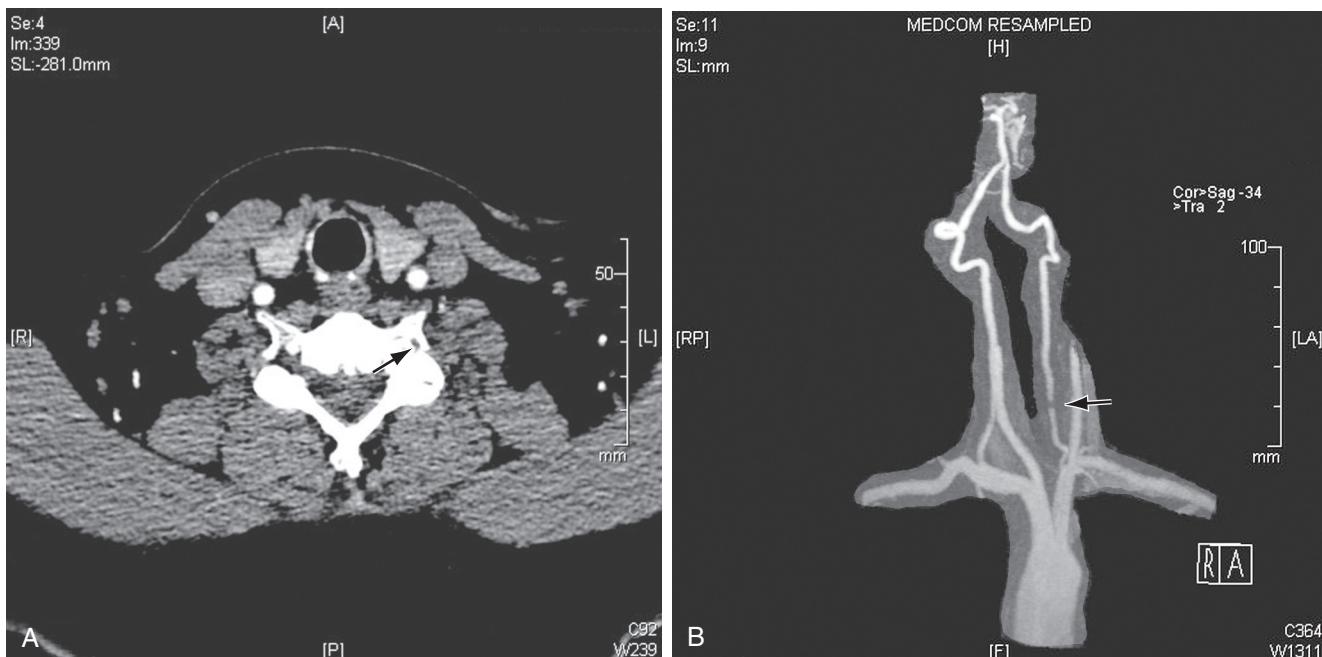
### V1 Segment = atherosclerosis e aign

The most common atherosclerotic lesion of the VA is origin stenosis, with a prevalence of 20%–40% in patients with cerebrovascular disease.<sup>8</sup> The lesions are usually smooth and fibrotic with low embolic potential. Redundancy and kinks are common in the V1 segment, but only severe kinks with poststenotic dilatations can be responsible for hemodynamic symptoms.

*AVF diversion* ← *extinsic compression* ← *V2 Segment* ← *dissection* ← *anatomical* ← *fracture*

The most common pathology of the V2 segment is extrinsic compression by either bone or tendon. Compression can be by osteophytes,<sup>11</sup> the edges of the transverse foramina (Fig. 100.2), or intervertebral joints. Rotation or extension of the neck usually triggers compression of the VA in this segment. Extrinsic VA compression by musculotendinous structures is common in patients with an abnormally high level of entry into the transverse processes of the spine, usually C4 or C5, due to sharp angulation resulting from the abnormal level of entry (Fig. 100.3).

The V2 segment is a frequent site for development of traumatic or spontaneous arteriovenous fistulas. This occurs because fixation of the adventitia of the VA to the periosteum of the foramina makes the vessel vulnerable to luxation/subluxation



**Figure 100.2** (A) Computed tomography (CT) and (B) magnetic resonance angiography (MRA) images demonstrating large osteophytes occluding the vertebral artery at C5.



**Figure 100.3** (A) Vertebral magnetic resonance angiography (MRA) (with the carotid image subtracted). (B) Arch and four-vessel MRA.

injuries in this area. The close proximity of the artery to its surrounding venous plexus results in an arteriovenous fistula when the artery and vein are damaged in continuity. The VA may tear completely or incompletely (dissection) as a consequence of stretch injury after brisk neck rotation or hyperextension.

Although most vertebral artery aneurysms occur intracranially, the V2 segment is the most common site of extracranial aneurysmal degeneration (Fig. 100.4). Two-thirds of all extracranial VA aneurysms involve the V2 segment, with most as pseudoaneurysms secondary to trauma or dissection.<sup>12</sup> True degenerative extracranial VA aneurysms are rare, accounting for less than 1% of all VA lesions.<sup>13</sup> In one review, all patients with a true extracranial VA aneurysm had some form of connective tissue disorder.<sup>12</sup> Most extracranial vertebral aneurysms are asymptomatic and found incidentally. Some present with symptoms including: a palpable neck mass, dizziness, headaches, and/or neurologic deficit from cerebral ischemia or nerve compression. Rupture is rare. Because the natural history is unknown, ligation with or without reconstruction is most often recommended for large extracranial vertebral aneurysms.<sup>12</sup>

Dissection, fibromuscular disease, arteritis, and embolizing atherosclerotic plaques can also be identified in the V2 segment. Disease in the second segment of the VA can result in extracranial occlusion or stenotic lesions in the intraforaminal segment, which commonly give rise to emboli.

V3 Segment *< trauma* *< dissection* *I* *occlusion*  
*AVF* *pseudoaneurysm*

The most common problems at the V3 level relate to trauma and dissection; they include occlusive lesions, arteriovenous fistulas, and pseudoaneurysms. Extracranial VA dissection occurs most



**Figure 100.4** V2 segment true aneurysm (arrow) in a patient with connective tissue disorder. Also note the left common right subclavian and right external carotid aneurysms.

commonly in the V3 segment because the artery is mobile and, therefore, vulnerable to mechanical injury. The first two cervical vertebrae are the most mobile of the spine, 50% of neck rotation occurs between C1 and C2. The VA is redundant at this level to allow the arc of displacement of the transverse process of the atlas (80 degrees), to which the VA is attached. Clinically, extracranial vertebral dissection may present with severe occipitocervical neck pain with associated dizziness, vertigo, double vision, ataxia, and dysarthria.<sup>14</sup> Dissection may be associated with fibromuscular dysplasia; but can also occur in a normal artery after seemingly trivial trauma (Fig. 100.5). VA dissection often follows neck hyperextension or rotation and has been associated with practicing yoga, painting a ceiling, coughing, vomiting,



**Figure 100.5** Intramural dissection of the vertebral artery at the V3 segment in a 40-year-old woman with Klippel–Feil syndrome and subluxation of the atlantoaxial joint.



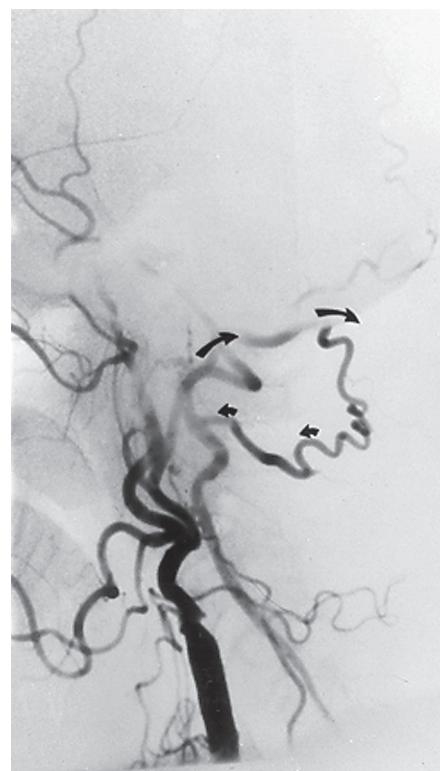
**Figure 100.6** Distal V2 segment pseudoaneurysm resulting from dissection.

sneezing, and cervical chiropractic manipulation.<sup>15,16</sup> Vertebral dissection is rare, with an incidence of 1 per 100,000, but it is a significant cause of stroke in a young and otherwise healthy population.<sup>17</sup> In one study, 62% of dissections observed serially with angiography completely resolved.<sup>18</sup> The remaining dissections went on to vessel occlusion, remained stenotic, or developed pseudoaneurysmal dilation and/or AV fistulas (Fig. 100.6). Half of the patients diagnosed with extracranial VA dissection will be asymptomatic, 21% will experience mild neurologic sequelae, 25% will suffer moderate to severe deficits, and 4% will die.<sup>19</sup> Notably, there appears to be no relationship between recanalization and neurologic outcome.<sup>20</sup>

An arteriovenous fistula results from rupture of the wall of the VA into its surrounding venous plexus. In long-standing fistulas, the pulsatile mass formed by the fistula and its dilated venous channels is called an arteriovenous aneurysm.

The VA may be compressed in the pars atlantica of the third segment between the occipital ridge and the arch of the atlas. In these patients, symptoms of low flow are usually precipitated by head extension or rotation. The V3 segment is rarely affected by significant atherosclerosis.

When the VA is occluded in the V1 or V2 segments, it usually reconstitutes at the V3 segment by collaterals from the external carotid via the occipital artery (Fig. 100.7) or collaterals from the ipsilateral subclavian artery via branches of the thyrocervical trunk (Fig. 100.8).<sup>21</sup> Because of this collateral network, the distal vertebral and basilar arteries usually remain patent despite a proximal VA occlusion. This finding is crucial for developing appropriate surgical strategy.



**Figure 100.7** The distal vertebral and basilar arteries being fed by an occipital artery collateral in a patient with proximal vertebral artery occlusion.



**Figure 100.8** The distal vertebral and basilar arteries fed by a thyrocervical trunk collateral in a patient with proximal vertebral artery occlusion.

## V4 Segment

Similar to the V3 segment, the fourth segment (V4) is infrequently affected by atherosclerosis. This segment is also prone to arteriovenous fistula formation and aneurysmal degeneration. Advanced atherosclerotic disease of the basilar artery is generally a contraindication to the reconstruction of VA lesions.

## PATIENT SELECTION FOR VERTEBRAL ARTERY RECONSTRUCTION

### Anatomic Considerations

The minimal anatomic requirement to justify VA reconstruction for hemodynamic symptoms would be greater than 60% stenosis in both VAs, if both are patent and complete or 60% stenosis in the dominant VA if the contralateral is hypoplastic, ends in a posteroinferior cerebellar artery, or is occluded. A single normal VA is typically sufficient to adequately perfuse the basilar artery regardless of the patency status of the contralateral VA. Unlike carotid artery disease, the mere presence of stenoses in an asymptomatic patient is not an indication for reconstruction.

### Etiologic Considerations

#### Low Flow

For patients with hemodynamic symptoms, it is essential to rule out systemic causes of ischemia before advising evaluation of the vertebrobasilar arteries as the etiology. In the later years

### BOX 100.2

#### Routine Testing for the Potential Diagnosis of Vertebrobasilar Ischemia

- Cardiology consultation
- Echocardiography
- Holter monitoring
- Medication review
- Serum electrolytes
- Neurology consultation
- Thyroid function tests
- Audiology/ear, nose, throat evaluation
- Magnetic resonance imaging

### BOX 100.3

#### Nonvascular and Cardiac Conditions that Cause or Mimic Vertebrobasilar Ischemia

- Cardiac arrhythmia
- Pacemaker malfunction
- Cardioemboli
- Labyrinthine dysfunction
- Tumors of the cerebellopontine angle
- Use of antihypertensive medications
- Cerebellar degeneration
- Myxedema
- Electrolyte imbalance
- Hypoglycemia

of life, VA stenosis is a frequent arteriographic finding and dizziness in the elderly is common. The presence of both cannot necessarily be assumed to have a cause–effect relationship. The indication for intervention in patients with hemodynamic symptoms depends on the ability to demonstrate insufficient blood flow to the basilar artery. Other common systemic causes of hemodynamic ischemia, include orthostatic hypotension, poorly regulated antihypertensive therapy, arrhythmias, heart failure, malfunction of pacemakers, and anemia.

#### Emolic

Patients who present with VBI secondary to embolization from lesions in vertebral or subclavian arteries should be considered for treatment regardless of the status of the contralateral artery. Surgical or endoluminal intervention is warranted if medical treatment fails. Surgical intervention is not indicated in asymptomatic patients' radiographic findings alone.

Patients who present with nonatherosclerotic lesions such as aneurysm, dissections, and fistulas may also be considered as potential candidates for VA reconstruction.

### Differential Diagnosis

Identification of patients who may benefit from VA reconstruction begins with exclusion of other causes of symptoms (Box 100.2). These other conditions include inappropriate antihypertensive medication use, cardiac arrhythmias, anemia, brain tumors, and benign vertiginous states. A thorough investigation must rule out these causes including inner ear pathology and internal carotid artery stenosis/occlusion (Box 100.3).

The evaluation should include assessment of the precise circumstances associated with symptom development. Any systemic mechanism that decreases the mean pressure of the basilar artery may be responsible for hemodynamic symptomatology, and affected individuals may or may not have concomitant vertebral artery stenosis or occlusion. Symptoms from orthostatic hypotension, a drop of 20 mm Hg in systolic pressure on rapid standing, often occurs in older individuals with poor sympathetic control of their venous tone. This causes excessive pooling of blood in the veins of the leg and resulting transient hypotension.

Because certain prescription medications can mimic VBI, patient medications require thorough review. In fact, excessive use of antihypertensive medications is the most common etiology of posterior circulation symptoms and can also cause hemodynamic posterior circulation ischemia by decreasing perfusion pressure, and inducing severe orthostatic hypotension.

A cardiac source is the second most common cause of VBI, especially in older adults; evaluation includes a 24-hour Holter monitor and echocardiography. Arrhythmias may cause symptoms as a result of decreased cardiac output. In addition, transesophageal echocardiography may be useful in patients with a suspected embolic mechanism to rule out a cardiac source.

In patients with a combination of orthostatic hypotension and occlusive lesions, the hemodynamic problem may not respond to medical treatment; in such cases reconstruction of a diseased VA is indicated.

Investigation must also exclude inner ear pathology, including rare tumors of the cerebellopontine angle, and other benign vertiginous states.

When patients present with a combination of anterior and posterior hemispheric symptoms, investigation of the great vessels and the carotid circulation is warranted. Significant great vessel or carotid occlusive lesions may warrant reconstruction to alleviate symptoms.

An important aspect of the history is identifying triggering events, such as positional or postural changes. This is followed by a thorough physical examination, which includes palpation, auscultation, pulse examination, and comparative arm blood pressures (recumbent and standing). Physical examination can alert the physician to the possibility of subclavian steal in patients with differences in brachial blood pressure greater than 25 mm Hg or with diminished or absent pulses in one arm. The diagnosis of reversal of vertebral artery flow can be made accurately by noninvasive indirect methods and demonstrated directly by duplex imaging of the reversal of flow in the VA.

Patients may relate their symptoms to turning or extending the head. These dynamic symptoms usually appear on turning the head to one side and are caused by extrinsic compression.<sup>11</sup> To differentiate this from dizziness or vertigo secondary to labyrinthine disorders that appear with head or body rotation, the patient should attempt to reproduce the symptoms by first turning the head *slowly* and then repeating the maneuver *briskly*, as in shaking the head from side to side. In labyrinthine disease, the sudden inertial changes caused by the latter (brisk) maneuver result in immediate symptoms and nystagmus. Conversely, with extrinsic vertebral artery compression, a short delay occurs before imbalance develops.

## Diagnostic Testing

Once a suspicion of VBI has been entertained, only a few diagnostic tests are available.

### Duplex Ultrasonography

Although duplex ultrasound is excellent for detecting lesions in the carotid artery, it has significant limitations with VA pathology. Direct visualization of the second portion of the vessel is difficult because of its intraosseous course through the transverse processes of C2 to C6. The usefulness of duplex ultrasound lies in its ability to confirm reversal of flow within the VA and detect changes in flow velocity consistent with a proximal stenosis.<sup>22</sup> In addition, ultrasound imaging can diagnose pathology of the great vessels and confirm subclavian steal.

### Computed Tomography and Magnetic Resonance Imaging

MRI is another modality that provides a safe, noninvasive, detailed evaluation of both the extracranial and intracranial vasculature as well as structures within the posterior fossa. Contrast-enhanced magnetic resonance angiography (MRA) with three-dimensional reconstruction and maximum image intensity techniques provides full imaging of the vessels, including the supra-aortic trunks and the carotid and VA (see Fig. 100.3). MRA can also diagnose VA flow reversal.

Transaxial MRI can readily diagnose both acute and chronic posterior fossa infarcts. Brain stem infarctions are often missed by CT because they tend to be small and the CT resolution in the brain stem is poor. In patients who are candidates for VA reconstruction, brain MRI is performed preoperatively to ascertain whether infarctions have taken place in the vertebrobasilar territory. Transaxial MRI is particularly important in patients suspected of having suffered embolic infarction in the posterior circulation.

CT angiography can readily identify occlusive lesions and has the advantage of being able to demonstrate significant osteophytic lesions that may impinge on vertebral flow.

### Arteriography

Despite the technologic advances in MRI and CT evaluation, selective subclavian and vertebral angiography remains the best imaging modality for preoperative evaluation of patients with VBI. Some consider angiography mandatory before endovascular intervention or surgical reconstruction. Arteriographic investigation necessitates systematic positions and projections to evaluate the vertebrobasilar system from its origin to the top of the basilar artery. This begins with an arch view, which determines the presence/absence of a VA on each side, VA dominance, and aberrant vessel anatomy. The most common anomalous origin is the left VA originating from the aortic arch in 6% of individuals. A much rarer variant is the right VA, arising from the innominate or right common carotid artery, most often in patients with aberrant retroesophageal right subclavian artery. Arch views must be obtained in at least two projections: right and left posterior oblique views. The most common site of disease, the VA origin, may not be well imaged

with ultrasound or MRA and can often be displayed only with oblique projections, not part of the standard aortic arch evaluation. An origin stenosis may be missed in standard views because of superimposition of the subclavian artery. Additional oblique projections may be needed to displace the subclavian artery to obtain a clear view of the VA origin. The presence of poststenotic dilation in the first centimeter of the VA suggests a significant origin stenosis. Visualization of the second segment (V2) is accomplished in the oblique arch views in conjunction with selective subclavian injections. An effort should be made to attempt to angiographically identify the point of entry of the VA into the transverse processes. An abnormally low entry at C7 instead of C6 is associated with a short V1 segment, which can create challenges for reconstruction at the V1 level.

Patients with suspected VA compression should undergo dynamic angiography, with provocative positioning. Arteriography is required to demonstrate extrinsic dynamic compression of the VA. This is performed either with the patient sitting up, with bilateral brachial injections, or, if transfemoral approach is used, in Trendelenburg position with the head resting against a block. These positions mimic the effects of the weight of the head on the spine, which changes its curvature and decreases the distance between C1 and C7. This longitudinal compression often enhances the extrinsic compression effects caused by osteophytic spurs. In these positions, images should be obtained with extension or rotation provoking symptoms.<sup>23</sup> The VA may be normal in one position and occluded by extrinsic compression in the other (Fig. 100.9). Finally, delayed imaging should be performed to demonstrate reconstitution of the

extracranial VA through cervical collaterals. Delayed views are of the utmost importance in identifying a patent V3 segment, which can be exploited as a distal target for revascularization. Finally, the basilar artery should be seen clearly in a lateral projection. Subtracted views are needed to eliminate the temporal bone density. In the Towne anteroposterior view, routinely used in neuroradiology, the basilar artery is foreshortened and therefore the resolution is poor.

## VERTEBRAL ARTERY RECONSTRUCTIVE PROCEDURES

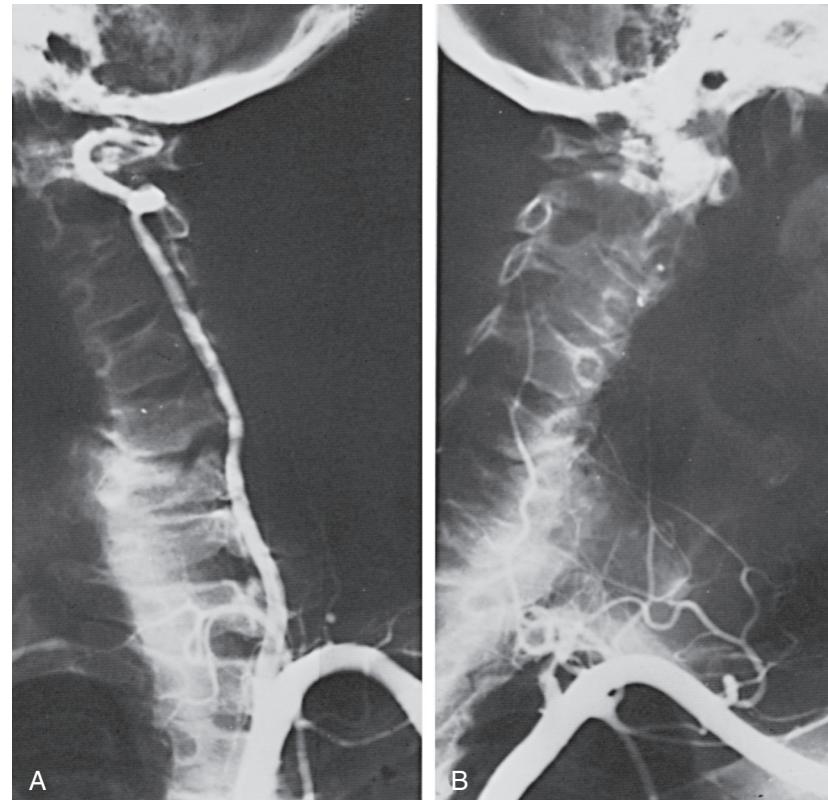
Accumulated experience has shown that with appropriate surgical intervention, predictable resolution of hemodynamic symptoms and cessation of embolic events can occur.

### Disease Location

The location of disease will dictate the type of surgical reconstruction. With rare exceptions, most VA reconstructions are performed to relieve an ostial stenosis (V1 segment) or stenoses, dissection, or occlusion of its intraspinal component (V2 and V3 segments).<sup>24</sup>

### V1 Segment

Several operations are described for treating V1 ostial lesions.<sup>25,26</sup> Transposition of the proximal VA to the carotid artery is most common. Alternately, bypass using saphenous



**Figure 100.9** A patient with a single vertebral artery showing minimal extrinsic compression (A) when the neck is rotated to the right and occlusion (B) when the neck is rotated to the left. (From Berguer R. Surgical management of the vertebral artery. In: Moore WS, ed. *Surgery for Cerebrovascular Disease*. New York: Churchill Livingstone; 1986.)

vein can be performed from either common carotid artery or subclavian artery.<sup>27,28</sup> Lastly, subclavian–vertebral artery endarterectomy can be performed, but is fraught with technical challenges.

### V2 Segment

Although the V2 segment is the site of a wide variety of pathologic conditions, it is rarely accessed surgically due to its interosseous position. The most common indication for exposure is hemorrhage, which, when untreatable endoluminally, is best managed by proximal and distal ligation. After complete V2 occlusion, patency of the distal extracranial segment is often maintained by collaterals from the external carotid or subclavian artery. Ligation at C1–C2 level and bypass to the V3 segment may be indicated for embolizing V2 pathology.

### V3 Segment

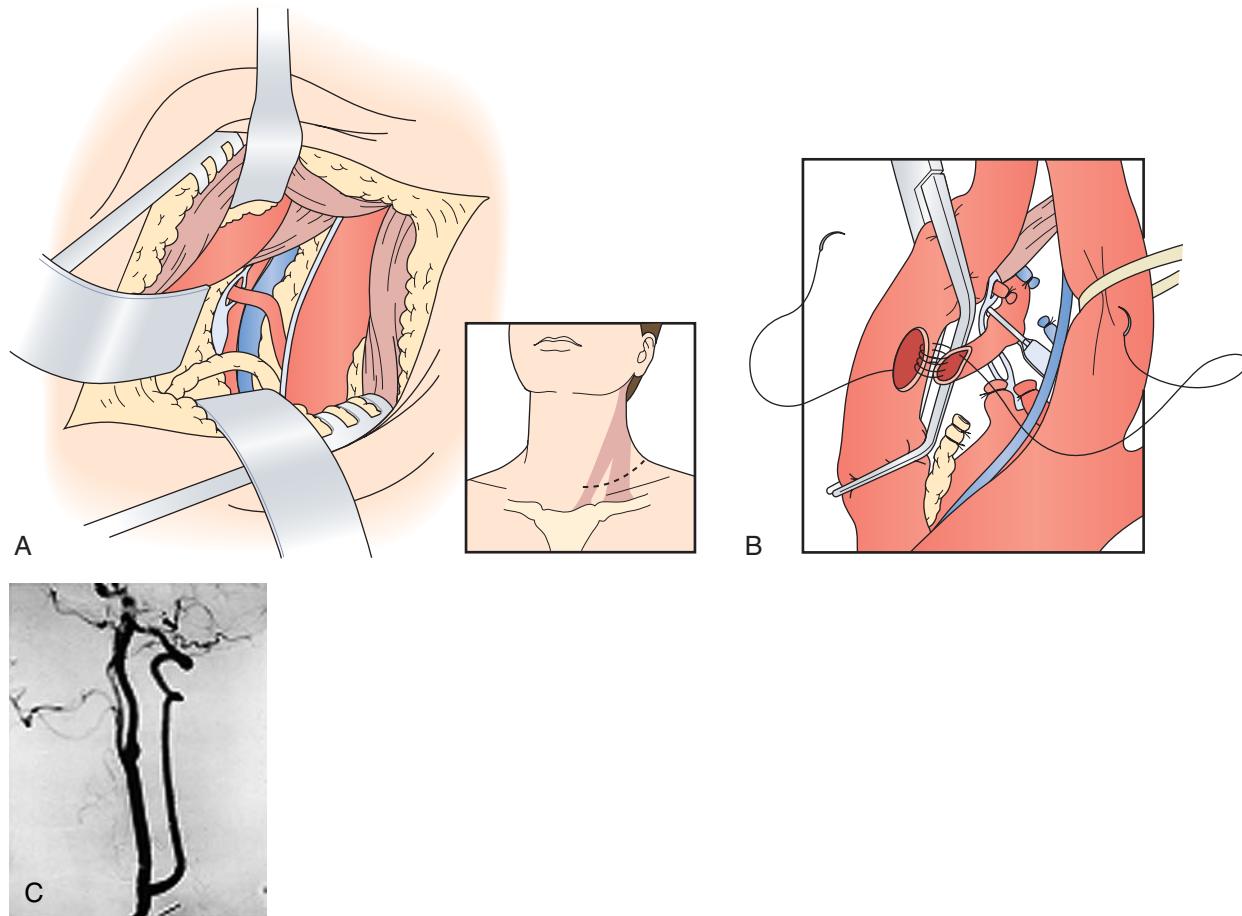
Reconstruction of the V3 segment is usually performed with saphenous vein bypass from the common carotid, subclavian, or proximal VA.<sup>21,25</sup> Alternatively, radial artery can be used as a conduit. Transposition of the external carotid or hypertrophied occipital artery into the distal VA, or transposition of the distal VA into the internal carotid artery, has also been described.

### Suboccipital Segment

For more distal pathology, the VA can also be accessed surgically above the level of the transverse process of C1. Surgical exposure at the suboccipital segment requires resection of the C1 transverse process and part of its posterior arch. Reconstruction at this level is limited to saphenous vein bypass from the distal internal carotid artery. Bypasses above the level of C1 (suboccipital) are technically demanding and are rarely required.

### Transposition of the Proximal Vertebral Artery into the Common Carotid Artery

The approach to the proximal VA is the same as for subclavian-to-carotid transposition (see Ch. 57, Cerebrovascular Exposure). The incision is placed transversely one fingerbreadth above the clavicle and directly over the two heads of the sternocleidomastoid muscle (Fig. 100.10). Subplatysmal skin flaps are created to provide adequate exposure. Dissection is carried down directly between the two bellies of the sternocleidomastoid, and the omohyoid muscle is divided. The internal jugular vein is retracted laterally and the carotid sheath entered. The



**Figure 100.10** (A) Access to the proximal vertebral artery between the sternocleidomastoid muscle bellies. (B) Transposition of the proximal vertebral artery to the posterior wall of the common carotid artery. (C) Proximal vertebral-to-common carotid transposition. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)

carotid artery should be exposed proximally as far as possible, which is facilitated if the surgeon temporarily stands at the head of the patient and looks down into the mediastinum. The vagus nerve should be left with the common carotid to prevent traction injury from lateral displacement.

After the carotid artery has been mobilized, the sympathetic chain is identified running behind and parallel to it. On the left side, the thoracic duct is divided with ligatures. Accessory lymph ducts – often seen on the right side – are also ligated and divided. The entire dissection is medial to the prescalene fat pad that covers the scalenus anticus muscle and phrenic nerve.

The vertebral vein is next identified emerging from the angle formed by the longus colli and scalenus anticus and overlying the VA and, at the bottom of the field, the subclavian artery. The vein is ligated in continuity and divided. Below the vertebral vein lies the VA. It is important to identify and avoid injury to the adjacent sympathetic chain. The VA is dissected superiorly to the tendon of the longus colli and inferiorly to its origin from the subclavian artery. The VA is freed from the sympathetic trunk. Preserving the sympathetic trunks and the stellate or intermediate ganglia resting on the artery usually requires freeing the VA from these structures, and after dividing its origin, the latter is transposed anterior to the sympathetics.

Once the artery is fully exposed, an appropriate site for reimplantation in the common carotid artery is selected. The patient is given heparin systemically. The distal portion of the V1 segment is clamped below the edge of the longus colli with a microclip placed vertically to indicate the orientation of the artery and to avoid axial twisting during its transposition. The proximal VA is oversewn with 5-0 polypropylene suture immediately above the stenosis. The artery is divided at this level and brought to the common carotid artery; its free end is spatulated for anastomosis.

After cross-clamping the carotid artery, an elliptical 5- to 7-mm arteriotomy is created posterolaterally with an aortic punch. The anastomosis is performed with continuous 6-0 or 7-0 polypropylene suture while avoiding tension on the fragile VA. Before completion, standard flushing maneuvers are performed, and the suture is tied to reestablish flow (Fig. 100.10C).

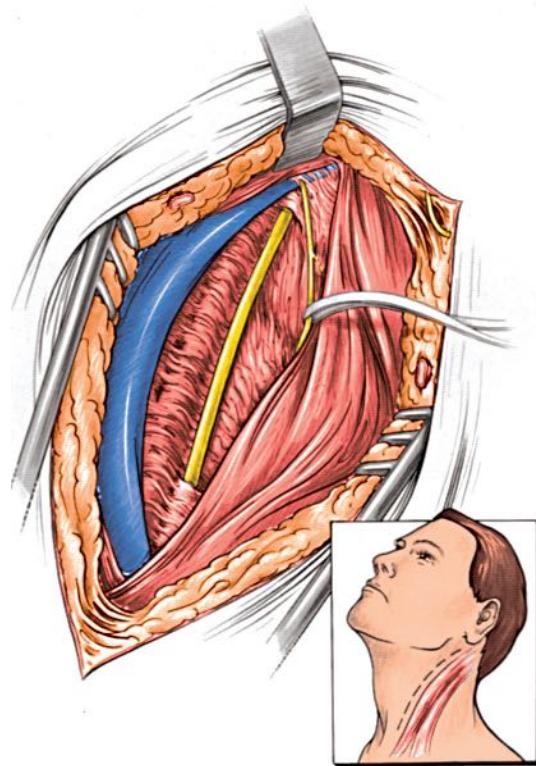
When simultaneous carotid endarterectomy is planned, the VA is approached through the standard carotid incision extended inferiorly to the head of the clavicle. With this approach, the sternocleidomastoid muscle is lateral and the field is narrower.<sup>29</sup>

### Distal Vertebral Artery Reconstruction

#### Common Carotid–Vertebral Artery Bypass

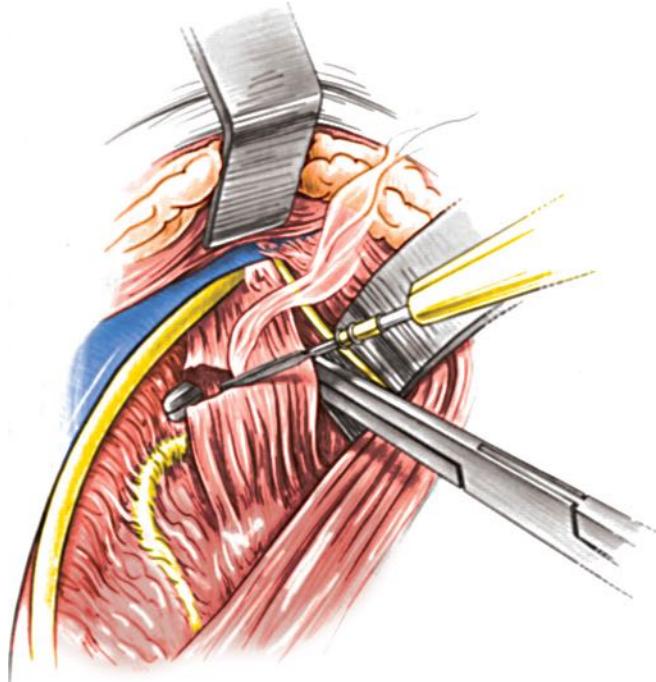
Reconstruction of the distal VA is generally done at the C1–C2 level. Rarely, the reconstruction is done between C1 and the base of the skull via a posterior approach. Although various techniques can be applied to revascularize the VA in its V3 segment (between the transverse processes of C1 and C2), the approach is the same for all procedures.<sup>21,30</sup>

The incision is made anterior to the sternocleidomastoid muscle, the same as for a carotid operation, and is carried superiorly to immediately below the earlobe (Fig. 100.11). The

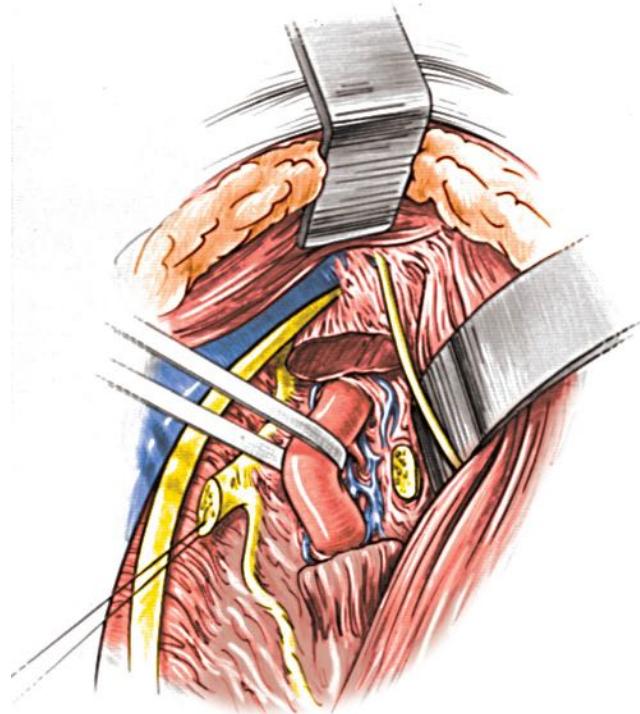


**Figure 100.11** Retrojugular approach and isolation of the spinal accessory nerve. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)

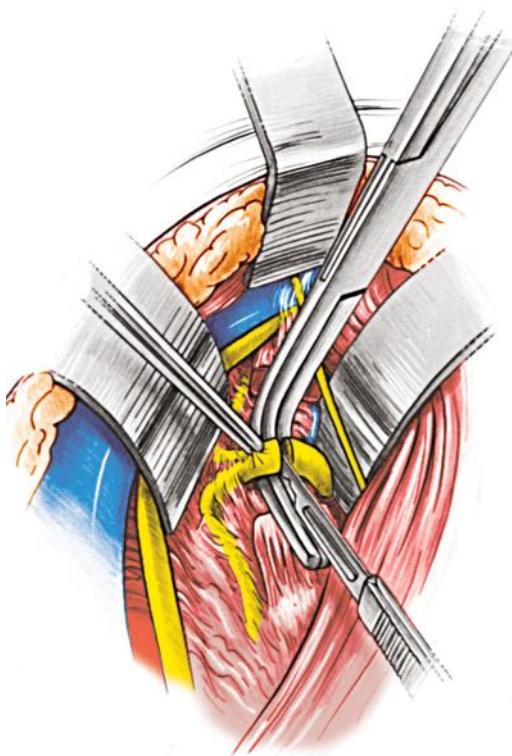
dissection proceeds between the internal jugular vein and the anterior edge of the sternocleidomastoid to expose the spinal accessory nerve. The nerve is followed cranially as it crosses in front of the transverse process of C1, which can easily be felt by the operator's finger. The levator scapulae muscle is identified by removal of the overlying fibrofatty tissue. With the anterior edge of the levator scapulae identified, the anterior ramus of C2 is identified. The levator scapulae is transected from its origin on the C1 transverse process (Fig. 100.12). The C2 ramus divides into three branches after crossing the VA. The artery runs below, in contact with the nerve and perpendicular to it. The ramus is cut (Fig. 100.13) before its branching; underneath it, the VA can be identified. A small minority of patients may develop noticeable but self-limiting posterior scalp numbness as a result of cutting the ramus. The artery is freed from the surrounding veins with care, as venous bleeding is difficult to control at this level. Before encircling the artery with fine silicone vessel loops (Fig. 100.14), one must ensure that a branch from the occipital collateral artery does not enter the posterior aspect of the VA at this location. Tearing of this collateral vessel complicates preparation of the vessel. Once the VA has been encircled, the distal common carotid artery is dissected and prepared to receive a saphenous vein graft. There is no need to dissect the carotid bifurcation. The location selected for the proximal anastomosis of the saphenous vein graft on the common carotid artery should not be too close to the bifurcation, because cross-clamping at this level may fracture underlying atheroma.



**Figure 100.12** Dividing the levator scapulae over the C2 ramus. The vagus, internal jugular vein, and internal carotid artery are anterior to the muscle. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)



**Figure 100.14** After the vertebral venous plexus is dissected away, the vertebral artery is slung with a polymeric silicone (Silastic) loop for clamping and anastomosis. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)



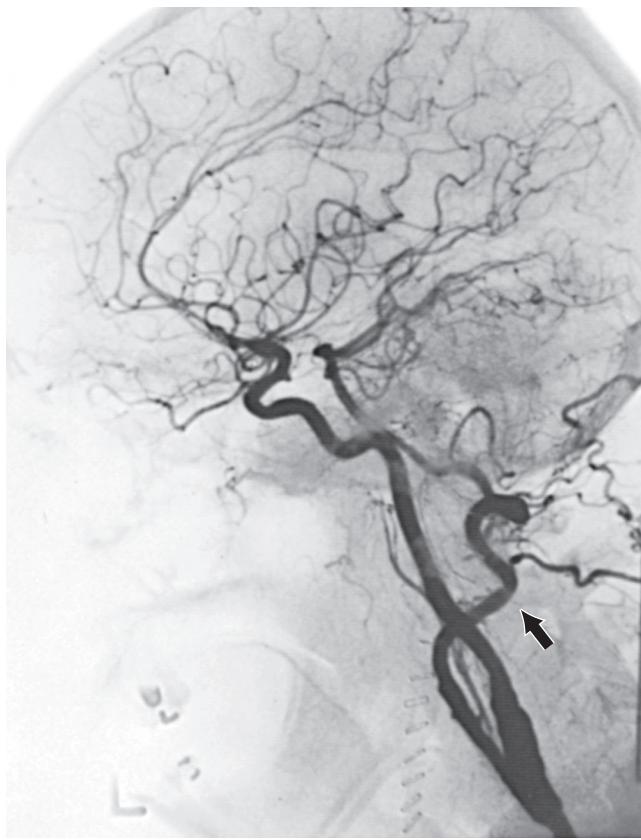
**Figure 100.13** Dividing the anterior ramus of C2 to expose the underlying vertebral artery running perpendicular to the anterior ramus. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)

A saphenous vein graft or other suitable conduit is prepared. A valveless segment facilitates back bleeding of the VA after completion of the distal anastomosis. The patient is given intravenous heparin. The VA is elevated by gently pulling the loop and is occluded with a small J-clamp to isolate this segment for an end-to-side anastomosis. The VA is opened longitudinally with a coronary scalpel for a length adequate to accommodate the spatulated vein. End-to-side anastomosis is performed with continuous 7-0 polypropylene. The distal anastomosis is assessed for backflow, and if satisfactory, a small clamp is placed on the vein graft proximal to the anastomosis and the J-clamp removed to restore flow through the VA.

The graft is passed beneath the jugular vein. The common carotid artery is then cross-clamped, an elliptical arteriotomy is made in its posterior wall with an aortic punch, and the proximal vein graft anastomosed end to side with continuous 6-0 polypropylene. Before the anastomosis is completed, standard flushing maneuvers are performed. Next, the VA is occluded with a clip immediately below the anastomosis to functionally create an end-to-end configuration. In the absence of suitable common carotid artery, the ipsilateral subclavian artery can be used.

#### Alternative Options for V3 Reconstruction

The distal VA may also be revascularized via the external carotid artery (ECA), either directly by means of transposition of the ECA to the distal VA or by bypass graft to the ECA



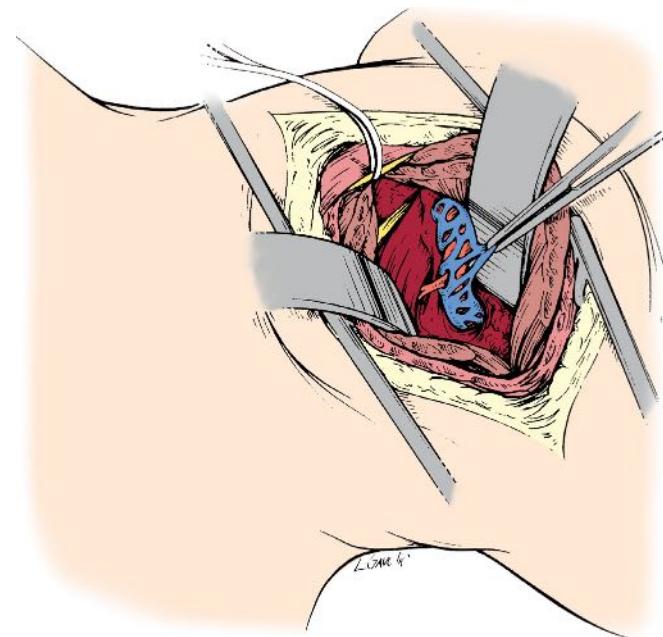
**Figure 100.15** Arteriogram of a transposition of the external carotid artery to the distal vertebral artery. This patient had previously undergone internal carotid endarterectomy. (From Berguer R, Kieffer E. *Surgery of the Arteries to the Head*. New York: Springer-Verlag; 1992.)

(Fig. 100.15). Another method of revascularization of the distal VA is transposition of this vessel into the distal cervical internal carotid artery below the transverse process of C1. This technique is particularly applicable for patients with inadequate saphenous vein or those in whom the ECA cannot be used because of unsuitable anatomy.

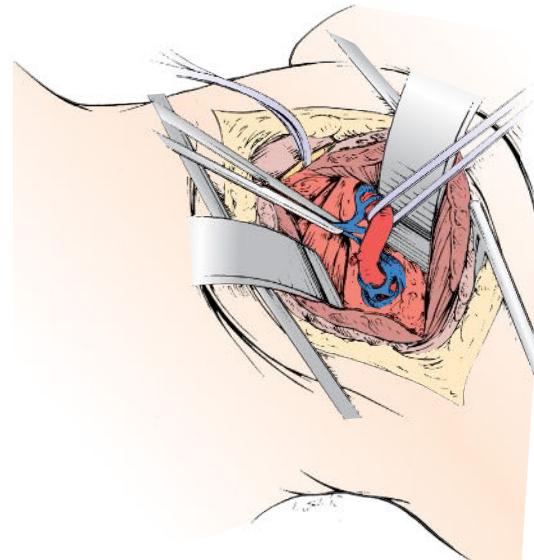
A small number of patients have disease that extends up to the level of C1 and require revascularization in the most distal segment of the extracranial VA.<sup>31–33</sup> To accomplish this, the VA must be exposed in its pars atlantica, where the artery runs parallel to the lamina of the atlas before entering the foramen magnum.

#### Posterior Suboccipital Vertebral Artery Bypass

For more distal pathology, the VA can also be accessed surgically above the level of the transverse process of C1. Surgical exposure at the suboccipital segment requires resection of the C1 transverse process and part of its posterior arch. Reconstruction at this level is limited to saphenous vein bypass from the distal internal carotid artery. Bypasses above the level of C1 (suboccipital) are technically demanding and rare. To accomplish this, the vertebral artery must be exposed in its pars atlantica, where the artery runs parallel to the lamina of the atlas before entering the foramen magnum (Figs. 100.16 and 100.17).



**Figure 100.16** The pars atlantica of the distal vertebral artery exposed and surrounded by a dense venous plexus.



**Figure 100.17** Exposure of the pars atlantica of the vertebral artery from its exit from the transverse foramen of C1 to its entrance into the dura mater.

## OPERATIVE RESULTS

### Perioperative Outcomes

Perioperative complication rates differ for proximal versus distal reconstruction. Perioperative complications that can follow any reconstruction include stroke, bleeding, thrombosis, and nerve injury. Intraoperative completion imaging with digital angiography is useful and should be considered for all types of VA reconstruction. Reparable technical flaws may be identified, and repair can prevent reconstruction failure.

### Proximal Reconstructions

The technically easier proximal operations have been reported to have a combined stroke and death rate of 0.9%.<sup>22</sup> Among patients undergoing proximal operations in one report, no deaths or strokes occurred in those who underwent only a vertebral reconstruction. When proximal VA reconstruction is combined with a carotid operation, the observed stroke and death rates increase to 5.7%.<sup>22</sup> Berguer et al.<sup>22</sup> reported four instances of immediate postoperative thrombosis (1.4%). Three of the four patients had vein grafts interposed between the VA and the common carotid because of a short V1 segment. The grafts kinked and thrombosed. Other complications that are particular to proximal reconstruction include vagus and recurrent laryngeal nerve palsy (2%), Horner's syndrome (8.4%–28%), lymphocele (4%), and chylothorax (0.5%).

### Distal Reconstructions

Operations on the distal VA carry higher stroke and death rates. These have a combined stroke and death rate of 3%.<sup>34</sup> The immediate graft thrombosis rate is 8%, and spinal accessory nerve injury occurs in 2% of patients.<sup>35</sup>

### Long-Term Outcomes

Results after both proximal and distal VA reconstruction are generally equal to or better than those reported in series reviewing other forms of extracranial cerebrovascular reconstruction.<sup>34,36</sup> After proximal vertebral-to-common carotid transposition, patency rates at 5 and 10 years equal or exceed 95% and 91%, respectively. When selected appropriately, more than 80% of patients have relief of their symptoms after proximal surgical reconstruction.<sup>36</sup>

For distal bypass reconstruction, patency rates of 87% and 82% should be expected at 5 and 10 years.<sup>34,36</sup> Seventy percent of patients undergoing distal VA reconstruction are dead at 5 years, mostly from cardiac disease, whereas 97% of survivors are stroke free. Symptoms are expected to be cured in 71% of patients and improved in an additional 16%.<sup>34,36</sup>

Predictably, in patients treated for severe hemodynamic symptoms who also suffer from compensatory high blood pressure, appropriate reconstruction and reperfusion of the brain stem results in significant improvement in their hypertension.

## ENDOVASCULAR THERAPY

Over the last two decades, a growing number of case reports and small nonrandomized case series suggest that endovascular intervention may be safe and technically feasible.<sup>37–48</sup> Endovascular access to the VA is relatively straightforward. Patients are pretreated with dual-therapy aspirin and clopidogrel. The procedure can be performed under local anesthesia, enabling continuous neurologic monitoring. Most cases are performed from a femoral approach (93%), although transbrachial (3%) and transradial (5%) are gaining traction.<sup>49</sup> The stenotic lesions are crossed and treated with 0.014- or 0.018-in systems

and small coronary-diameter balloons and stents. Procedures can be performed with or without the assistance of embolic protection, although vertebral arteries are usually too small to accommodate most distal protection devices. One large review found distal protection used in only 2% of cases.<sup>49</sup>

Periprocedural risks include access complications, distal embolization and stroke, arterial rupture, stent malposition and vessel thrombosis or dissection. Later, restenosis and stent fracture are not uncommon.

Overall, retrospective reviews suggest that endoluminal vertebral artery intervention is reasonably safe, although a selection bias exists. A 2005 Cochrane review identified 313 interventions for VA stenosis, with just over half using stent placement as part of the treatment. The technical success rate was 95%, and the 30-day stroke and death rate was 6.4%.<sup>50</sup> The Cochrane group concluded that although angioplasty with stenting for VA stenosis is technically feasible, evidence is currently insufficient to support its routine application.

A subset of 16 patients treated within the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS 2001) represents the only report of a randomized controlled trial comparing endoluminal therapy with best medical care for symptomatic vertebral stenosis. No 30-day strokes or deaths occurred in either group, although two of eight patients who underwent endoluminal therapy experienced transient ischemic symptoms. Furthermore, with a mean follow-up of 4.5 years, no posterior circulation strokes were noted in either group.

Despite high technical success rates, VA angioplasty alone, especially when used for the treatment of disease at the origin of the vessel, appears to have an unacceptably high rate of restenosis. Adjuvant stent placement seems to add to clinical durability, although stents carry inherent morbidity of their own, such as malposition and potential stent fracture. In their series of 105 patients who underwent endovascular stenting for symptomatic VA disease, Jenkins et al. achieved 100% radiographic improvement (residual stenosis ≤30%). The authors reported an immediate (30-day) periprocedural risk of death of 1% and periprocedural complication rate of 4.8%. Complications included transient ischemic attack, flow-limiting dissection, hematoma, and access-site problems. At 1 year of follow-up, six patients had died and five had experienced a vertebrobasilar stroke; at approximately 2.5 years of follow-up, 70% of patients remained symptom-free, but 13% had restenosis requiring retreatment.<sup>51</sup>

In the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA) trial, 18 patients with extracranial VA disease underwent angioplasty and stenting. Technical success (determined as less than 50% residual stenosis following treatment) was achieved in 17 (94%) of the 18 patients. No periprocedural neurologic complications were observed. The investigators reported 6-month restenosis rates of 50%, with 39% symptomatic.<sup>52</sup>

A recent systematic review of the available literature noted a weighted mean technical success rate of 97%. The authors estimated the mean periprocedural stroke and death rate from

combined angioplasty and stenting to be approximately 1.1%. Transient ischemic events occurred in 1.5% of patients. Recurrent symptoms occurred in 8% of patients within a reported follow-up range of 6 to 54 months, and greater than 50% restenosis developed in 23% of the subset of patients who underwent follow-up imaging.<sup>49</sup>

Late stent fracture with concomitant in-stent restenosis may be a problem plaguing endoluminal therapies that target lesions at the VA origin. Anatomically, the VA takes origin from the subclavian artery at a near right angle. In addition, the first portion of the subclavian artery has relative mobility, whereas the VA becomes fixed as it passes into the transverse foramen of C6. This particular anatomy may create unique mechanical forces that make stent fracture more likely than it is for other parts of the body.

The use of drug-eluting stents to impede neointimal hyperplasia and prevent restenosis has been well established in the coronary arteries and may be beneficial in the treatment of vertebral disease.<sup>53</sup> Ogilvy et al. reported a series of patients with the longest follow-up thus far (21 months); for these patients, drug-eluting stents were used in stenosis of VA origin. The authors found that the incidence of in-stent restenosis (>50% diameter) decreased from 38% in patients who received non-drug-eluting stents to 17% in those who received drug-eluting stents.<sup>54</sup> Other reports also suggest decreased restenosis rates with drug-eluting stents; however, many have mean patient follow-up times of less than 1 year.<sup>55,56</sup> Treatment with drug-eluting stents requires long-term dual antiplatelet therapy. It remains unclear whether differing stent makeup will have a significant impact in the outcomes of patients who undergo interventions of the VA.

With the exception of the small subset of patients from CAVATAS 2001, only retrospective case series exist for endoluminal therapies for the treatment of VA disease, as with open surgical techniques. Currently no level I data support the routine application of angioplasty and stenting of the VA over best medical therapy. The multicenter, randomized Vertebral Artery Stenting Trial (VAST), which was designed to prospectively analyze the impact of percutaneous vertebral interventions over medical therapy for stenting of intracranial or extracranial vertebral artery stenosis, was stopped due to regulatory requirements but after enrolling 115 subjects the authors were able to conclude that stenting of symptomatic VA stenosis is associated with a major

periprocedural vascular complication in about one in 20 patients and that the risk of recurrent vertebrobasilar stroke under best medical treatment alone was low, questioning the need for and feasibility of a phase 3 trial.<sup>57</sup>

## CONCLUSION

Surgical or endovascular reconstruction of the VA is often a viable option and should be considered in symptomatic patients with appropriate atherosclerotic lesions or other vasculopathy in whom medical therapy has failed. Open techniques for revascularization of the VA have proven clinical durability and acceptable surgical morbidity in experienced hands. Endoluminal techniques, which have gained momentum over the past decade, have shown clinical feasibility but have yet to deliver on durability benchmarks set by open surgical revascularization. For each individual patient who suffers from medically refractive VBI, practitioners must carefully balance the risks of surgery versus the limitations of endoluminal intervention before recommending intervention.

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A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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# Brachiocephalic Artery Disease: Surgical Treatment

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Based on a previous edition chapter by Kristofer M. Charlton-Ouw, Wande B. Pratt,  
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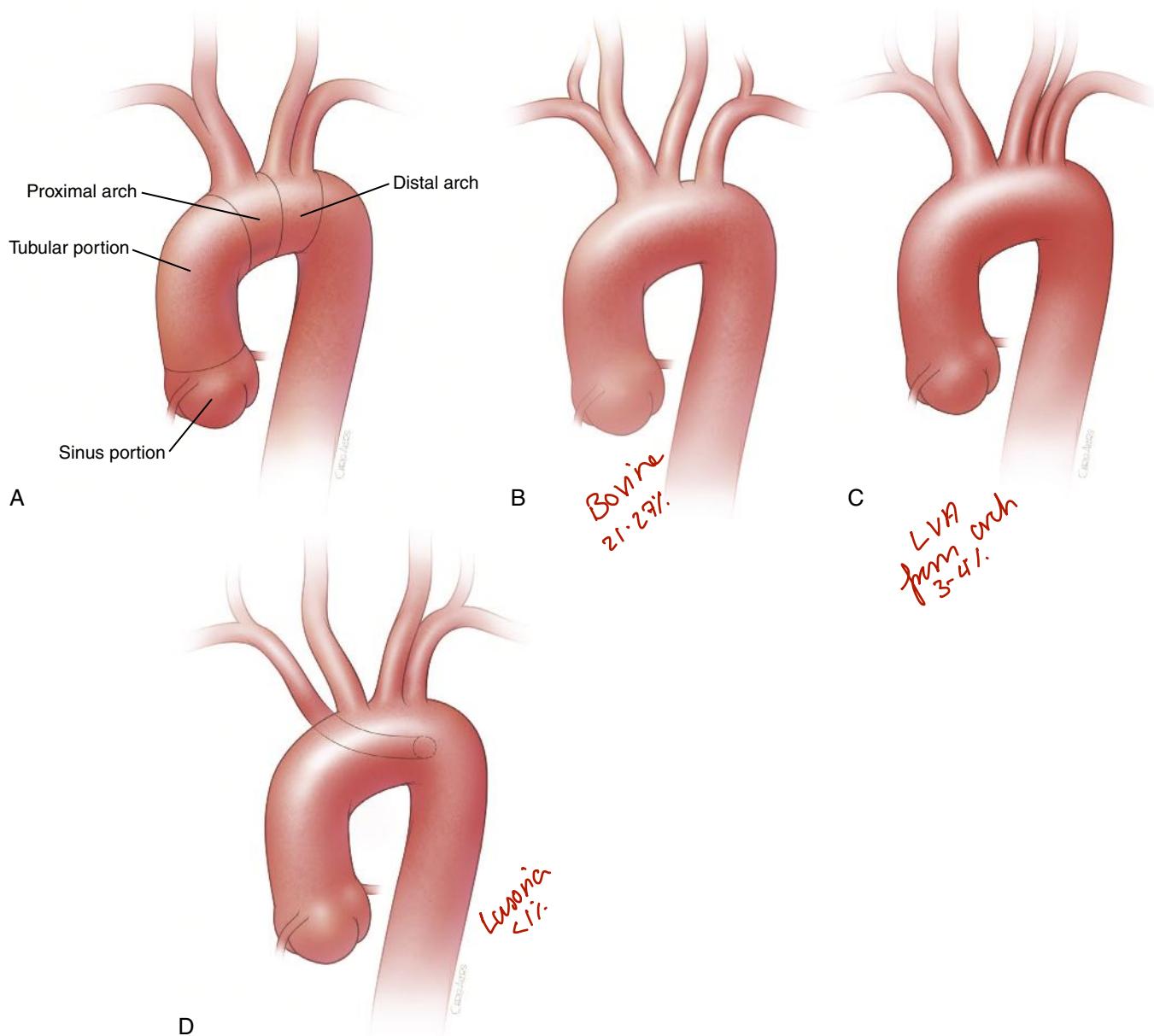
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## INTRODUCTION

The brachiocephalic arteries constitute the **aortic arch branches**, including the innominate, left common carotid (LCCA), and left subclavian arteries (LSCA), also known as the **supra-aortic trunks (SAT)** or great vessels. SAT disease is predominantly **atherosclerosis with steno-occlusive lesions**. **Aneurysms**, arterial **dissection**, isolated or extending from the aortic arch, **arteriopathies**, radiation changes, and **traumatic injury** can occur. These may lead to **upper extremity ischemia** such as **claudication** or **thromboembolism**, and **neurologic ischemia** including **stroke**, **transient ischemic attack**, and **vertebrobasilar subclavian steal**. Neurologic symptoms may be related to **thromboembolism**, or, in the case of multi-vessel disease, **global ischemia**. In those with internal mammary coronary grafts, **coronary steal** may occur. Rarely, compressive or inflammatory symptoms such as hoarseness, dysphagia, dyspnea, or cough may develop. This chapter discusses open reconstruction for SAT disease.

## ANATOMIC VARIANTS

The “normal” arch is a left-sided arch with distinct origins of the innominate artery, LCCA, and LSCA, present in 70%–75%<sup>1–5</sup> (Fig. 101.1). A **common shared origin** of the innominate and LCCA, “bovine arch,” is the most common variant, seen in 21%–27% of individuals. The **left vertebral artery** originates directly from the arch in 3%–4% of individuals.<sup>1–5</sup> An **aberrant right subclavian artery (ARSA)**, originating posterior and distal to the LSCA, occurs in 0.8%–1% of the population. It is due to abnormal involution of the 4th aortic arch and persistence of right dorsal aorta fusing with the right 7th intersegmental artery, and is more common in women.<sup>6,7</sup> A variety of rare patterns constitute the remaining variants.<sup>4</sup> Ethnic differences are reported with less variation in published series from Asia and the bovine pattern is more frequently seen in Africa and South America.<sup>5,8,9</sup> Links between aortic arch pathology and anomalous brachiocephalic branching is suspected.<sup>10</sup> Recognition of anatomic variants is important in assessing and treating patients with SAT disease.



**Figure 101.1** Normal and Variant Aortic Arch Anatomy. (A) The normal aortic arch consists of three separate innominate artery, left common carotid artery and left subclavian artery origins in 70%–75% of individuals. (B) The most common variant is the mis-named “bovine” configuration in which the left common carotid artery arises with or from the innominate artery. This is present in 21%–27%. (C) The next most common variant involves the left vertebral artery originating directly from the aortic arch in 3%–4%. (D) An aberrant right subclavian artery, originating distal and posterior to the left subclavian is found in up to 1% of human aortic arches.

## DIAGNOSTIC EVALUATION

When symptoms suggest SAT disease, comprehensive physical examination including carotid and upper extremity pulse assessment and bilateral arm pressures should be performed. Carotid duplex ultrasound may identify elevated velocity flow, parvus–tardus waveforms, reversal of vertebral flow, or concurrent carotid disease<sup>11,12</sup> (see Ch. 22, Vascular Laboratory: Arterial Duplex Scanning). Upper extremity noninvasive studies including pulse volume recordings and segmental pressures help appreciate the degree of central flow reduction.

Axial imaging is key to visualizing the aorta and SAT. CTA and MRA have replaced conventional aortography for diagnosis.<sup>13,14</sup> Aortography and selective arteriography are now largely utilized for endovascular intervention, but may still occasionally serve for disease definition. Body habitus, claustrophobia, metallic implants and renal disease limit or alter use of CTA and MRA. MRA signals drop out at slower flow rates, in areas of complex flow patterns, or with movement, overestimating stenosis. MR also allows for important brain imaging (see Ch. 30, Magnetic Resonance Imaging and Arteriography). CTA is usually completed more rapidly but can be limited by dense

lesion calcification, which is common. Vessel wall and lesion characteristics are better appreciated on CTA. It is particularly helpful in assessing ascending aortic and SAT quality for anatomic or extra-anatomic reconstruction suitability (see Ch. 29, Computed Tomography). Transesophageal echocardiography (TEE) or intraoperative epi-aortic ultrasound may be of value in characterizing the aorta for clamping.

## INDICATIONS FOR REVASCULARIZATION

### Occlusive Disease

Atherosclerosis, although the most common SAT pathology, is infrequently encountered clinically, accounting for <9% of cerebrovascular lesions.<sup>15</sup> Aortic arch branch vessels account for <5% of cerebrovascular operations.<sup>16,17</sup> The subclavian arteries develop significant disease more frequently than the innominate or LCCA. Hemodynamic patterns and shear stress changes in the arch predispose the SAT origins and proximal trunks to plaque development.<sup>18,19</sup> The LSCA is most frequently involved.<sup>20</sup> Most patients with SAT atherosclerosis are in their early sixties, typically Caucasian, with extensive smoking histories, and multiple atherosclerosis risk factors.<sup>21</sup> Approximately 20%–40% of patients have multi-vessel involvement. Trans-sternal repair is performed more often in patients with multi-vessel disease.<sup>22</sup>

The most common form of non-atherosclerotic occlusive disease is giant cell arteritis (see Ch. 138, Vasculitis and Other Uncommon Arteriopathies) and Takayasu disease (see Ch. 140, Takayasu Arteritis). Both have acute inflammatory phases with systemic symptoms and vessel wall inflammation.<sup>23</sup> In the chronic phase, fibrosis and tapering stenosis or occlusion develop. Takayasu arteritis more frequently involves SATs and is the etiology in 20% of patients requiring reconstruction in the western hemisphere, with the majority having multi-vessel disease.<sup>24</sup> Takayasu arteritis predominantly affects females in their 20s and 30s. The highest incidence is in the Far East and in individuals of eastern descent. Radiation-induced arteritis can lead to great vessel atherosclerosis and stenosis decades after treatment.<sup>25,26</sup>

The decision point in SAT occlusive disease management is symptoms. Symptoms are neurologic in 50%–90% and upper extremity in 10%–40% of cases. Stroke, transient ischemic attack, hypoperfusion, embolism, or claudication may be seen and present in both territories in up to 40%.<sup>22,24,25,27</sup> Lesions can lead to subclavian steal syndromes. Subclavian–coronary steal causes angina with internal mammary coronary grafts. Subclavian–vertebral steal leads to vertebrobasilar symptoms and vertebral artery flow reversal.<sup>27–30</sup> Asymptomatic lesions should generally be managed medically. Indications for reconstruction without symptoms include innominate and/or subclavian lesions proximal to hemodialysis access or peripheral bypasses, or severe disease proximal to prior or planned internal mammary coronary revascularization.<sup>30</sup> It should also be considered to allow accurate blood pressure management in

patients with intractable control and disease leading to erroneous monitoring.<sup>31</sup> Finally, failure of endovascular therapy is an indication for open surgical SAT revascularization.

## OTHER INDICATIONS

### Trauma

Blunt and penetrating SAT injury has a spectrum of severity ranging from minimal intimal injury, dissection, mural hematoma and pseudoaneurysm, to partial or complete transection with hemorrhage and extremis. Upper extremity ischemia, neurologic event, or compression of vital structures may be present. Pseudoaneurysm formation may present acutely or late. Blunt or penetrating SAT injury represents 3%–10% of arterial injuries.<sup>32,33</sup> Unlike the distal aortic arch, which is fixed to the posterior mediastinum leading to a higher likelihood of torsion and deceleration blunt injury, SAT are not tightly fixed and blunt injury is less common. Penetrating trauma is more common and may affect any SAT vessel (Fig. 101.2). Assessment should be directed by examination and mechanism. Most patients with major blunt deceleration injuries or chest and thoracic inlet penetrating injuries who are not in extremis should undergo CTA (see Ch. 181, Thoracic Vascular Trauma). Urgent repair of traumatic SAT injury is indicated for patients with hemorrhage, critical extremity ischemia, and compression of vital structures. If possible, resuscitation and correction of physiologic abnormalities should be accomplished prior to repair, particularly if open reconstruction is planned. Minor asymptomatic injuries can be medically managed with anti-thrombotic agents and monitored for resolution. Most clinically occult low-grade injuries remain stable or resolve.<sup>34–36</sup> Stroke from blunt injuries most commonly occurs at the time of injury or soon afterward. Recurrent stroke is infrequent on medical management.<sup>37</sup> In follow-up of medically managed SAT injuries, surgical repair should be directed to new symptom onset; recurrent thromboembolic events despite medical therapy; and enlarging or symptomatic pseudoaneurysms.

### Dissection

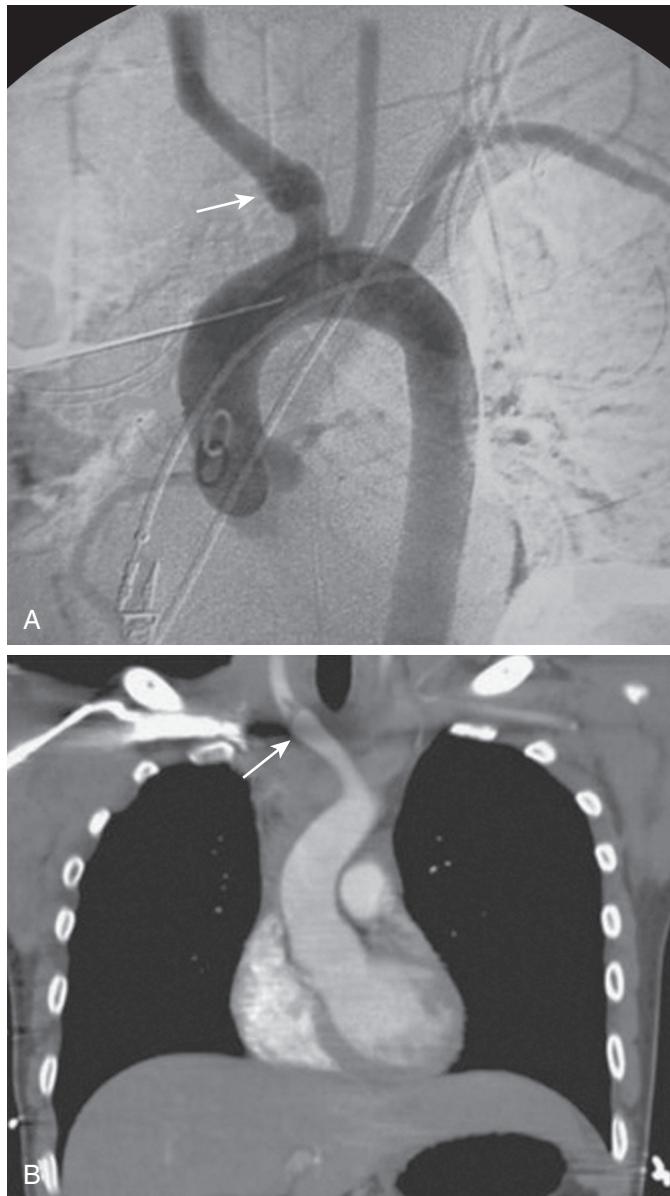
Dissection of SAT occurs spontaneously or as extension from the aortic arch. In patients with aortic dissection extension into the CCAs, 19% of patients present with stroke.<sup>38</sup> Even with aortic repair, SAT dissection persists. Subclavian artery dissection can cause posterior circulation neurologic events, arm ischemia or myocardial infarction when internal mammary coronary grafts are present. Healing remodeling or anatomically stable dissection are the most common outcomes. Degeneration with aneurysm or thromboembolic events are rare.<sup>39</sup> Spontaneous brachiocephalic dissection with subacute retrograde aortic extension has been described.<sup>40</sup> Similar to cervical carotid dissection, initial medical management with antithrombotic agents for 3 to 6 months is the treatment of choice. A randomized trial demonstrating a low risk of recurrent stroke with anticoagulant or antiplatelet agents in

carotid dissection has led to similar practice for brachiocephalic dissection.<sup>41</sup> Patients with initial rupture and hemorrhage, pseudoaneurysm, associated mobile thrombus, or early rapid enlargement should be repaired. Enlarging aneurysm, recurrent thromboembolic events, or persistent/progressive severe carotid stenosis are late indications for repair.

## Aneurysm

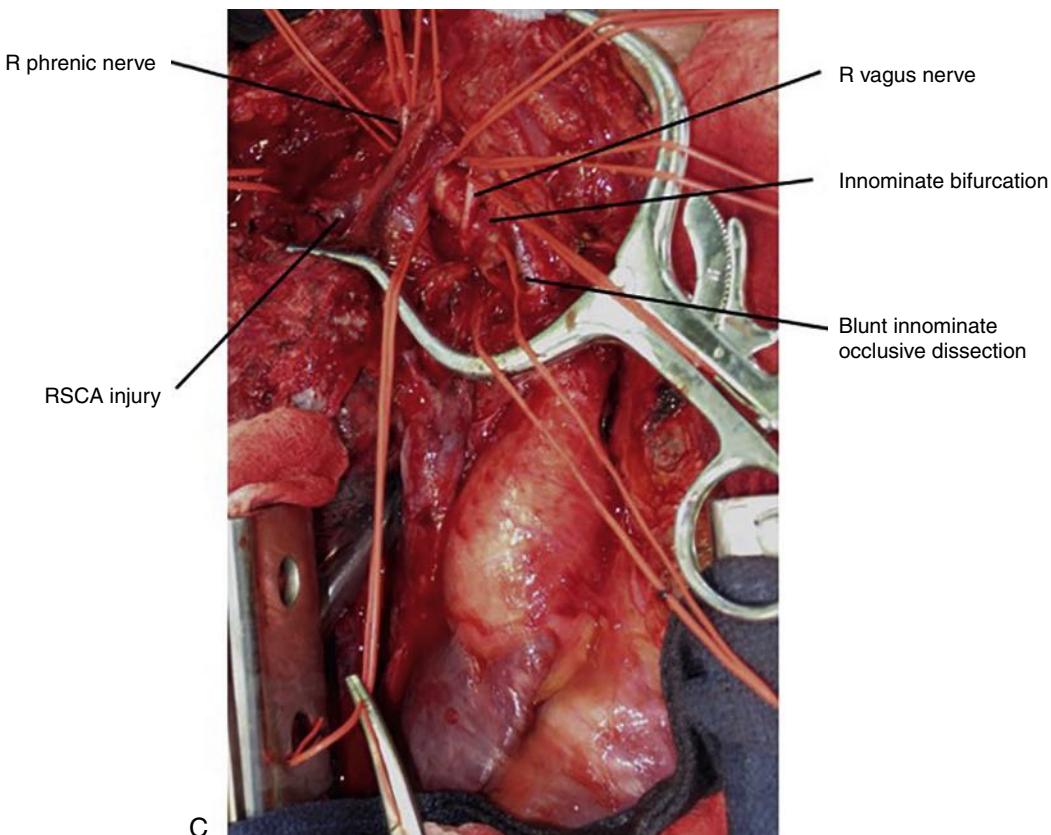
True, isolated, proximal brachiocephalic artery aneurysms are rare, most frequently occurring in the subclavian artery and less frequently in the innominate and LCCA.<sup>42,43</sup> They usually occur in continuation with adjoining aortic arch aneurysms, or may be related to arterial thoracic outlet syndrome (see Ch. 125, Thoracic Outlet Syndrome: Arterial). Patients younger than 50 years should be screened for genetic disorders, such as

Loeys–Dietz and Marfan syndromes. A painless pulsatile mass may be palpated or seen. Symptoms include chest, arm, upper back or neck pains, upper extremity and neurologic thromboembolization, hemodynamic vertebrobasilar events, compressive symptoms such as dyspnea, dysphonia, dysphagia, cough, cervical radiculopathy/brachial plexopathy, and hemoptysis or hematemesis due to aerodigestive erosion. Symptomatic thromboembolization is the most frequent presenting symptom.<sup>43–45</sup> Thrombosis of subclavian aneurysms as small as 2 cm has been reported.<sup>45</sup> Symptomatic aneurysms should be repaired. Isolated brachiocephalic aneurysms may be identified incidentally on axial imaging, and this is how most are now identified. These patients are usually asymptomatic with small aneurysms (<3 cm) and the natural history is slow growth and rare complications.<sup>42</sup> It has been recommended that smaller, asymptomatic aneurysms be repaired due to the concern for



**Figure 101.2** Blunt Traumatic Injury. Aortogram (A) and CTA (B) showing blunt traumatic injury to the distal innominate artery (arrows).

*Continued*



**Figure 101.2, cont'd.** (C) Sternotomy with right suprACLAVICULAR extension exposure for blunt and penetrating injuries from an explosive device. The right subclavian injury was penetrating laceration with hemorrhage. The innominate artery injury was blunt with intimal disruption and occlusion of the bifurcation. Both injuries were able to be opened and debrided. Longitudinal arteriotomy of the innominate on to the left common carotid allowed for intimal flap resection/endarterectomy and was closed primarily; the subclavian required interposition grafting with reversed saphenous vein. RSCA, right subclavian artery.

thromboembolism. However, based on recent data, surveillance in asymptomatic individuals, with selective repair in those with thrombus burden or growth may be considered.<sup>42</sup> Open repair is associated with significant mortality and morbidity. Kieffer and colleagues reported 11% perioperative mortality after open repair of innominate aneurysm, but included ruptured and infected cases with most associated with arch aneurysm.<sup>44</sup> Bower et al. reported a 30-day mortality of 8.2%, with all deaths occurring in urgent/emergent cases. Interestingly, late survival was worse in those with innominate aneurysms.<sup>43</sup> Unfortunately, it is uncommon for the anatomy to be suitable for isolated brachiocephalic endovascular repair, although it may be an option in select cases<sup>46</sup> (see Ch. 102, Brachiocephalic Artery Disease: Endovascular Management). Proximal occlusion with cervical surgical revascularization may be appropriate in cases when traditional resection and revascularization is technically challenging. Aortic endovascular grafts may provide this proximal occlusion<sup>46</sup> (Fig. 101.3). This is an important consideration in treatment of ARSA aneurysms. Tissue of the persistent 4th aortic arch and the 7th intersegmental artery in this anomaly is prone to degeneration and aneurysm, called Kommerell diverticulum. This may be associated with aortic aneurysms. A normal caliber ARSA causing compressive symptoms, or a degenerative ARSA aneurysm should be repaired.

Options include traditional open aortic reconstruction and right subclavian artery (RSCA) revascularization<sup>47</sup>, right subclavian revascularization and ligation with thoracic endovascular aortic graft exclusion (TEVAR), and total endovascular repair using<sup>48</sup> TEVAR and periscope right subclavian endograft.<sup>47,48</sup> Thoracic aortic aneurysms or dissections, even without SAT disease, are a current indication for SAT revascularization (arch debranching) to permit more proximal endograft seal zone (see Ch. 80, Thoracic Aortic Aneurysms: Endovascular Treatment).

## Infection

Rarely, infections, including syphilis and tuberculosis, can lead to aneurysmal degeneration of SAT, in particular the subclavian artery. Bacteremic seeding of SAT disease can lead to infected aneurysm or pseudoaneurysm.<sup>49</sup> ARSA can fistulize into the esophagus.<sup>50</sup> In patients with prolonged intubation or tracheostomy, or mediastinal processes, trachea-innominate fistula may occur. Traditional treatment involves innominate ligation.<sup>51</sup> When diagnosed, infectious brachiocephalic aneurysms or pseudoaneurysms should be repaired regardless of size. Patients should receive long-term systemic antibiotics. Depending on organism virulence and anatomy, treatment includes ligation and/or resection, debridement, soft tissue coverage, and extra-anatomic or *in situ* repair.



**Figure 101.3** A 36-year-old patient with large LSCA aneurysm and no identifiable connective tissue disorder. Aneurysm, broad-based, obliterating the outer distal arch curve, causing pseudo-coarctation and significant arch tortuosity (A). Ascending aorta–innominate–LCCA bypass debranching with LCCA to LSCA CSB and SCA ligation away from the mediastinum, followed with TEVAR of arch to zone 0 (B). At 1 year, CTA shows SCA aneurysm treated well and sac excluded and significantly reduced with good perfusion throughout brachiocephalic reconstructions (C). This type of SAT aneurysm requires aortic-based management for occlusion.

## REVASCULARIZATION

### General Considerations

Physiologic and anatomic characteristics must be considered within the context of operative goals in determining the most appropriate method of revascularization. The option for hybrid endovascular and open procedures are becoming more widely performed, allowing less surgical exposure to revascularize the brachiocephalic arteries. **Extra-anatomic cervical revascularization** is more suitable for patients with severe comorbidities and advanced physiologic age. Patients who are less likely to tolerate sternotomy include those with advanced pulmonary dysfunction, nutritionally and metabolically frail patients, and those with previous sternotomy. Anatomically appropriate candidates for cervical repair are classically those with single arterial occlusive lesions of the CCA or proximal subclavian arteries. Cervical multiple vessel reconstruction is also considered in high surgical risk individuals with one good inflow artery, or when this can be created with endovascular means.<sup>52</sup> As noted, when SAT occlusion is planned, as in the case of TEVAR seal zone extension or brachiocephalic aneurysm, cervical reconstruction can be pursued. **Transthoracic revascularization** is offered to younger patients with comorbidity profiles tolerant of sternotomy. It is best suited for lesions requiring more than one bypass target, such as occlusive lesions involving the innominate artery or multiple SAT. Patients with SAT disease and coronary artery or cardiac structural disease may benefit from concomitant anatomic reconstruction. Patients may also benefit from reperfusion of an asymptomatic LSCA lesion not amenable to endovascular treatment if the left internal mammary artery is needed for coronary bypass.<sup>30</sup> In patients requiring extended landing zone for TEVAR, supra-aortic vessel debranching can be performed for planned coverage of the great vessels.

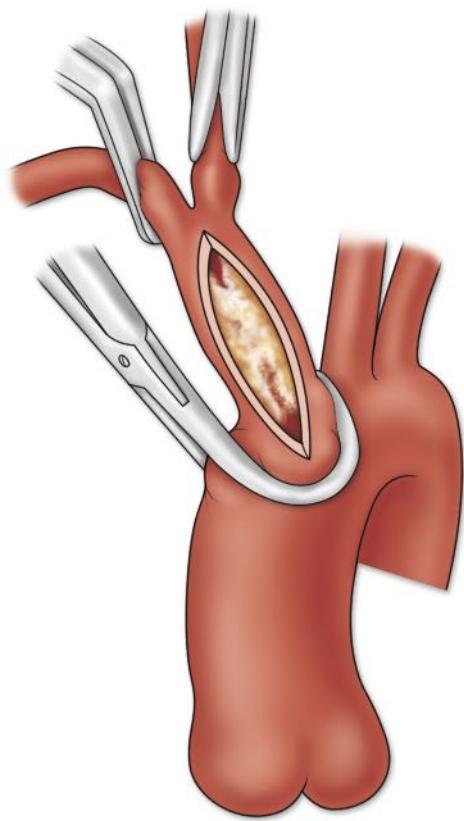
### Transthoracic Revascularization

#### Endarterectomy

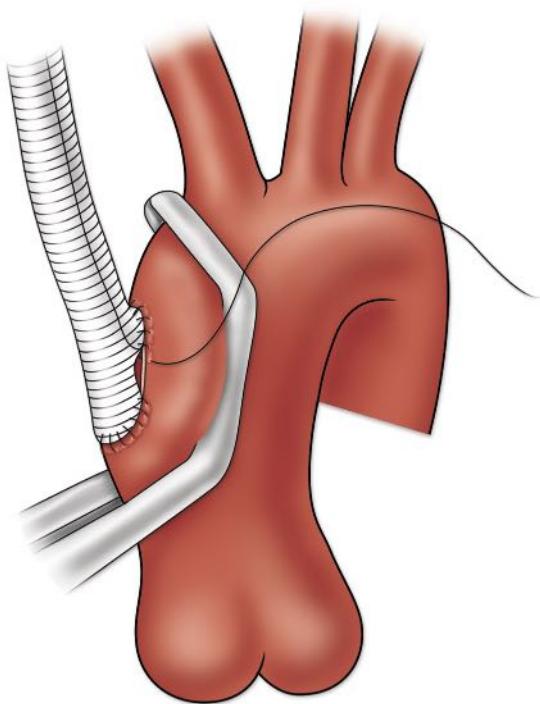
Endarterectomy was described first in the LSCA in 1958 and in the innominate in 1961 by DeBakey, with subsequent success.<sup>53–60</sup> In general, operative stroke occurs in 3%–7% and mortality in 5%–7% of cases. It is best employed in focal lesions within an artery's mid to distal section with the contiguous aortic arch uninvolved, and little disease into the right CCA and SCA. This technique requires fastidious attention to clamping of arteries at sites free of disease, careful creation of a clean endarterectomy surface, and diligent shaping of smoothly transitioning endpoints. It is rarely performed in the innominate and other brachiocephalic arteries due to frequent contiguous aortic arch disease. The proximal clamp is a partial occlusion J-type clamp placed onto the aortic arch at the innominate origin (Fig. 101.4A) Adventitial compromise requiring bypass graft conversion occurs in 5% of cases.<sup>60</sup> In addition to potential embolization and dissection, a risk of endarterectomy relates to inadvertent obstruction of the nearby LCCA with proximal clamping resulting in bilateral hemispheric ischemia. To avoid this, there must typically be at least 15 mm between the vessel origins.<sup>25</sup> Even when treating isolated symptomatic innominate artery atherosclerosis, LCCA proximity or bovine configuration may contraindicate endarterectomy.

#### Bypass Grafts

Also described by DeBakey, bypass grafts are more commonly performed.<sup>53</sup> Inflow for anatomic grafts consists of a disease-free ascending aorta. Preoperative CTA is imperative to identify aortic and supra-aortic target vessel atherosclerotic burden and appropriateness for clamping and anastomosis. Calcification and thrombus are contraindications to clamping for ascending aortic-based grafts without circulatory support. Intraoperative confirmation can be achieved with TEE or

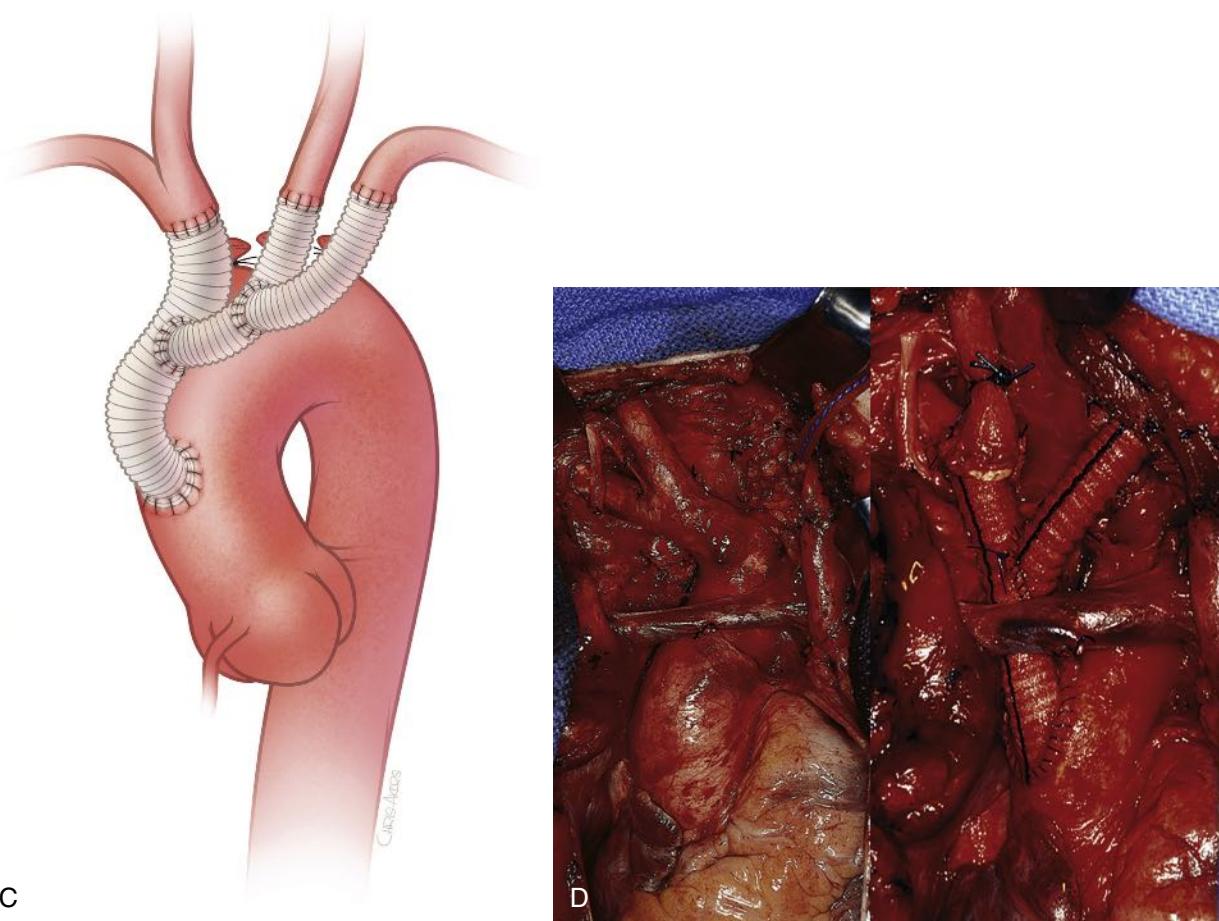


A



B

**Figure 101.4** Transthoracic, anatomic brachiocephalic revascularization can take several forms. All require the ascending aorta to be free of major calcification, thrombus and aneurysm. (A) Innominate endarterectomy is performed less frequently than bypass. Disease must be limited to the innominate trunk and no severe aortic "spill over" atheroma should be present. Distally both the RSCA and RCCA are controlled. There must be some 15 mm of distance between the innominate and LCCA origins to allow secure clamping of the innominate origin on the arch and maintain LCCA perfusion. Bypass from the ascending aorta mandates disease-free clamping at the anterolateral aspect (B).



**Figure 101.4, cont'd.** Single-vessel and multiple-vessel configurations may be constructed such as aorto-innominate, aorto-carotid, aorto-subclavian, or aorto-innominate-LCCA, and aorto-innominate-LCCA-LSCA (C). Separate RSCA and RCCA grafts may be needed also. With exposure and creation, it is usually apparent that pre-made bifurcated grafts are too bulky to allow perfect sternal closure and may kink. Separate sewn-on side-arm grafts commonly provide appropriate configuration (D).

epi-aortic ultrasound. Less invasive techniques for anatomic repair using mini-sternotomy or right anterolateral thoracotomy with tunneling may be considered.<sup>61,62</sup> Once sternotomy is performed, spatial restrictions of the thoracic cavity are assessed, with particular attention to the graft's dimensions and how it affects mediastinal space. Preformed bifurcated or multi-limb grafts can kink or compress underneath the sternum complicating closure. For this reason, it is critical to size and construct multi-limb grafts to minimize bulk (Fig. 101.4C,D). Bifurcated grafts can be avoided by constructing an ascending aorta to innominate bypass sewing smaller grafts end to side to this graft to supply the LCCA and LSCA as necessary. If space is compromised, aorto-innominate–LCCA grafts can be constructed with a left carotid–subclavian graft, either from the LCCA graft or native CCA, more cephalad and away from the substernal space (see Fig. 101.3).

The patient is systemically anticoagulated, and the systolic blood pressure reduced to 90 mm Hg, mean arterial pressure 70 mm Hg. A partial occlusion clamp is applied on the anterolateral aspect of the ascending aorta to minimize kinking and bulk (Fig. 101.4B). A properly sized collagen or gelatin

impregnated Dacron tube graft, usually 10–14 mm for innominate, and 6–10 mm for CCA/SCA, is beveled and sewn to the ascending aorta in an end-to-side fashion using 4-0 polypropylene suture. Polytetrafluoroethylene (PTFE) can also be used.<sup>63</sup> Shunting is rarely needed during innominate reconstruction, but is possible.<sup>24</sup> The aortic clamp is slowly released with the patient in the Trendelenburg position to assist de-airing, and the graft clamped. Once the aortic anastomosis is complete and stable, blood pressures may be liberalized. With multi-vessel reconstruction, the proximal anastomosis for LCCA bypass is then sewn end-to-side, via a side graft from this innominate bypass. It is important to construct the side branch anastomosis prior to completing the innominate bypass to avoid prolonged clamping of the RSCA and right common carotid artery (RCCA). For this reason, transposition of the LCCA is not usually possible. The side graft anastomosis is completed and clamped. Distal clamps are placed on the RSCA and RCCA and the innominate artery is clamped and transected beyond its diseased portion, oversewing the proximal stump with pledgeted 4-0 polypropylene suture. The innominate anastomosis is completed end-to-end with

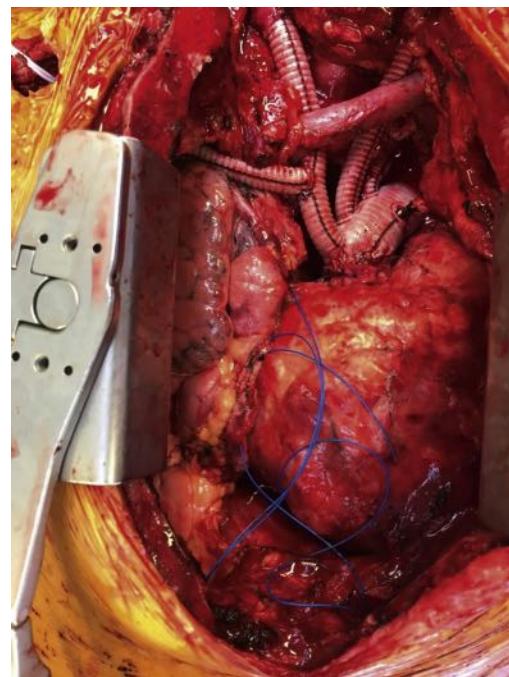
4-0 polypropylene suture re-establishing RSCA and CCA perfusion (Fig. 101.4D). This may require separate grafts to the RSCA and RCCA. The LCCA is the most common target for the side branch graft, which is placed under the preserved left brachiocephalic vein. The LCCA is transected and its origin over-sewn and end-to-end anastomosis performed. The LSCA may be transposed end-to-side onto the LCCA bypass, or a separate side graft from the LCCA bypass, or native CCA, to the LSCA can be performed. These configurations allow for comfortable sternal closure. Alternatively, cervical LSCA revascularization may be deferred and staged to a later time if necessary.<sup>24,25</sup> Operative conduct is similar but less involved for single vessel aorto-carotid and aorto-subclavian bypass (see Ch. 55, Thoracic and Thoracoabdominal Vascular Exposure).

### Total Aortic Arch Replacement

When the ascending aorta or transverse arch has significant atheromatous plaque, thrombotic debris, or is aneurysmal, clamping has a prohibitive embolic stroke risk. SAT revascularization can occur with total arch reconstruction.<sup>64</sup> This requires cardiopulmonary bypass (CPB), deep hypothermic circulatory arrest, and antegrade or retrograde cerebral perfusion. A prefabricated branched graft is used with side-branches for CPB (Fig. 101.5). Antegrade cerebral perfusion requires a patent distal innominate and RCCA to receive the CPB inflow from cannulation or grafts to either the innominate or right axillary artery, or selective cannulas into SAT vessels. This technique may be limited by SAT disease. Retrograde cerebral perfusion involves pumping cooled, oxygenated blood from CPB cannulas into the superior vena cava with enough pressure to direct blood flow back into the brain. With this technique, the need for a patent distal innominate artery is unnecessary and operative time may be shorter.

### Transthoracic Operative Results

DeBakey performed the first aorto-brachiocephalic bypass.<sup>53</sup> Crawford subsequently published results of direct brachiocephalic endarterectomy and bypass in 1962 with a 30-day mortality of 7.5%.<sup>65</sup> In 1983, Dr. Crawford reviewed 43 patients and reported stroke and 30-day mortality rates of 6.9% and 4.7%, respectively.<sup>66</sup> He subsequently reported the mortality in their experience improved from over 20% to almost 5% in the decade after SAT bypass.<sup>67</sup> There have been many reports with reasonable initial and long-term results after transthoracic SAT revascularization (Table 101.1). Kieffer reported 2.9% stroke, 1.5% myocardial infarction, and 5.2% mortality rates, with 5- and 10-year patency rates of 98.4% and 96%, respectively.<sup>59</sup> Rhodes reported 7% stroke, 3% myocardial infarction, and 3% mortality, with 5-year 80% primary patency.<sup>24</sup> In 100 consecutive transthoracic reconstructions, Berguer reported operative stroke and death in 16% with a 6% mortality in isolated SAT procedures.<sup>68</sup> However, this increased to 29% with concomitant cardiac operations. Primary patency was 94% and 88%, and stroke-free survival was 87% and 81% at 5 and 10 years, respectively. Cormier,



**Figure 101.5** Redo-arch replacement with total reconstruction for growing innominate aneurysm and symptomatic LCCA dissection stenosis using arch branch prosthesis. Performed under DHCA with right axillary cannulation for antegrade perfusion. Left carotid bypass to distal CCA after carotid endarterectomy. Separate prefabricated LSCA and RCCA bypass grafts. After rewarming, during CPB weaning, right axillary conduit graft is sewn to RCCA graft to complete total arch reconstruction.

using PTFE, found 1 stroke (1.9%) and 1 death (1.9%) in 53 patients.<sup>63</sup> Transthoracic reconstruction outcomes from the Texas Heart Institute were reported in 2005.<sup>22</sup> Takach reported 113 anatomic revascularizations with mortality of 2.7%, stroke 2.7%, and myocardial infarction 1.8%. Ten-year patency was 94% with freedom-from-stroke at 85%. One-third of transthoracic operations also involved coronary bypass; however, this did not significantly affect mortality. In a 2014 National Surgical Quality Improvement Program report, Daniel detailed 30-day stroke, MI and mortality of 1.2%, 0%, and 2.4%, respectively, in 83 direct anatomic revascularizations.<sup>21</sup> In a 2011 literature review, 1650 patients undergoing transthoracic brachiocephalic reconstruction were assessed.<sup>69</sup> The mortality rate was 7.8% and stroke occurred in 3.8%. In other reports mortality has ranged from 2.7% to 22%.<sup>22,67</sup> Transthoracic revascularization results in appropriately selected, fit patients have continued to improve; however, the risk is not negligible. It is still not appropriate for asymptomatic patients, and additive risk of concomitant cardiac and other arterial procedures is undefined.

### Postoperative Management

Sternal closure is critical. Post-sternotomy disruption occurs in up to 5% of patients leading to a nearly 50% mortality.<sup>70</sup> Patients are observed in a monitored unit for 24 hours. Strict blood pressure management is instituted, and aspirin given. Mediastinal drains are removed once drainage

**TABLE 101.1** Select Transthoracic Brachiocephalic Revascularization Results

Series Author	Year	# Patients	Mortality %	Stroke %	MI %	SURVIVAL %		PATENCY %	
						5-year	10-year	5-year	10-year
Crawford <sup>65</sup>	1962	67	7.5	NA	NA	NA	NA	NA	NA
Crawford <sup>67</sup>	1969	122	9.8	NA	NA	NA	NA	NA	NA
Liljeqvist <sup>87</sup>	1979	85	6.0	9.0	NA	NA	NA	NA	NA
Crawford <sup>66</sup>	1983	43	4.7	6.9	NA	NA	NA	NA	NA
Brewster <sup>56</sup>	1985	37	3.4	6.9	NA	NA	NA	NA	NA
Cormier <sup>63</sup>	1989	53	1.9	1.9	1.9	85	74	95	95
Cherry <sup>57</sup>	1989	26	3.8	0	3.8	NA	NA	NA	NA
Kieffer <sup>59</sup>	1995	135	5.2	2.9	1.5	78	52	98	96
Berguer <sup>68</sup>	1998	100	8.0	10	3	87	81	94	88
Azakie <sup>60</sup>	1998	94	3.0	6.3	2.1	85	65	NA	NA
Rhodes <sup>24</sup>	2000	92	3.0	7.0	3	88	NA	80	NA
Takach <sup>22</sup>	2005	113	2.7	2.7	1.8	100	68.5	NA	94
Daniel <sup>21</sup>	2013	83	2.4	1.2	0	NA	NA	NA	NA

MI, myocardial infarction; NA, not available.

is <150 mL/day. Further antithrombotic medication, if indicated, is instituted after 24–48 hours. Pulmonary toilet is aggressive and early mobilization a goal. Patients are discharged with post-sternotomy precautions, including not lifting more than 5 to 10 lbs, avoiding upper extremity or chest weight-bearing exercises, and limiting arm abduction to less than 90 degrees for 6 weeks. After the initial postoperative visit, we monitor patients with physical examination along with duplex ultrasound of the extracranial carotid and subclavian systems and the graft itself every 6 months for two years and then annually thereafter. CTA is reserved for concerns in surveillance.

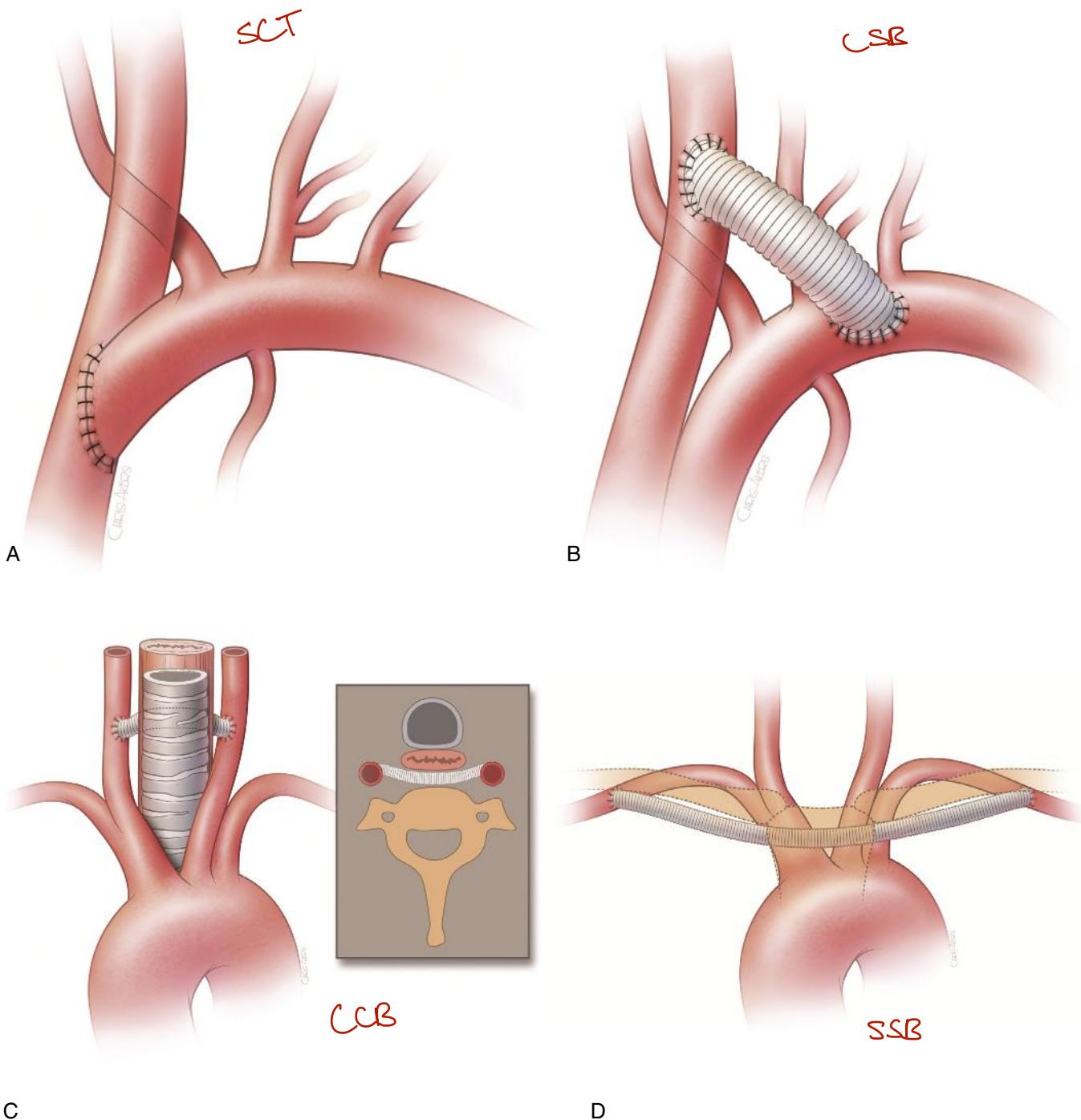
## Extra-Anatomic Revascularization

### Subclavian–Carotid Transposition

Subclavian to carotid artery transposition (SCT) is effective and durable, and frequently compared to carotid–subclavian bypass (CSB).<sup>71</sup> SCT demands a slightly different set of anatomic criteria and is contraindicated when internal mammary artery to coronary artery bypass has been performed, as clamping can cause myocardial ischemia and infarction. The vertebral arteries must also be assessed prior to performing SCT. An ipsilateral vertebral artery terminating in a posterior inferior cerebellar artery (PICA) or contralateral vertebral artery occlusion are both contraindications to SCT as posterior stroke may occur with temporary subclavian clamping. Relative contraindications include a long, tortuous ipsilateral vertebral artery which can kink and occlude, and an early branching vertebral artery making safe ligation of the subclavian artery proximal to the vertebral artery difficult and prohibitive.

The SCT requires no prosthetic, offering durability in the form of patency and resistance to infection. While wound infections in the neck are rare, reoperations are challenging as

prosthetic graft removal is necessary. Patency rates favor SCT compared to CSB. Cina et al. reported 5-year patency rates of 99% and 86% for SCT and CSB, respectively.<sup>72</sup> SCT offers the advantage of a single anastomosis compared to CSB, but is tempered by the need to secure the SCA proximally with risk of bleeding with stump retraction. SCT is performed through a transverse supraclavicular incision centered on the heads of the sternocleidomastoid muscle. Sub-platysmal flaps are created. The sternocleidomastoid (SCM) is retracted medially with partial division of the clavicular head in most cases. The carotid sheath is entered, the internal jugular (IJ) vein dissected free and retracted, to expose the CCA. The omohyoid muscle is divided and the CCA circumferentially mobilized. If left-sided exposure is performed, the thoracic duct is identified and ligated; accessory lymphatic channels on either side are identified and ligated to avoid lymph leak. The IJ is retracted laterally, and exposure of the SCA and its proximal branches proceeds after division of the vertebral vein. The medial anterior scalene muscle can be divided to provide SCA control distal to the thyrocervical trunk and internal mammary branches. Care to avoid a medial phrenic nerve is necessary. Both the CCA and SCA are exposed as possible into the mediastinum. Once the thyrocervical trunk, vertebral and internal mammary arteries are controlled, the patient is anticoagulated, and the proximal SCA clamped and transected proximal to the origin of the vertebral artery. The transected stump is over-sewn first as loss into the chest can be disastrous. For this reason, we place two pledgeted, 4-0 polypropylene sutures at the proximal subclavian clamp before transection. The sutures are tied, left long and secured. If clamp control is lost after transection the sutures can be elevated, preventing retraction. The subclavian stump is ligated with running suture and interrupted, pledgeted sutures. The clamp is slowly released with no retraction by stay sutures. Once satisfied with hemostasis, the artery is released into the chest. The CCA is then rolled slightly to expose



**Figure 101.6** Common Extra-Anatomic SAT Bypass Grafts. (A) Subclavian–carotid transposition. (B) Carotid–subclavian bypass. (C) Carotid–carotid bypass: tunneled either retropharyngeal or antetracheal. (D) Axillo–axillary bypass: tunneled subcutaneously epistemally.

the posterolateral wall and clamped. A longitudinal lateral arteriotomy is made and opened with an arterial punch. The free, transected SCA is brought to the CCA. With proper mobilization there is ample length for a tension-free anastomosis. An end-to-side anastomosis is created with 5-0 polypropylene suture. (Fig. 101.6A). Because of tight spaces and acute angles, a parachute technique is preferred. Shunting is usually unnecessary. The incision is closed over a closed-suction drain.

#### Carotid–Subclavian Bypass

The CSB is the most common cervical extra-anatomic operation. It has utility in thoracic aortic, SAT, and cervical arterial disease. With improvements in balloon-expandable stent technology, moderately diseased SAT inflow vessels can be treated to optimize flow through CSB, thus making this bypass applicable across SAT disease distributions. The CSB conduit can be either Dacron or PTFE (Fig. 101.6B). Counterintuitively, autogenous vein has lower patency rates and is avoided. Some

suggest PTFE has superior patency.<sup>73–75</sup> Ziomek compared different conduits with 18 prosthetic grafts, 13 autogenous vein and 5 SCT. The 5-year patency rate for prosthetic grafts was 94.1%, and 58.3% with autogenous bypasses ( $P < 0.01$ ).<sup>76</sup> In a larger cohort of 60 reconstructions examined later, results were consistent: 25 PTFE (5-year patency, 95.2%  $\pm$  4.6%), 15 Dacron (5-year patency, 83.9%  $\pm$  10.5%), 11 autogenous vein (5-year patency, 64.8%  $\pm$  16.5%), and 9 SCT (5-year patency, 100%).<sup>73</sup> Statistical significance was not achieved due to the small sample size.

**Operative outcomes are similar between CSB and SCT.** Assessing 702 CSB and 87 SCT, Madenci showed no significant differences in combined operative stroke and death (5.1% vs. 6.9%;  $P = 0.45$ ).<sup>77</sup> However, CSB had slightly lower long-term patency. In a systematic review of 516 CSB and 511 SCT procedures, the patency rates were 84% and 99%, respectively, over 5 years ( $P < 0.001$ ).<sup>72</sup> Again noted was prosthetic superiority to vein (86% vs. 74%;  $P = 0.0006$ ). In 287 CSBs, Takach reported operative mortality of 1%, stroke 2.1%, MI 0.3%, and 15-year primary patency of 86.5%.<sup>28</sup> While SCT has higher patency rates and may be more infection-resistant, these advantages must be weighed against the versatility and ease of CSB. CSB can be used with most vertebral artery variants and when the internal mammary artery is to be preserved. Both anastomoses are end-to-side, and no subclavian artery ligation is needed. Furthermore, SCT can only provide flow from the carotid to the ipsilateral subclavian artery. CSB may also provide carotid perfusion.

A transverse supraclavicular incision is made centered on the lateral edge of the sternocleidomastoid (SCM), more lateral than for SCT. The platysma is divided and sub-platysmal flaps created. The SCM is retracted medially with partial division of the clavicular head. The carotid sheath is entered and the IJ retracted to expose the CCA. The vagus nerve is identified and the CCA is encircled after sufficient mobilization. The omohyoid muscle is divided and scalene fat pad dissected lateral to the IJ and retracted laterally and superiorly. Careful ligation of the thoracic duct and all its tributaries during fat pad dissection requires meticulous attention. The phrenic nerve overlying the anterior scalene muscle is identified, mobilized and protected. The muscle is then divided sharply at the first rib conscious of the brachial plexus laterally. This enables exposure of the subclavian artery. Further mobilization of the SCA can be achieved medially by ligation of the thyrocervical trunk and the costocervical trunk posteriorly. Sufficient SCA length is obtained for control and arteriotomy just lateral to the thyrocervical trunk.

The patient is systemically anticoagulated. An 8-mm standard-wall PTFE or Dacron graft is typically used. The SCA is notoriously fragile. Atraumatic clamps and attention to their use is important. Performing the SCA anastomosis first allows for graft manipulation and anastomotic hemostasis in a narrow, deep wound. Performing the CCA anastomosis first establishes inflow and defines proper graft position. An aortic punch is helpful when fashioning the arteriotomies. After clamps are applied and the arteriotomy created, the graft is sewn end-to-side with 5-0 polypropylene suture. The graft is passed under the IJ, flushed, and cut to appropriate length. The phrenic nerve is

left posterior to the graft. When it is more lateral in position it may sometimes be over the SCA anastomotic hood. The second anastomosis is completed end-to-side, after clamping the graft close to the initial anastomosis. The CCA anastomosis is on the posterolateral aspect. If the procedure is performed for CCA disease, the SCA anastomosis is created first to minimize carotid ischemic time. When the indication is symptomatic, ulcerated CCA plaque, we transect and ligate the CCA distal to the plaque and perform an end-to-end anastomosis. The graft can be brought posterior to the sternocleidomastoid and sewn onto the carotid bifurcation after endarterectomy. The incision is closed over a closed-suction drain.

### Carotid–Carotid Bypass

The carotid arteries are exposed via longitudinal incisions over the anterior border of both SCMs. The IJs are reflected laterally as the carotid sheath is entered. The CCAs are mobilized and the vagus nerves identified and avoided. The pharynx and cervical spine are palpated medially in both wounds. A tunnel is created using sharp and blunt dissection between buccopharyngeal fascia behind the pharynx and esophagus and the prevertebral fascia until there is enough room to pass an 8-mm externally supported PTFE graft. This retropharyngeal route, described by Berguer and Gonzalez, can be opened for up to two vertebral body lengths for various cross-configurations.<sup>78</sup> Some prefer to route the bypass subcutaneously anterior to the trachea. However, the retropharyngeal route eliminates risk of skin erosion, may enable cross-transposition of the carotid artery, and allows for safe tracheostomy or sternotomy in the future (Fig. 101.6C). The patient is anticoagulated and the inflow carotid artery is clamped and the anastomosis performed medially. The graft is flushed and clamped with donor artery flow re-established. The target carotid is clamped and an end-to-side or end-to-end anastomosis created. The target carotid can be ligated proximally if symptoms from a lesion were present or the bypass is for creation of an endograft landing zone. Endarterectomy may also be performed if needed. The distal anastomosis can be sewn to the carotid bifurcation after endarterectomy or end-to-end after eversion endarterectomy. Operative complications are <4%, and patency as high as 90% at 5 years<sup>78–80</sup> (see Ch. 57, Cerebrovascular Exposure).

### Axillo–Axillary and Subclavian–Subclavian Bypass

Axillo–axillary bypass is a rare alternative to CSB when common carotid inflow is compromised in patients not candidates for more extensive reconstructions. It is largely performed for arm symptoms and vertebrobasilar insufficiency.<sup>81,82</sup> It can also be performed when long segment subclavian artery disease obviates more proximal revascularization and the contralateral axillary artery is patent. It has occasionally found utility in debanding for zone 0 TEVAR.

The bilateral axillary arteries are exposed with transverse incisions inferior to the lateral third of each clavicle (Fig. 101.6.D). The pectoralis major is split parallel to its fibers and the axillary artery identified posterior to the deep pectoral fascia. The artery is exposed at and medial to the pectoralis minor where it is less mobile with arm abduction.

The bypass is constructed with prosthetic graft tunneled subcutaneously anterior to the sternum and sewn in end-to-side fashion, bilaterally. This procedure, while safer for patients with elevated cardiopulmonary and carotid risk profiles, carries potential hazards due to subcutaneous tunneling across the chest. Complications may include graft compression, skin erosion with graft infection, and risk of bypass damage with future sternotomy. A cervical subclavian–subclavian bypass via retropharyngeal approach avoids subcutaneous tunneling risks of bilateral phrenic nerve and thoracic duct injury<sup>78,83</sup> (Fig. 101.7) (see Ch. 59, Upper Extremity Vascular Exposure).

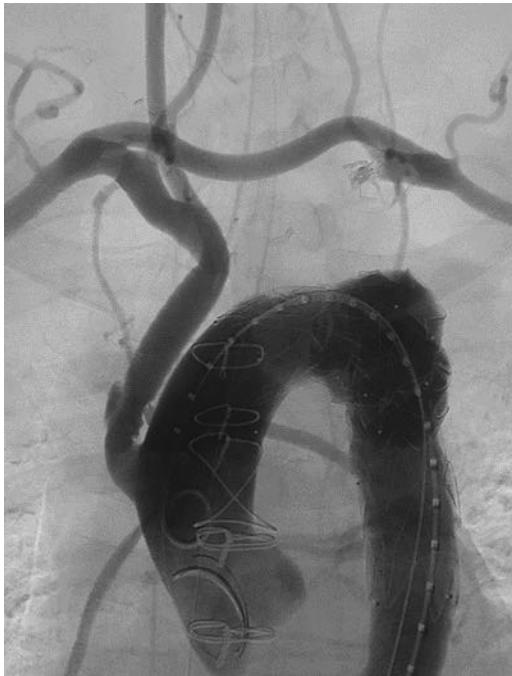
The safety of axillo–axillary bypass has been demonstrated. In a review of 16 studies including 426 patients, with a mean follow-up of 51 months, the stroke and mortality rates were 1.1% and 0.5%, respectively.<sup>83</sup> Reported series document excellent durability, with primary patency at 5 and 10 years of 90% and 88%, respectively.<sup>81,82</sup>

### Carotid–Contralateral Subclavian Bypass

Retropharyngeal cross-revascularization can be performed if the contralateral target for carotid inflow is the subclavian artery. Standard carotid exposure with a supraclavicular transverse incision for subclavian exposure is necessary.<sup>78</sup> Carotid anastomoses can be performed end-to-end or end-to-side, with end-to-side subclavian anastomosis with attention to vertebral perfusion or an internal mammary coronary graft.

### Extra-Anatomic Operative Results

Perioperative morbidity and mortality are generally lower with cervical revascularization than transthoracic reconstruction



**Figure 101.7** A 55-year old asymptomatic man 20 years after open repair of blunt aortic injury, with enlarging anastomotic aneurysm and occluded left carotid system. Aorto-innominate, subclavian–subclavian graft and LSCA ligation proximal to vertebral artery for debranching followed with TEVAR.

(Table 101.2). However, long-term patency rates are inferior. In a 1999 report, stroke, myocardial infarction, and mortality rates were 3.8%, 3%, and 0.5%.<sup>29</sup> Five- and 10-year survival rates were 72% and 41%, with 5- and 10-year patency rates of 91% and 82%. In a 2007 report, 5-year cumulative patency was 92% in 143 patients with cervical brachiocephalic artery revascularization with stroke, myocardial infarction, and mortality rates of 1.4%, 4.3%, and 0.7%.<sup>80</sup> In another study, there were no significant differences in mortality, stroke, MI, or 10-year survival rates between transthoracic and extra-thoracic revascularization.<sup>22</sup> However, 10-year patency was 94% with anatomic, and only 60% with extra-thoracic reconstruction ( $P = 0.002$ ). Analysis of National Surgical Quality Improvement data demonstrated similarly low perioperative composite stroke, myocardial infarction, and death rates between approaches, but a higher complication rate in sternotomy patients. Transthoracic reconstructions were associated with longer hospital length of stay, more transfusions, and higher rates of sepsis and venous thromboembolism.<sup>21</sup> Among cervical reconstructions reported prior to 2011, operative mortality was 1.5% and the stroke rate was 2.9%.<sup>69</sup> Today there appears to be a growing preference for endovascular, hybrid, or extra-thoracic revascularizations as the first-line approach, except in the most fit of patients with multiple-vessel SAT disease for whom a well-performed anatomic reconstruction may be appropriate.

### Impact of Concomitant Carotid Endarterectomy and SAT Revascularization

Up to 30% of surgical SAT reconstruction involve concomitant carotid endarterectomy (CEA),<sup>29</sup> and the impact of this is not definitively established. In one report, combining CSB or CST with CEA was associated with a stroke risk of 3.6% compared to 0.34% for CSB/CST alone.<sup>84</sup> AbuRahma described a 2.7% stroke and 2.7% death rate at 30 days in 37 patients undergoing combined CSB and CEA, with 5-year patency 85%.<sup>85</sup> Recently, we queried the National Surgical Quality Improvement Program comparing 1245 patients undergoing isolated open SAT revascularization to 270 undergoing SAT reconstruction and CEA. After risk-adjustment and propensity matching, we found no significant differences in stroke, death or MI at 30 days with composite stroke, death, and MI in 5%–6%. We concluded adding CEA to open SAT reconstruction adds negligible risk.<sup>86</sup>

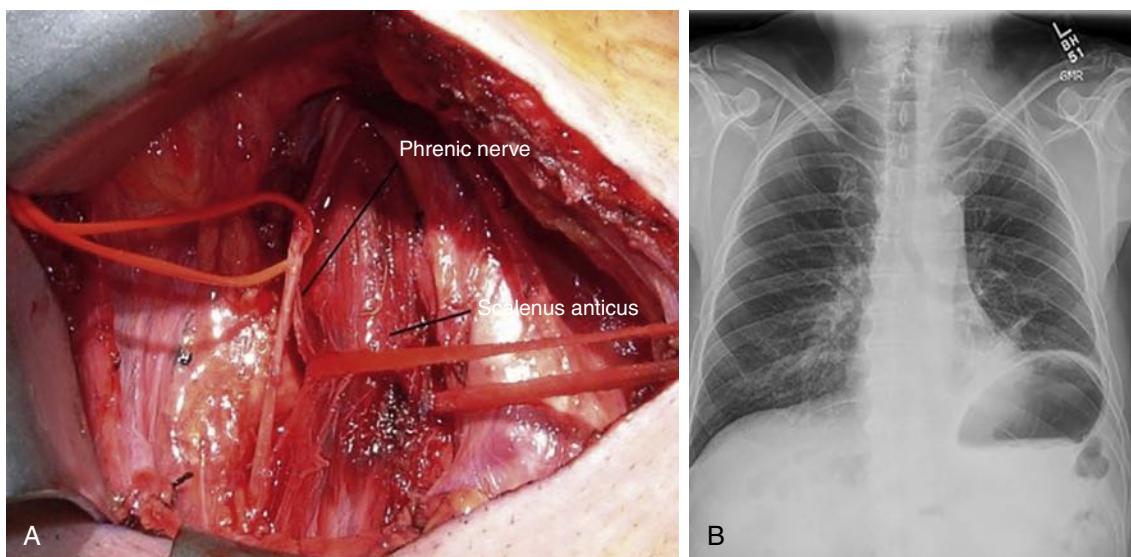
### Postoperative Management

Postoperative management of cervical reconstruction involves strict blood pressure control, aggressive pulmonary toilet and immediate mobilization. Aspirin is given with antithrombotic medications, starting 24–48 hours postoperatively. A postoperative chest X-ray to assess for phrenic nerve palsy and discussion of diaphragmatic physical therapy is important (Fig. 101.8). After supraclavicular incisions, closed-suction drains are removed when patients eat with no evidence of lymphatic leak. Occasionally, recurrent laryngeal nerve palsy from vagal retraction or arterial dissection can occur. Horner syndrome is usually temporary. Patients

**TABLE 101.2** Select Cervical Brachiocephalic Revascularization Results

Series Author	Year	Patients/ Type	Mortality %	Stroke %	MI %	SURVIVAL %		PATENCY %	
						5-year	10-year	5-year	10-year
Crawford <sup>67</sup>	1969	177 CSB	2.3	NA	NA	NA	NA	NA	NA
Crawford <sup>66</sup>	1983	99 CSB	1.0	2.0	NA	NA	NA	NA	NA
Vitti <sup>91</sup>	1994	124 CSB	0.8	0	2.4	83	59	94	94
Schardey <sup>88</sup>	1996	108 SCT	0	1.9	NA	83	NA	100	NA
Berguer <sup>29</sup>	1999	182 All	0.5	3.8	3	72	41	91	82
Mingoli <sup>82</sup>	1999	61 Ax-Ax	1.6	0	0	93	67	87	83
AbuRahma <sup>75</sup>	2000	51 CSB	0	0	2	86	57	96	92
Cina <sup>72</sup> Systematic Review	2001	27 SCT	0	0	NA	NA	NA	NA	NA
		516 CSB	1.2	6.6		86		84	
		511 SCT	1.2	4.4		85		99	
Ozvath <sup>79</sup>	2003	24 Car-Car	0	4	0	NA	NA	50	NA
Byrne <sup>80</sup>	2007	143 All	0.7	1.4	4.3	NA	NA	NA	NA
Domenig <sup>89</sup>	2008	150 SCT	0.7	1.3	0	80	51	NA	NA
Takach <sup>28</sup>	2011	287 CSB	1.0	2.1	0.3	88	73	94	89
Madenci <sup>77</sup>	2013	789 CSB/SCT	2.9	3.3	NA	NA	NA	NA	NA
Illuminati <sup>90</sup>	2018	45 CSB	2.2	2.2	0	71	NA	96	NA
AbuRahma <sup>85</sup>	2020	37 CSB+CEA	2.7	2.7	0	NA	NA	85	NA

Ax-Ax, axillo–axillary bypass; Car-Car, carotid–carotid bypass; CEA, carotid endarterectomy; CSB, carotid–subclavian bypass; MI, myocardial infarction; NA, not available; SCT, subclavian–carotid transposition.



**Figure 101.8** (A) Normal anatomic location of the phrenic nerve sitting on and just medial to the anterior scalene muscle underneath the scalene fat pad, and medial to the brachial plexus. (B) Postoperative left hemidiaphragm paralysis after CSB, usually transient, from traction. Some patients may require diaphragm physical rehabilitation.

are monitored with physical examination and duplex studies every 6 months for 24 months, then annually with CTA reserved for concerns in surveillance.

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# Brachiocephalic Artery Disease: Endovascular Management

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## INTRODUCTION

Brachiocephalic arterial disease presents a complex surgical challenge due to the frequent involvement of other arch vessels, choice of inflow and access, as well as the inherent risks of complex surgery, embolization, and cerebral ischemia.<sup>1</sup> This process may affect the aortic arch and/or its branches, including the innominate, the proximal right subclavian (RSCA) and right common carotid (RCCA), the left common carotid (LCCA) and the left subclavian (LSCA) arteries. Early management of brachiocephalic arterial disease involved open surgery (see Ch. 101, Brachiocephalic Artery Disease: Surgical Treatment) via a

transthoracic approach<sup>2,3</sup> with high morbidity and mortality rates.<sup>4</sup> The extra-anatomic approach offered a variety of options for poor sternotomy candidates or those with severely calcified aortas, but often with a reduction in long-term patency rates.<sup>1,5,6</sup> As endovascular techniques have evolved, management has included a wider variety of options with acceptable results, decreased risks, and faster recovery times.

## DISEASE PREVALENCE

A great deal of the information on patients with occlusive disease of the arch vessels comes from reports of open surgical

series.<sup>7–10</sup> A detailed understanding of the anatomy of the aortic arch is a necessity for planning. The most common cause of arch vessel disease is atherosclerosis. In evaluations for carotid bifurcation occlusive disease, 5% to 15% of patients are found to have concomitant arch vessel disease.<sup>11–14</sup> The prevalence of arch disease in patients without bifurcation disease is approximately 1.5% to 2.0%. In patients with coronary artery disease, the prevalence is 4% to 7%,<sup>15–18</sup> and greater than 11% in those with significant coronary disease. The LSCA is involved most often, followed by the innominate and LCCA, which are both affected approximately 30% of the time.<sup>12,19</sup> Less common causes of arch vessel disease include Takayasu arteritis, radiation-induced injury, aneurysm, and dissection.

## PROCEDURE PLANNING

### Imaging Studies

#### Duplex Ultrasound

Ultrasound imaging of the supra-aortic vessels is often the initial imaging modality. Velocity information can provide insight into the degree of stenosis, and often the visualization of calcification can provide information regarding the nature of the occlusive process.<sup>20–22</sup> However, the anatomic discrimination necessary to guide intervention can be obtained only with more detailed imaging. Lesions of the brachiocephalic arteries are often located proximal to the reach of ultrasound in the mediastinum or behind the clavicle. As a result, significant lesions may manifest by very low velocities in the CCA since they are measured distal to these lesions (see Ch. 22, Vascular Laboratory: Arterial Duplex Scanning).

#### Computed Tomography and Magnetic Resonance Angiography

The most frequently employed methods for assessing the anatomy of the aortic arch are computed tomographic angiography

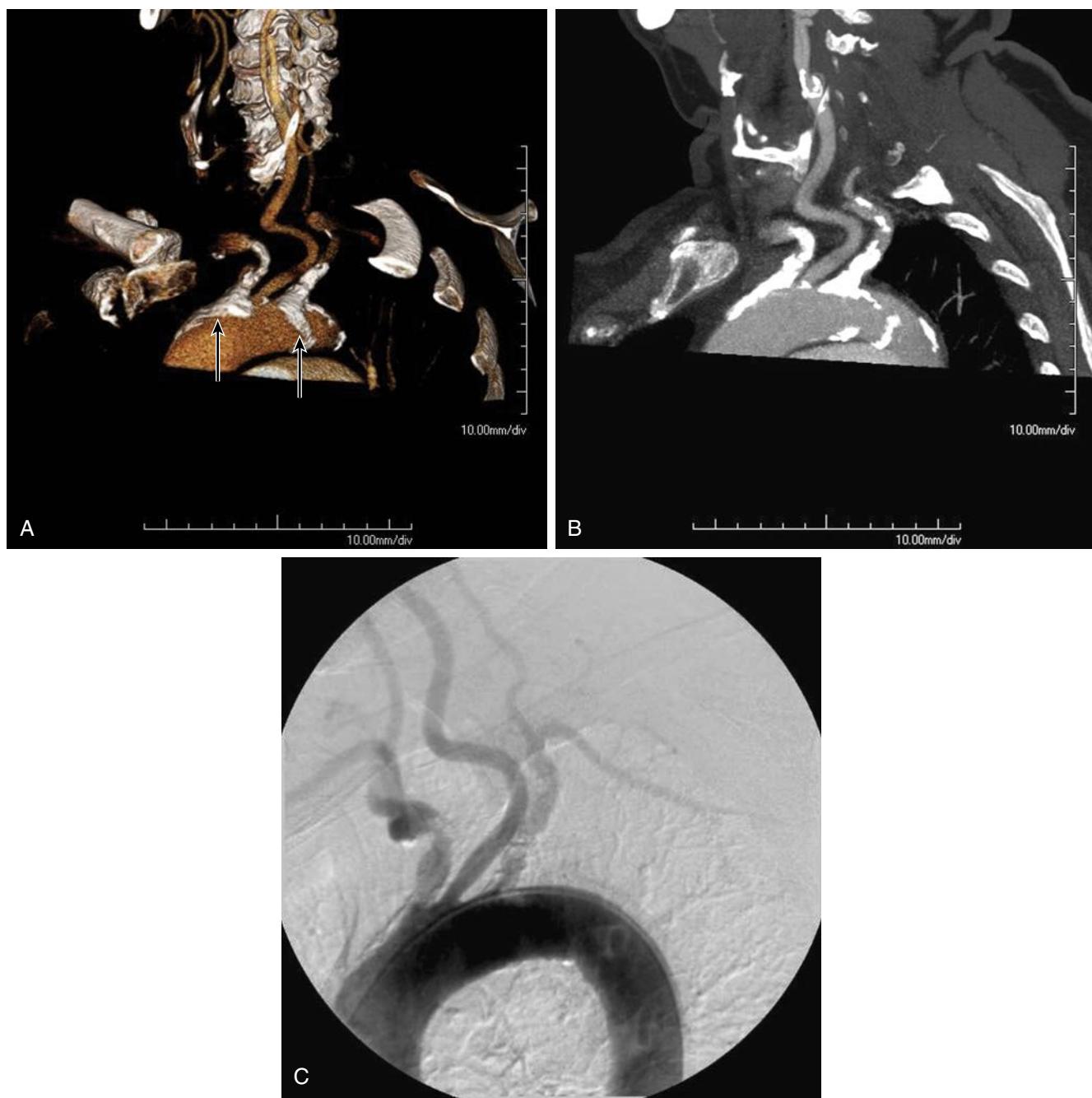


**Figure 102.1** “Bovine arch” anatomy with common origin of innominate and left common carotid artery.

(CTA) and magnetic resonance angiography (MRA) (see Ch. 29, Computed Tomography and Ch. 30, Magnetic Resonance Imaging and Arteriography). Axial imaging has the advantage of avoiding catheter manipulation within the aortic arch and its potential complications. CTA and MRA can be used to evaluate both aneurysmal and occlusive disease, assess the degree of stenosis or occlusion, lesion morphology, vessel configuration and other factors that are very helpful for planning revascularization. MRA is not as helpful in assessing the degree of calcification. Both CTA and MRA can define the intracranial circulation. The source images can be reformatted into three-dimensional models of the aortic arch and its branches to allow excellent visualization of the relevant anatomy with precise measurements. The presence and pattern of arch variants or anomalies will alter the complexity and influence the surgical or interventional approach.<sup>23</sup> The usual anatomic makeup of the aortic arch involves three arch vessels: the innominate or brachiocephalic artery gives rise to the RSCA and RCCA; the left CCA; and the left SCA. In up to 20% of individuals, the LCCA originates from the innominate artery in a “bovine” configuration, or as a common trunk, thus leaving only two main brachiocephalic branches from the aortic arch (Fig. 102.1).<sup>23</sup> In as many as 6% of individuals, the left vertebral artery originates from the aortic arch directly, between the LCCA and LSCA. Finally, aberrant origin of the subclavian arteries (<1%), with or without an associated Kommerell diverticulum and/or a right-sided aortic arch, are best displayed on preprocedural axial imaging studies. There is also variability in the aortic arch as to whether the great vessels arise from the ascending aorta or the “top” of the arch.<sup>24</sup> Aortic arch classification type significantly alters case planning and assessment of complexity. Elderly patients, especially those with years of hypertension, tend to have elongated or tortuous arches from which the branches are more likely to arise from the ascending arch, thus making cannulation and device passage from a femoral approach more tortuous and challenging. Given the wealth of information that affects procedural planning, every patient should have contrast enhanced axial imaging study pre-operatively. CTA offers the added value of a clear understanding of surrounding structures and better discrimination and visualization of calcification (Fig. 102.2).

### Arteriography

Procedural planning and determination of the degree of stenosis can be achieved with axial imaging alone in most patients and angiography is typically performed as part of the therapeutic intervention to treat identified disease. In performing catheter-directed imaging, care must be utilized, as disease of the arch vessels is often associated with or directly caused by “spillover” disease of the aortic arch itself, in which aortic arch disease has extended into its branches. Catheter manipulation may potentially dislodge plaque and cause emboli. Flush aortography is performed with a pigtail catheter. As the arch progresses to the patient’s left, it also moves from anterior to posterior within the mediastinum. Arch imaging is best performed in a left anterior oblique (LAO) projection to “open up” the arch. The flush catheter is positioned proximal to the origin of the



**Figure 102.2** (A) CT three-dimensional surface rendering of the aortic arch showing severe calcific disease of the origins of the innominate and left subclavian arteries (arrows). (B) Maximum intensity projection images of the same patient reconstructed from the CT scan. (C) Arteriogram of the same patient. Note extensive calcification at the origins of the innominate and proximal left subclavian arteries.

innominate artery. Axial imaging can aid in determining the angle to which the imaging gantry should be rotated to provide an optimal view. Images obtained from aortography are used to help identify vessel origins, degree of vessel stenosis, and the type of catheter or guide that may be necessary to cannulate the vessels. Calcification of the aortic arch branches can also be used as a guide under fluoroscopy.

Angiographic imaging of the innominate bifurcation is best performed in an RAO projection. This orientation separates the origins, allowing individual assessment of the RCCA and

RSCA origins and visualization for treatment of either vessel (Fig. 102.3). The origins of the vertebral arteries (VA) are best viewed with a slight cranio-caudal angulation of the image intensifier since they usually arise from the posterior aspect of the subclavian artery.

VAs

## DISEASE DISTRIBUTION

It is particularly important to understand the high-risk anatomic features to avoid missteps and negative consequences.

Brachio  
spinalis

High- and low-risk lesion features are noted in Table 102.1. There is wide variability in technical success, with failure rates ranging from 0% to 40%.<sup>25–28</sup> The lesions most treated are at the origin of the LSCA, LCCA or innominate artery. Less commonly, lesions involve the innominate bifurcation or the origins of the RCCA or SCA, the body of either CCA, or the LSCA. Whereas SCA occlusion has typically been managed with aggressive endovascular approaches, occlusion of the innominate or CCA has more often been treated with open techniques, given concern of potential cerebral embolization. Patients with diffuse disease should be considered for surgical bypass or medical management, while focal lesions are usually best treated with endovascular techniques. Occasionally, a patient with carotid bifurcation disease presents with tandem inflow lesions (see below). Knowledge of the anatomic relationships of the disease to other vessel origins is critical. For example, when intervening in the LSCA, it is imperative to know the location of the LVA origin to avoid injury. Additionally, it is essential to recognize that intervention in the origin of any arch vessel can have an impact

on the orifice of closely located neighboring vessels (Fig. 102.4). In all arch interventions, knowledge of the status and location of neighboring vessels allows planning to prepare for and mitigate risk of occluding or injuring closely located arch branches.

## ENDOVASCULAR THERAPY

Initial endovascular intervention in the supra-aortic trunks involved balloon angioplasty alone.<sup>29–37</sup> Success varied from 80% to 95%, and recurrence rates were 8% to 25% at 1 to 2 years. Since the introduction of stents, the principal interventional therapeutic approach has become primary stent placement, either bare metal or covered.<sup>26,38–43</sup> This approach offers added control of the procedure with the ability to manage dissection and residual stenosis and more reliably achieve a satisfactory immediate technical result than with angioplasty alone.

### Stents

Large series demonstrate patency rates of 77% to 100% over an 18- to 24-month period. Although some suggest selective stenting, most clinicians practice primary stenting in this anatomic bed,<sup>44,45</sup> with balloon-expandable stents being most utilized. There has been no randomized trial of primary versus selective stenting of arch branch lesions. If the lesion is in the body of the artery, and especially if there is substantial tortuosity or significant caliber change along the artery, self-expanding stents can be considered. Additionally, heavily calcified innominate artery occlusive disease may lead to early stent occlusion due to stent compression. Balloon-mounted covered stents have more recently become an important option for supra-aortic vessel intervention, offering more precise deployment and increased radial force with less likelihood of in-stent restenosis due to intimal hyperplasia. A recent study reviewed both balloon-expandable (44) and self-expanding (5) stents to treat 48 consecutive symptomatic patients with innominate or subclavian artery occlusive lesions. Results include a technical success 96%, clinical success 94%, and primary patency of 91.7% and 77% at 12 and 24 months, as well as secondary patency of 96.5% and 91.7% at 12 and 24 months.<sup>46</sup> Another retrospective review of 27 lesions treated with both self-expanding and balloon-mounted stents documented a 100% technical success for stenotic lesions and 57% technical success for occlusive lesions with no periprocedural or post-procedural complications during 18 months mean follow-up.<sup>47</sup> A recent retrospective study reviewed outcomes for 16 patients with symptomatic LSCA occlusions who were treated with balloon-expandable stents. Technical success was 93.8% with one failure due to inability to cross the lesion and no major or minor complications. Patency at two years was 93.3% with one asymptomatic restenosis.<sup>48</sup> Covered stents have also been used to treat aneurysms and traumatic injury of arch vessels.<sup>49–52</sup> Reports document excellent acute success in trauma or aneurysm treatment and patency of the devices has been maintained; repeat interventions have occasionally been necessary for the treatment of either kinks or angulation within the prosthesis. There remains little information regarding the use of drug-eluting stents for

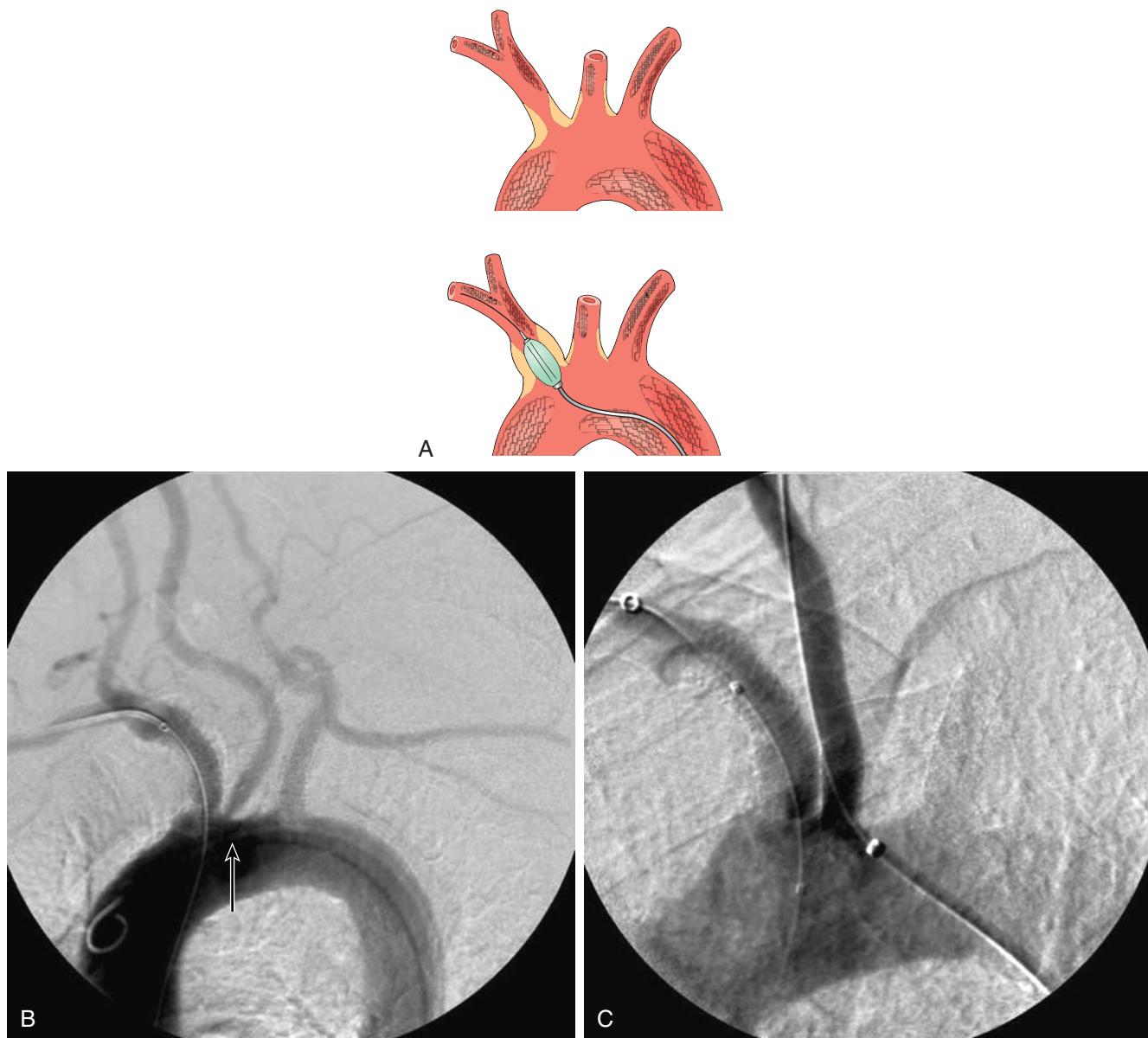


**Figure 102.3** Maximum separation of the origins of the branches of the innominate artery in a right anterior oblique projection of approximately 20 degrees.

**TABLE 102.1**

**Favorable and Unfavorable Characteristics of Arch Vessel Disease**

Favorable	Unfavorable
Stenosis	Occlusion
Concentric lesions	Eccentric lesions
Vessel origin at top of arch or distal	Vessel origin in ascending aorta
Absence of calcium	Heavy calcification
Nonulcerated plaque	Ulceration
Asymptomatic	Symptomatic
Nonostial lesions	Ostial lesion
	Plaque abutting vertebral artery origin



**Figure 102.4** (A) Treatment of a neighboring arch vessel can force treatment of an adjacent arch branch. After treatment of the innominate artery, the left common carotid can be impinged on by a shift of aortic plaque, thus necessitating intervention in the left common carotid origin. (B) A successfully treated innominate artery has shifted aortic plaque, which resulted in stenosis at the origin of the left common carotid artery (arrow). (C) Treatment of the common carotid origin and simultaneous protection of the innominate artery's stented origin.

the treatment of supra-aortic trunk<sup>53</sup> occlusive disease. In addition, stents should be avoided at the first rib compression of the subclavian–axillary artery.

## PERIOPERATIVE MEDICAL MANAGEMENT

### Antiplatelet Agents

There are no useful data on antiplatelet therapies for intervention in the supra-aortic trunks and recommendations are based on inference from use in patients with cerebrovascular disease and those requiring carotid bifurcation intervention (see Ch. 42,

Antiplatelet Agents). All patients with peripheral or cerebrovascular disease should be maintained on aspirin,<sup>53,54</sup> and this is standard therapy for aortic arch interventions. The use of clopidogrel for the treatment of patients with atherosclerotic vascular disease provides a reduction in risk when combined with aspirin in this population.<sup>55</sup> The combination of aspirin and clopidogrel has shown benefit when used as the periprocedural antiplatelet regimen in carotid stenting and should be used in this application.<sup>56–58</sup> Clopidogrel drug resistance is common and can lead to periprocedural ischemic complications in patients undergoing endovascular stent implantation.<sup>59–61</sup> Ticagrelor and Prasugrel have a lower incidence of resistance and can be used as a substitute for those patients with clopidogrel

resistance; however both may be associated with more remote bleeding complications.<sup>62</sup> The addition of glycoprotein IIb/IIIa inhibitors to the dual antiplatelet therapy has not been shown to reduce embolic events and may significantly increase intracranial hemorrhagic complications.<sup>63–65</sup> Based on this information, dual aspirin and clopidogrel therapy is recommended as standard antiplatelet regimen for arch branch intervention. In patients without a long-term indication for dual antiplatelet therapy, the clopidogrel may be stopped after 30 days but may be continued for 6 months if there is a periprocedural indication that longer-term therapy may be of value.

### Intraprocedural Heparin

Heparin is typically used as the intraoperative anticoagulant for intervention in the arch vessels, and there are no meaningful data assessing alternative strategies.<sup>66</sup> The use of bivalirudin in carotid interventions has been reported,<sup>67</sup> and may be a safe alternative. A recent meta-analysis reviewed studies comparing heparin to bivalirudin in percutaneous peripheral interventions including carotid interventions. The authors conclude bivalirudin use is associated with lower all-cause mortality, bleeding, and access site complications.<sup>68</sup> Data via randomized trials are needed to confirm those results and without additional data the routine use of bivalirudin cannot be recommended. Currently heparin administration adequate to maintain activated clotting times of between 250 to 300 seconds is recommended. Reversal of the heparin with protamine after intervention is reasonable and without evidence of associated thromboembolic events.<sup>69</sup>

## TECHNICAL DETAILS OF ENDOVASCULAR MANAGEMENT

A comprehensive plan includes intended access location, whether multiple access sites are desired, appropriate sheath caliber and length intended as the treatment platform, and balloons and stents of correct size, shaft length and required wire compatibility. After arch angiography, selective catheterization is performed of the relevant vessels. In most instances, this is best achieved with simple curve catheters. Options include the vertebral (Cook, Inc., Bloomington, IN), Headhunter (Cook, Inc.), angled Glide (Terumo, Tokyo, Japan) catheters, and many others. Simple curve catheters allow access to most vessels and advancement of the catheter if necessary. When angulation of the arch mandates an increased angle on the catheter, alternatives include Vitek (Cook, Inc.), and Simmons (multiple manufacturers) catheters. The use of complex curve or reverse-curve catheters may be required when the arch is tortuous, the LCCA must be cannulated in a bovine arch configuration, or in type III arches. The complex curve catheter must be reformed in the aortic arch which can increase risk for embolic complications. Once selective access has been obtained, the vessel can be imaged, and intervention performed. Complex curve catheters are not as easily advanced, due to the major secondary curve on the catheter, and requires a longer length of wire in the branch in order to advance.

Brachial or radial access for intervention in the subclavian arteries and the innominate artery can provide an approach to treat an obstructive lesion that might otherwise prove impossible to revascularize from the femoral route. Retrograde access to the carotid arteries can also be obtained through open exposure of these vessels when needed.

### Left Subclavian Artery Intervention

Many of the techniques described in this section are applicable to interventions in the other arch vessels. The LSCA is most frequently treated among the arch branches and can be managed via retrograde, antegrade or a combined approach. Preservation of the VA and often the internal mammary artery (IMA) is imperative. History of a prior left IMA to the coronary arteries is essential to elicit.

After arch aortography with either a 4- or 5-F flush catheter, an exchange is made for a selective catheter. After accessing the vessel origin, a steerable, 0.035-in. Glidewire (Terumo Cardiovascular Systems, Ann Arbor, MI) is passed across the lesion into the distal vessel. If a stiff Glidewire is used, it can be left in place, and a long 6-F or 7-F sheath is advanced from the groin over this wire, to the origin of the lesion. A 70-cm length sheath is usually adequate, but a 90-cm length sheath may be required in a very tall patient. If the Glidewire used has less support, wire exchange for either a Rosen (Infiniti Medical, Menlo Park, CA) or Storz (Cordis, Bridgewater, NJ) or Supracore (Abbott) wire can be performed, and the sheath then advanced. If the arch is tortuous and additional stability is required, the exchange wire can be advanced further to the brachial artery. This may be the case if there is no stump of subclavian artery from the arch and the tip of the sheath must be maintained in stable position with its tip in the arch. The vessel origin and the area of disease are positioned within the center of the imaging field to minimize distortion from parallax. Predilation with a 4- to 6-mm angioplasty balloon allows accurate determination of size and ensures easier passage of the stent. Frequently predilation is performed with a balloon that is longer than the lesion to allow fixation of the balloon at either end of the stenosis. The balloon diameter chosen for predilation should be slightly smaller than the distal vessel so that dissection is not induced. In the case of proximal SCA lesions, this will limit the potential for damage to the origin of the VA. This technique also allows imaging of the distal extent of the lesion to gauge proximity of the VA and IMA origins to facilitate their preservation. The length and diameter of the stent selected should be sufficient to ensure that the lesion is covered fully, and the vessel is expanded to its true size and not that of a post-stenotic dilated segment. The stent should not extend beyond the origin of the VA. Ideally, for orificial lesions, the stent should extend approximately 1 to 2 mm into the aortic arch to fully cover any arch plaque. If a balloon-expandable stent is undersized, it will allow further expansion by dilation with a larger diameter balloon. It is important to know the limits of expansion of the stent while still retaining the strut architecture, which provides adequate radial resistance to compression. If the proximal extent of the stent has been positioned partially in the aorta, it is helpful to “flare” this end of the stent by dilating it

with a slightly larger balloon, or the shoulder of the treatment balloon to a higher pressure. This further opens the vessel origin and reduces protrusion of the stent into the aortic lumen, which can be an impediment to future interventions.

In some situations, the interventionalist may choose to place the stent in “protected” fashion through the lesion to prevent difficulty with passing through tight lesions. To do so, the sheath and dilator are passed through the lesion and the sheath remains within the lesion until the stent is advanced to the correct location. Typically, for orificial disease, a balloon-expandable stent is positioned just at the origin of the vessel. The sheath is then withdrawn to expose the stent. In this approach, the operator must ensure that the stent is positioned appropriately before and during withdrawal of the sheath. The sheath tip must be maintained near the lesion for support of the devices being passed and for any arteriography that is required through the sheath.

### Vertebral Artery Protection

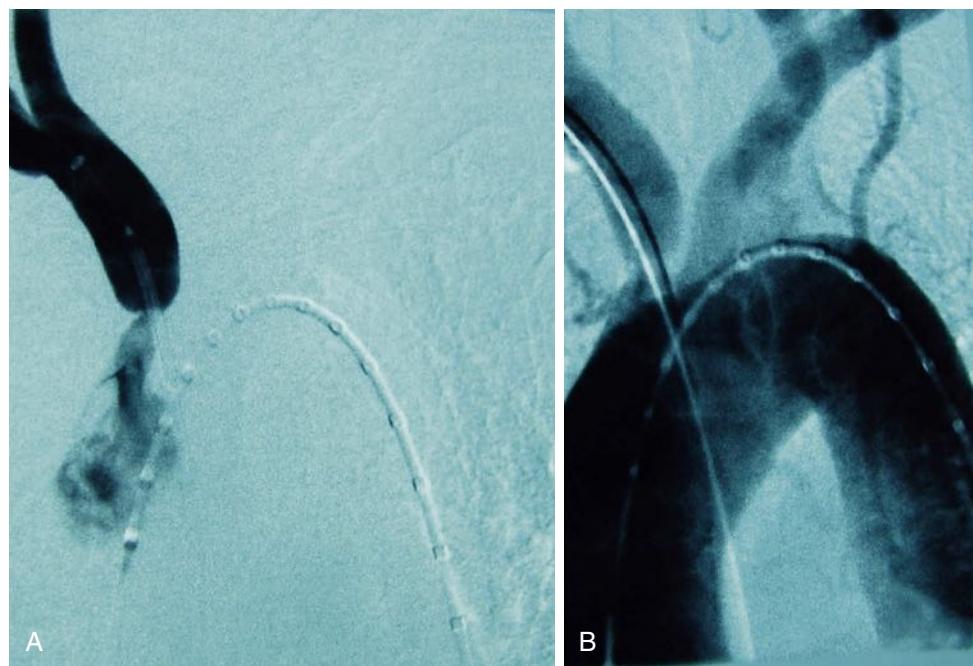
The preoperative plan should include non-encroachment of the SCA stent onto the VA origin. If this cannot be achieved, consideration should be given to open reconstruction. When the lesion approaches the VA origin, it is important to “protect” this vessel. Using a slightly larger sheath, an 0.014-inch buddy wire can be placed into the origin of the VA. The VA origin can be stented, if necessary, to maintain patency. If it is desired to have a wire in the VA throughout the LSCA stent procedures, the wire can be placed from a different direction using an alternative access (e.g., radial approach), or in buddy wire technique. An 0.035-inch compatible stent advances over both wires. As the stent delivery catheter tip approaches where the wire paths diverge, the limit of stent placement just short of the VA origin can be ascertained.

Embolic protection of the VA during endovascular intervention has been described but is not routinely used. The baseline

risk of embolic complications with intervention is low and the risk of adverse events related to insertion of a protection device remains undefined,<sup>70</sup> but includes the potential risk of vertebral dissection with manipulation of the vessel. In the setting of subclavian steal, normalization of flow takes some time to occur after stenting, and there is inherent protection related to the preexisting reversed flow in the VA.<sup>71</sup>

### Brachial Access

Retrograde brachial access can be helpful for traversing proximal occlusions in the LSCA. With flush occlusion of the vessel origin, it can be challenging to traverse via aortic access. In certain difficult situations, through-and-through access may be necessary to ensure adequate purchase within the vessel for delivery of the device. Access to the brachial or radial artery is obtained as noted earlier, and a long 5- or 6-F sheath is positioned just distal to the occlusion. A Glidewire is used in conjunction with an angled catheter to traverse the occlusion. It is important to ensure re-entry into the aorta because it is relatively easy to enter a dissected plane, which can cause aortic dissection. Once it is confirmed that the wire has traversed the lesion and entered the descending aorta, the catheter can be introduced, and the wire removed; blood should exit the catheter freely. In the absence of free flow of blood, the catheter can be assumed to be in a plane outside the vessel lumen; therefore, a different path must be created. With the return of blood flow, angiography should be performed to confirm position within the aortic arch. After luminal access has been confirmed, treatment of the lesion can proceed. The stent is positioned 1 to 2 mm into the aorta. When positioning the stent, imaging can be difficult from the brachial sheath. The lesion can be crossed with the sheath and dilator as described above, prior to placement of the stent (Fig. 102.5). Alternately, groin access that has been



**Figure 102.5** (A) Retrograde contrast injection may be difficult through a severe arch lesion. (B) Transfemoral arch aortography provides optimal imaging when positioning the stent.

obtained for arch aortography can be helpful. The wire is positioned within the flush catheter around the aortic arch. This wire then creates a fluoroscopic marker for the aortic wall, so that the location of the SCA origin can be identified. This technique is particularly helpful in performing retrograde interventions. Most LSCA occlusions can be crossed, especially with escalation to a bi-directional approach. However, care must be taken to avoid extensive subintimal arch dissection.

## Radial Access

Transradial access was first described in the coronary circulation in 1989,<sup>72</sup> followed by the first successful transradial coronary stent implantation, 1993.<sup>73</sup> Since then, transradial access for coronary interventions has grown and has been adopted by many interventionalists and vascular surgeons. It has successfully been used in a variety of visceral, aortic, and peripheral interventions with a low site complication rate and high technical success rate and is proven to decrease bleeding complications and diminish renal dysfunction.<sup>74–76</sup> Reports have demonstrated that the use of this access site for the retrograde treatment of subclavian and innominate disease is safe, comparable with brachial access.<sup>77,78</sup> Particularly in obese or advanced age patients, transradial access should be considered.<sup>79,80</sup> Transradial access can achieve “patent” hemostasis, thus minimizing the risk of post procedural radial artery thrombosis to 0.9%.<sup>81</sup> Further, radial artery occlusion is often clinically silent and does not preclude the use of the artery for future interventions.<sup>74,82,83</sup> Limitations include atherosclerosis, anatomic variations such as a tortuous or hypoplastic vessel or a radial loop, device size and length for intervention, and gender, as females tend to have smaller radial arteries.<sup>74,84</sup> Prior to access, ultrasound is used to ensure the vessel is patent, of adequate caliber, >2 mm, and has no aberrant anatomy. A modified Barbeau test is used to ensure adequate collateral circulation. The Barbeau test is done by placing a transcutaneous pulse oximeter on the tip of the index finger and monitoring waveform with and without radial artery occlusion. Resultant waveforms are classified A–D with Barbeau Class A and B deemed appropriate for access (Fig. 102.6). This screening test identified only 1.5% of patients as being unsuitable candidates for transradial access.<sup>85</sup> A 4-F micropuncture system is used to access the artery under ultrasound guidance. A 6-F Glidesheath slender (Terumo, Somerset, NJ) is introduced over the 0.018-inch micropuncture wire. To combat vasospasm, a “transradial cocktail” bolus of 200 µg nitroglycerin, 2.5 mg verapamil, and 3000 units of unfractionated heparin is instilled via the sheath. Once the procedure is completed, a TR band is applied to achieve patent hemostasis.<sup>81</sup>

## Innominate Artery Interventions

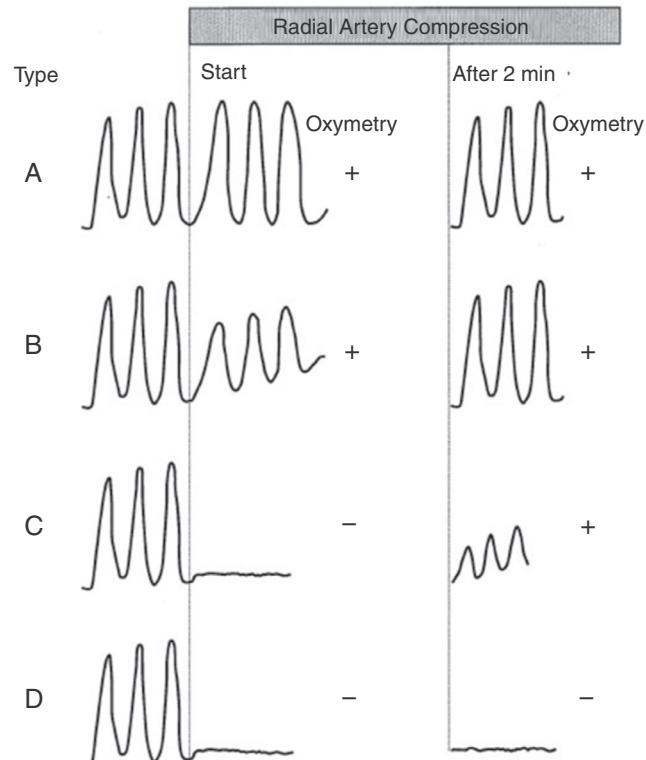
Interventions in the innominate artery are the most challenging of the supra-aortic trunk vessels. The large diameter and short length contribute to the challenge to ensure a stable treatment platform, as does preservation of the innominate artery bifurcation. Intervention may expose the patient to a risk of

embolization in both carotid and vertebral distributions. There are options to minimize the potential for cerebral embolization, including protection during intervention (see below). In most circumstances innominate interventions completed from a femoral access do not use protection devices.

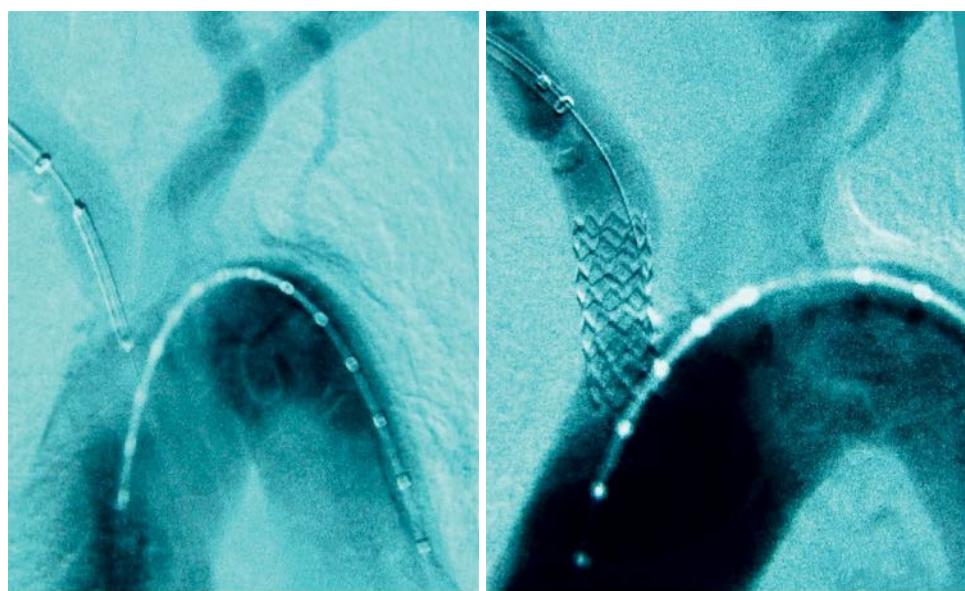
In treating innominate artery disease, it is important to understand where the origins of the branches are in relation to the disease process. The innominate origin is best visualized with the image intensifier in the LAO position, but the bifurcation is best visualized in RAO. It may be necessary to add either caudad or cephalad angulation to the RAO projection to isolate the branch origins. It is imperative to ensure that the distal aspect of the stent be understood in relation to the bifurcation. The length of the stent should be carefully considered.

## Cannulation of the Arch Branches

Because the innominate artery often has the most difficult angulation, it can be challenging to engage its orifice in a diseased artery. As with the LSCA, access via the brachial or radial artery may allow access and visualization of the distal aspect of the plaque (Fig. 102.7). A through-and-through technique can also be used by snaring the wire, once crossed, and bringing it through the alternative access site. In some instances, the second access may be utilized so that a wire or a protection device can be placed. Normally, if access to the innominate origin from the groin has not been achieved easily within 15 minutes,



**Figure 102.6** The Barbeau Test. Drawing representing the four types of ulno-palmar arch patency findings with PL and OX, as recorded with the finger clamp applied on the thumb (A) No damping of the pulse tracing immediately after compression; (B) damping of pulse tracing; (C) loss of pulse tracing followed by recovery within 2 min, and (D) loss of pulse tracing without recovery within 2 min. (Reprinted with permission from the American Heart Association.<sup>85</sup>)



**Figure 102.7** Balloon-expandable stent placed in the innominate artery with slight extension into the arch. Origin of the innominate is best visualized in LAO projection.

brachial or radial access should be considered. Extensive attempts in patients with significant origin disease exposes them to unnecessary risk. With pre-interventional imaging revealing a significant angle to the innominate origin, which will make femoral access challenging, it may be worthwhile to consider brachial or radial access as the primary approach. In most situations, when the brachial or radial approach is used, the distal brachial wire is left in the ascending aorta so that the angle of stent placement is closer to the angle of blood flow. It is important to recognize that when “through and through” access is required, the native angle of the innominate artery can be distorted.

### Carotid Protection

If there is concern about the need for protection in the carotid distribution and transfemoral access has proved challenging, the wire from the arm can be snared and brought out through the femoral access. This allows a catheter to be brought through the lesion from below and a guide to be positioned at the vessel origin. The through-and-through wire can be used to provide support, holding the guide in place, and a protection device can be placed from either the arm or the groin; the lesion can then be treated from the groin. If the protection device has been placed from the groin, the intervention should be performed over the protection device’s wire, which allows capture and removal of the protection device through the stent rather than around it.

In most instances, there is a low risk of embolization, and the lesion can be treated using the simplest approach without a protection device. As discussed earlier, when access from the arm is used, the femoral wire can be left around the arch to assist in identifying the vessel origin. Some surgeons approach innominate lesions via a cervical CCA cutdown, affording both simple access to the lesion and embolic protection by direct carotid clamping and flushing.



**Figure 102.8** Treatment of the innominate artery branch origins with a kissing-stent technique to preserve both origins. Note the innominate artery branch origins are best visualized in RAO projection.

### Innominate Branches

RSCA intervention tends to be more difficult than LSCA due to visualization and anatomic location of stenoses which tend to develop in the very short segment between the RSCA and VA origins.<sup>86</sup> In addition, whereas extension of the proximal end of the stent into the arch from treatment of a LSCA lesion is desirable, the extension of the proximal end of the RSCA stent would project it into the innominate bifurcation and proximal RCCA. Disease in branches of the innominate artery usually occurs at the vessel origins; in many instances it requires kissing-stent technique to avoid impingement on the origin of the other vessel (Fig. 102.8). This can be performed from single femoral access with a larger sheath for introduction

of two-stent delivery systems. An alternative approach involves simultaneous access from the groin and arm. Wire access to the RCCA is obtained through the groin, and the arm approach provides access through the SCA. Simultaneous positioning of stents can thus be achieved, and imaging from the sheaths in both locations allows excellent visualization of the proximal and distal aspects of the occlusive lesion. Simultaneous stent deployment allows preservation of both ostia.

### Left Common Carotid Artery Interventions

Interventions in the LCCA most commonly involve the vessel origin as it arises from the aortic arch but may also occur in bovine configurations. When the vessel originates from the arch, intervention is performed similarly to the LSCA approach. Access to the vessel is obtained with the least angled catheter possible, and a decision is made regarding the use of either a guide catheter or sheath for stent delivery. If access is tenuous because of vessel angle off the aorta, a “buddy wire” can be positioned in the external carotid artery to maintain the guide or sheath position at the vessel origin. A protection device is then advanced and deployed within the ICA. Intervention is performed over the protection device wire, which is subsequently captured and removed. The buddy wire is removed last ensuring that the access sheath remains stable.

When access to the LCCA origin proves challenging, the interventionalist must decide whether to attempt retrograde access through open carotid exposure or to proceed to surgical revascularization. Several factors contribute to this decision, including extent of disease in other arch vessels, particularly the LSCA; significant disease in the carotid bifurcation, which may be addressed by simultaneous carotid endarterectomy (CEA) and retrograde intervention; and a history of prior neck operations or radiation therapy. It is important to remember that an alternative approach may be safer than persisting in attempting access in a very diseased arch.

### Innominate and Left Common Carotid Interventions in Combination with Carotid Endarterectomy

Repair of an inflow lesion is required in less than 5% of patients who require carotid intervention.<sup>87,88</sup> In those who need both, a hybrid approach has emerged as a safe and efficacious option. Only flow-reducing inflow lesions need treatment, and with the proliferation of CTA and MRA, lesions at the arch vessels’ origins are commonly detected. One clinical clue is the presence of a palpable CCA pulse in the neck, which implies that the proximal lesion is not flow-limiting; in addition, the duplex image of the cervical CCA waveform will be blunted in proximal flow-reducing lesions and velocities may be severely reduced.

The hybrid approach as described by Moore and Schneiders<sup>89</sup> involves proceeding with surgical exposure of the carotid bifurcation and internal carotid in standard fashion for endarterectomy. Once exposed, the internal carotid can be clamped

to avoid cerebral embolization, and intervention on the common or innominate lesion is performed under that protection either prior to or after standard endarterectomy. Access is gained into the CCA below the level of bifurcation disease, and a hydrophilic wire is passed through the lesion. This is then exchanged for a stiff wire, and angioplasty and/or stenting conducted in the normal fashion. After the intervention has been performed, a clamp is placed on the CCA above the stent but below the bifurcation disease. The artery is opened, and any embolic debris is flushed prior to final closing of the vessel. Performing CEA first avoids stagnant flow in the newly placed stent.

### Results of Innominate or Left Common Carotid Interventions in Combination with Carotid Bifurcation Endarterectomy

Scattered case series and meta-analyses have reported mostly favorable outcomes for this technique.<sup>90–93</sup> A meta-analysis of 13 studies published in 2011, with mean follow-up of 12–36 months, reported technical success rate of 97%.<sup>90</sup> Stents were used in 61%, whereas the remainder underwent simple balloon angioplasty. Thirty-day mortality and stroke rates were 0.7% and 1.5%, respectively. Ten of the 129 total patients developed restenosis of the proximal lesion, with 70% of these patients having been treated with balloon angioplasty alone at the initial operation. Seven underwent reintervention, including repeat angioplasty ( $n = 4$ ) and bypass graft ( $n = 3$ ). The results seem to indicate that it is reasonable and efficacious, but further study is justified prior to widespread application. A review of large single-center series in 2016 reported less optimistic outcomes,<sup>91</sup> with 23 patients undergoing combined endarterectomy with proximal intervention, and noted dissection in the proximal intervention site in 3 patients, 2 of whom required additional stent placement and one of whom sustained stroke and death. There were two early strokes (9%) and one death (4%). These authors advised caution and advised that performance of this combined procedure should be limited to those with hemodynamically significant proximal stenosis. In a retrospective review of 7 patients over a 2-year period who underwent simultaneous, retrograde stenting of the proximal CCA/innominate artery with eversion carotid endarterectomy for severe tandem stenosis, no postoperative mortality, neurologic morbidity, cervical hematoma, or peripheral nerve injury was observed in any patient. In this small series, eversion carotid endarterectomy offered the advantage of direct introduction of the sheath into the CCA, saving time.<sup>92</sup> A more recent study reviewed 22 patients who underwent CEA with ipsilateral carotid artery stenting with a mean follow up of >5 years with mixed results. CEA was performed with a patch in 20 patients and eversion in 2 patients. Distal internal carotid artery clamping was performed in 90% of patients before ipsilateral carotid artery stenting. One dissection was created and successfully treated with stenting, 1 perioperative stroke occurred in a patient with symptomatic disease, 1 postoperative myocardial infarction occurred, 2 patients had cranial nerve injuries, and 1 patient expired within 30 days for unknown reasons.<sup>93</sup> These

**TABLE 102.2** Technical Success Rates for Arch Vessel Interventions

Series	Year	No. of Patients (Lesions)	Stenosis	Occlusion
Rodriguez-Lopez et al. <sup>43</sup>	1999	69 (70)	55/58 (95)	15/15 (100)
Sullivan et al. <sup>42</sup>	1998	83 (87)	76/77 (99)	6/10 (60)
Al-Mubarak et al. <sup>39</sup>	1999	38 (38)	34/34 (100)	2/4 (50)
Bates et al. <sup>38</sup>	2004	91 (91)	83/83 (100)	6/8 (75)
Brountzos et al. <sup>26</sup>	2004	48 (49)	42/42 (100)	5/7 (71)
Peterson et al. <sup>110</sup>	2006	18 (20)	20/20 (100)	N/A
Brountzos et al. <sup>46</sup>	2006	48(48)	N/A	46/48 (96)
Woo et al. <sup>47</sup>	2006	25 (27)	20/20 (100)	4/7 (57)
Song et al. <sup>103</sup>	2012	148 (148)	131/132 (99)	13/16 (81)
SCALLOP Registry <sup>99</sup>	2015	553 (560)	389/389 (100)	153/171 (89)
Karpenko et al. <sup>98</sup>	2017	245 (245)	122/125 (98)	110/120 (92)
Przewlocki et al. <sup>100</sup>	2017	411 (428)	355/356 (99)	54/71(76)
Akif Cakar et al. <sup>48</sup>	2018	16 (16)	N/A	15/16 (94)

more recent retrospective reviews conclude concomitant ipsilateral carotid endarterectomy and stenting is a safe and advantageous procedure with appropriate patient selection and careful surgical technique.<sup>92,93</sup> A technical maneuver that may help avoid complications during these hybrid treatments of tandem lesions is the use of a pigtail catheter placed from a femoral access into the arch and used to define the anatomy at the time of inflow stenting of the proximal LCCA or innominate artery when combined with endarterectomy. Retrograde angiography is usually inadequate since very little contrast typically traverses the critical lesion at the branch vessel origin and the contrast that does pass across the lesion is briskly carried away by non-opacified blood flow in the arch. In this situation, accurate delineation of the anatomy assists in optimal stent placement and coverage of the lesion and any associated post-angioplasty dissection.

## OVERALL RESULTS OF BRACHIOCEPHALIC INTERVENTIONS

Initial descriptions of endovascular treatment of arch vessel disease involved limited numbers of patients treated with angioplasty alone.<sup>30,94–96</sup> More recent studies demonstrated low complication rates, reasonable initial success and acceptable long-term results with selective stenting.<sup>94,97</sup> Stents have commonly been used as a primary method of treating occlusive lesions in this region. The initial technical results of reports of primary stenting are noted in Table 102.2. Complication rates range from 0% to 20%, with the majority consisting of access-related problems. Importantly, there were very few neurologic sequelae, with two strokes occurring in a single series,<sup>42</sup> both in patients undergoing combined endarterectomy and proximal branch intervention. In one of the larger series reported, Karpenko et al.<sup>98</sup> noted an incidence of TIA in one (0.8%) patient with stenosis and three (2.5%) patients with occlusion,

and no strokes were identified. They also noted an increased risk of stent thrombosis or in-stent restenosis in patients with stent length >40 mm. In an additional large study, the SCALLOP investigators<sup>99</sup> noted no TIA in patients with stenosis and two (1.2%) in patients with occlusion. Stroke rates were similar in both groups at 1.8%; however, in the SCALLOP registry, over 15% of patients had stents placed across the origin of the VA, a technique we would not recommend. A large-scale, long-term prospective study of over 400 patients with symptomatic subclavian or innominate artery stenosis or occlusion noted angiographic success rate of 99.7% in stenoses and 76.1% in occlusion, with freedom from restenosis at 82.6% and 77.9% at five and ten years, respectively. The major complication rate was 1.2%, with four embolic ipsilateral strokes and one intracranial hemorrhage.<sup>100</sup> In most of these series, the incidence of death and neurologic morbidity was low with no deaths in the three largest studies.<sup>98–100</sup>

Rupture is a rare but recognized risk. There are few reports on the incidence or management of brachiocephalic rupture. Options are like those in the event of rupture in other vessels during angioplasty and/or stenting.<sup>101</sup> This would typically include balloon occlusion to immediately control the injury and treatment with covered stent placement to control hemorrhage.

## RESULTS OF ENDOVASCULAR VS. OPEN BRACHIOCEPHALIC INTERVENTIONS

From the reported series published to date, endovascular patency rates appear lower than surgical reconstruction (Table 102.3). One-year patency rates vary from 88.5% to 97%, and 5-year patency varies from 77% to 89%. Recurrent stenosis can be treated by reintervention with 36-month and 60-month secondary patency rates of 90%<sup>38</sup> and 97.7%,<sup>99</sup> comparable to open surgery.

**TABLE 102.3** Patency Rates for Arch Vessel Interventions

Series	Patency Measure	PATENCY (%)				
		1 Year	2 Years	3 Years	4 Years	5 Years
De Vries et al. <sup>97</sup>	Duplex (>50%) + clinical symptoms	94	89	89	89	89
Przewlocki et al. <sup>27</sup>	Duplex (>50%) + clinical symptoms + arm pressure	88.5	83.6	N/A	N/A	77.2
Rodriguez-Lopez et al. <sup>43</sup>	Duplex (>50%)	92 100 <sup>a</sup>	82 96 <sup>a</sup>	73 90 <sup>a</sup>		
Bates et al. <sup>38</sup>	Arm pressure	97	91	83	N/A	77
AbuRahma et al. <sup>102</sup>	Duplex or angio + clinical symptoms	93		78		70
Palchik et al. <sup>105</sup>	Duplex (PSV ratio 3:1)	92	84	77		
Song et al. <sup>103</sup>	Duplex	91 95 <sup>a</sup>		78 91 <sup>a</sup>		67 86 <sup>a</sup>
Karpenko et al. <sup>98</sup>	Duplex (>70%) + clinical symptoms				89.8 (stenosis) 87 (occlusion)	
SCALLOP registry <sup>99</sup>	Duplex (>50%) and arm pressure	90.6 99.2 <sup>a</sup>		83.4 98.2 <sup>a</sup>		80.5 97.7 <sup>a</sup>
Akif Cakar et al. <sup>48</sup>	Duplex (>60%) + clinical symptoms	93.3	93.3			

<sup>a</sup>Secondary patency.

Several retrospective studies have compared the results of endovascular therapy for subclavian occlusive disease with outcomes from surgical reconstruction.<sup>102–105</sup> In the first of these studies, AbuRahma et al.<sup>102</sup> reports on 121 patients with stenting and 51 open carotid–subclavian bypass over a 13-year period at a single institution. The diagnosis of restenosis was based on the presence of an arm pressure differential together with appropriate duplex criteria. In the endovascular group, two completely occlusive lesions could not initially be crossed. Complication rates were 5.9% in the bypass group versus 14.9% in the endovascular group. Bypass complications included two phrenic nerve injuries, from which patients recovered within several months, and one nonfatal myocardial infarction. Endovascular complications included two distal embolic events treated by intervention, congestive heart failure, brachial artery thrombosis treated by thrombectomy, reperfusion, arm edema, pseudoaneurysm, procedure-related dissection and/or thrombosis treated by thrombolysis and stenting, and 11 minor complications (8 hematomas not requiring transfusion, 2 cases of headache and/or syncope, and 1 superficial wound infection). Overall, patients treated via endovascular approach experienced a major complication rate of 5.8%, similar to the major complication rate of surgical bypass. Primary patency rates for bypass at 1, 3, and 5 years were 100%, 98%, and 96%, respectively, versus 93%, 78%, and 70%, respectively, for endovascular therapy.

Another report compared the outcomes of 114 patients who underwent 137 procedures for subclavian artery stenosis treated by either primary stent placement (67 lesions) or carotid–subclavian bypass grafting (70 lesions).<sup>105</sup> Among lesions treated with endovascular therapy, 62 were successfully treated. Primary patency rates in the interventional patients were 78%, 72%, and 62%, respectively, at 1, 3, and 5 years, with assisted-primary patency rates at the same time points of

84%, 76%, and 76%. For patients who underwent surgical therapy, 1-, 3-, 5-, and 10-year patency rates were 95%, 92%, 90%, and 90%, respectively, and primary-assisted patency rates at the same time points were 97%, 97%, 95%, and 95%, respectively. There was no mortality in either group, and complication rates were similar: 20% in the open surgery group and 10% in the endovascular group. No cerebrovascular events occurred in either group.

In another single institution study of 76 patients treated over a 20-year period, 35 underwent surgical reconstruction and 41 had attempted angioplasty.<sup>104</sup> The 5-year secondary patency rate in the surgical group was 97%. In the endovascular group, there were failed attempts at treatment, six in the setting of occlusion, and one because of the development of a cerebellar infarct, at which point intervention was abandoned. There were four complications among these patients, including the one cerebellar infarct noted, two subclavian artery dissections requiring stenting, and one covered stent protruded into the aorta to an extent that necessitated surgical removal. The primary patency rate of successfully treated lesions was 82% at 4 years.

The most recent notable report<sup>103</sup> evaluated outcomes over 20 years in 252 patients who underwent balloon-expandable stent placement ( $n = 148$ ) or extra-thoracic bypass grafting ( $n = 104$ ). Of the bypass patients, 71 underwent axillo-axillary bypass and 33 carotid–subclavian bypasses. There were no perioperative deaths and no permanent neurologic deficits in either group. The overall complication rates were 6.1% in endovascular patients and 9.6% in surgical patients. Cumulative 1-, 3-, 5-, and 10-year primary (secondary) patency rates in the stent group were 91%, 78%, 67%, and 49% (95%, 91%, 86%, and 64%), versus 99%, 97%, 95%, and 89% (99%, 99%, 98%, and 94%) in surgical cases. The authors concluded that both therapies were safe and effective, while bypass was more

durable. Among patients with endovascular therapy failure, all were able to undergo surgical revascularization with a technical success rate of 100%.

When viewed together, long-term patency seems to be better with open surgical reconstruction than with endovascular therapy. However, endovascular therapy remains reasonable because it offers extremely low risk intervention, rapid recovery, outpatient or short hospital stays, early resumption of normal activities, and preservation of surgical options.

## ARCH INTERVENTION IN INFLAMMATORY CONDITIONS

Interventional therapy for inflammatory diseases (e.g., Takayasu arteritis) of these vessels mandates an understanding of the nature of the inflammatory process (see Ch. 140, Takayasu Arteritis). In most cases, treatment with anti-inflammatory medications is aimed at reducing the inflammatory state and not at decreasing the stenosis in the vessels. Revascularization procedures in these disease states are hampered by cell overgrowth and restenosis, and it is therefore important to ensure that the patient's disease is quiescent before vascular reconstruction. This includes normalization of inflammatory serum markers and improvement in systemic symptoms such as fevers and malaise. Nevertheless, occasionally cerebral ischemic symptoms develop that mandate acute attention to revascularization, even with an active inflammatory state. In this setting, reconstruction ideally with autogenous material carries the lowest risk of recurrence. Endovascular intervention in the setting of acute inflammation can be achieved, although immediate and long-term success rates appear lower than those achieved in patients with atherosclerotic disease, and recurrence rates are related to the degree of ongoing inflammation.<sup>106,107</sup> There is a suggestion that covered stents may be of some benefit in this scenario.<sup>108,109</sup>

After the inflammatory state has diminished, the residual lesion in question should be assessed. Improved endovascular outcomes are obtained with the treatment of short focal stenoses. Stent placement appears to have a distinct advantage over angioplasty alone. However, for complex lesions, especially long occlusions, it appears that autogenous reconstruction via arch vessel transposition offers recurrence rates that are about half those of endovascular therapy. There is limited data available regarding the use of covered stents in this setting, but it would seem likely that they might play a more significant role in treating these problems in the future.

## LONG-TERM MANAGEMENT AND SURVEILLANCE

Long-term management of this patient population includes appropriate medical therapy to address the underlying

atherosclerotic process to limit their overall risk for cardiovascular complications. This will involve appropriate medical therapy for comorbid conditions, including hypertension, hyperlipidemia, and diabetes. Smoking cessation should be a major component of therapy as well. Medical therapy for patients treated by stenting for arch vessel disease should include antiplatelet therapy, initiated before the procedure, and continued for at least 1 month as a combination of both aspirin (325 mg) and clopidogrel (75 mg) with a transition normally to clopidogrel alone after 1 month. However, there are no data to objectively define the optimal time frame for aggressive antiplatelet therapy.

After intervention in the arch distribution, it is important to maintain continued follow-up. These patients have a 15% to 25% risk for recurrent stenosis within the first 3 to 5 years, with about half of these recurrences being symptomatic. Follow-up should consist of an history and physical examination including bilateral arm pressure determination. In addition, duplex assessment of the arch vessels should be done every 6 months for the 18 to 24 months, with annual evaluation thereafter. If duplex is unable to assess the degree of stenosis within these vessels because of the location, CTA can be helpful in assessing the degree of stenosis. Repeat evaluations are recommended at 6-month intervals for the first 2 years after intervention and then annually.

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# Acute Limb Ischemia: Evaluation, Decision Making, and Medical Treatment

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Acute ischemia of the limb represents one of the toughest challenges encountered by vascular specialists. The diagnosis and initial assessment are largely clinical, and diagnostic errors can result in a high price to the patient – amputation or even death. Amputation and death rates remain high despite intervention, which is in contrast to major advances in the treatment of many

other vascular diseases. Acute ischemia is often an end-of-life condition that presents in a patient with multiple medical comorbidities. Therefore careful clinical assessment of the individual is as important as assessment of the limb. Unlike many other vascular conditions, there is no one definitive treatment; a variety of modalities are available, including anticoagulation,

operative intervention, thrombolysis, and mechanical thrombectomy. Selection of the most appropriate intervention or combination of interventions can be critical to the eventual outcome.

## Etiology and Pathology

Acute ischemia is the result of a sudden deterioration in the arterial supply to the limb. Excluding trauma and iatrogenic causes, there are two main reasons for acute ischemia to occur: arterial embolism and thrombosis. The distinction between thrombosis and embolism is important in terms of diagnosis and prognosis, but it may not be crucial when deciding on the form of treatment.

### Embolism

Embolism (from the Greek *embolos*, or “plug”) is the result of material passing through the arterial tree and obstructing a peripheral artery. Usually the source of the embolus is the heart, and the material is mural thrombus that has accumulated and then detached. The other main cause is atherosclerotic debris from a diseased proximal artery, often the thoracic aorta, in individuals with a heavy burden of atherosclerotic disease.

Once the embolus detaches, it passes easily through large arteries and lodges peripherally, usually at an arterial bifurcation, where vessels naturally narrow. Emboli can occlude any artery, but in the legs, the common femoral and popliteal arteries are commonly obstructed. Rarely large emboli, so-called saddle emboli, occlude the normal aortic bifurcation. In the upper extremity, the brachial artery bifurcation and the brachial artery at the takeoff of the profunda brachialis artery are frequent locations for emboli.

Emolic ischemia is usually catastrophic because it often occurs in otherwise normal arteries, without any established collaterals. Typically, the patient presents with an acute white leg, including a complete neurosensory deficit. Embolic occlusion is also progressive; the ischemia worsens as secondary thrombus forms both proximal and distal to the occlusion. The secondary thrombus is the plum-colored clot removed at embolectomy (Fig. 103.1). It is particularly important that this



**Figure 103.1** Embolic fragment in the center of the image, with the tail of secondary thrombus shown around it.

secondary thrombus is removed because it may be responsible for obstruction in smaller distal vessels. If the presentation is delayed, the secondary thrombus adheres to the arterial wall, making it particularly resistant to removal with an embolectomy catheter and less easily lysed by thrombolytic drugs.

### Cardiac Embolism

#### Atrial and ventricular

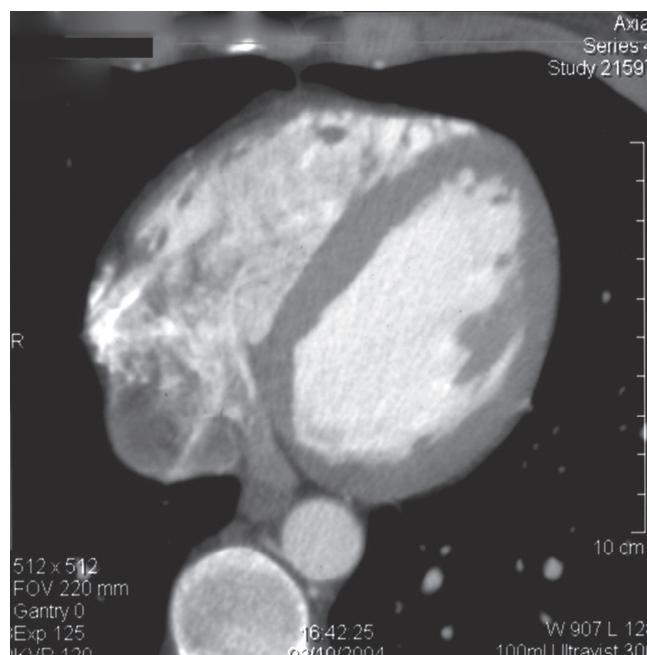
Embolism may occur in patients with otherwise normal arteries, with the embolic material usually arising from the heart. Embolic material from the heart usually consists of platelet-rich thrombus. Often it is organized, giving it the characteristic white surface on removal at embolectomy. The most common cause is atrial fibrillation; thrombus forms in the left atrial appendage as a result of stasis due to incoordinate contractions of the atrium and ventricle.

Mural thrombus, as a result of acute myocardial injury due to infarction, is a particularly dangerous cause of embolism. The patient has not only an ischemic extremity but also a high-risk medical condition (Fig. 103.2). Left ventricular aneurysm is also a high-risk cause of embolism, because these patients have a low cardiac output as a result of the previous infarct(s) that caused the aneurysm.

In the past, cardiac valve disease was the main cause of arterial embolism, but advances in the management of these patients have virtually eliminated this as a cause.<sup>1–3</sup> Instead, many patients now have artificial heart valves, and those with prosthetic valves are usually anticoagulated. Embolism is rare in patients with porcine replacement heart valves.

#### Paradoxical

Paradoxical embolism occurs when a clot from the venous system, usually deep venous thrombosis, travels through a patent



**Figure 103.2** Computed tomogram of the heart showing mural thrombus that caused brachial embolus (same patient as in Fig. 103.9).

foramen ovale into the arterial system. The clinical clue is acute arterial ischemia in a young patient with simultaneous deep venous thrombosis.<sup>4</sup>

### Endocarditis

Bacterial endocarditis is an infrequent diagnosis since the introduction of widespread echocardiography and antibiotics.



**Figure 103.3** Ulcerated Aortic Atheroma at Autopsy.

However, certain patient groups are at risk, including intravenous drug users, patients with indwelling arterial or venous lines, and those who are immunocompromised.

### Cardiac tumor

Atrial myxoma is a benign tumor of the left atrium that may fragment as it enlarges. Surgeons are advised to send the embolic material for histology if there is anything atypical about the material removed at embolectomy, or if the patient is young with no obvious reason for embolic disease.<sup>5</sup>

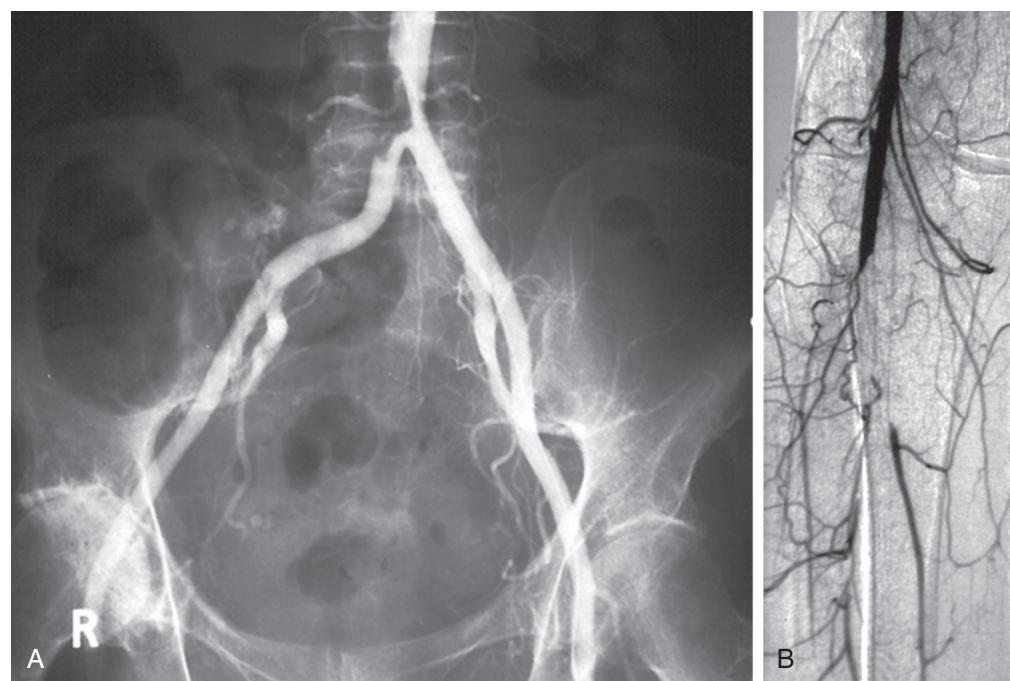
### Noncardiac Embolism

#### Atheroembolism

Another source of embolism is the native arteries themselves. Particularly in patients with extensive atherosclerotic disease in major arteries such as the aortic arch or the descending thoracic aorta, fragments of plaque or adherent thrombus may detach and cause symptoms that mimic cardiac embolism (Fig. 103.3). The embolic material may consist entirely of platelet-rich thrombus, similar to embolism. More sinister are fragments of atherosclerotic plaque that detach (Fig. 103.4); these are more difficult to remove at embolectomy and may irreversibly occlude small distal vessels (see Ch. 164, Portal Hypertension). Atheroembolism may occur spontaneously or may be precipitated by intraarterial manipulation of wires or catheters during cardiac or peripheral arterial interventions.

#### Aortic mural thrombi

Occasionally patients with hypercoagulable conditions develop an aortic mural thrombus in the absence of aortic pathology, which then embolizes to a limb. This should be suspected in a patient without atherosclerotic vascular disease and in whom the cardiac evaluation is negative. Although the acutely



**Figure 103.4** Angiogram showing aortic plaque (A) causing distal popliteal thromboembolism (B).

ischemic limb may need urgent treatment, the underlying aortic pathology can often be treated simply by anticoagulation, with resolution of the thrombus.<sup>6</sup>

## Thrombosis

Thrombosis results from blood clotting within an artery, which can be caused by progressive atherosclerotic obstruction, hypercoagulability, or arterial dissection.

### Atherosclerotic Obstruction

Thrombotic occlusion is most commonly the result of progressive atherosclerotic narrowing in peripheral arteries of the leg. Once a stenosis becomes critical, platelet thrombus develops on the stenotic lesion, leading to an acute arterial occlusion. The clinical manifestations are seldom as dramatic as those of embolization, because the progressive process of atherosclerotic narrowing results in the development of robust collateral circulation. Patients with atherosclerosis deteriorate in a step-wise fashion, as thrombosis supervenes on an arterial stenosis. The resulting symptoms of ischemia (usually the acute onset of claudication) improve as collateral vessels expand. Critical ischemia is the end result when this process occurs at multiple levels. Acute stroke or myocardial infarction is the result of atherosclerotic plaque disruption, which may be confirmed by plaque inspection at carotid endarterectomy or autopsy.<sup>7</sup> In the extremities, it is not known whether plaque disruption is a cause of acute-on-chronic arterial thrombosis, because the culpable plaque is rarely available for examination. It is possible, however, that the process of plaque disruption is the etiology in certain cases.

In patients with extensive atherosclerotic peripheral vascular disease, a reduction in cardiac output may produce acute limb ischemia by a global reduction in limb arterial perfusion. For example, if a patient with severe claudication develops a severe intercurrent illness resulting in shock (hypotension/global hypoperfusion), this may precipitate acute critical ischemia in the absence of thrombosis. It is important to recognize this phenomenon because it is the underlying disease, not the leg, that needs urgent treatment.

### Hypercoagulable States

*In situ* vessel thrombosis can also occur in the absence of atherosclerotic disease in states of hypercoagulability, low arterial flow, or hyperviscosity. These hypercoagulable states are associated predominantly with venous thrombosis, but thrombocytopenia in particular can cause arterial occlusion, usually in small vessels. Malignant disease is also linked mainly to venous thrombosis, but several authors have observed an association with acute arterial ischemia.<sup>8</sup> It may be worth screening patients with acute leg ischemia without obvious atherosclerosis for an underlying malignancy. Because the vessel thrombosis is often a marker of advanced malignancy, the outcome in these patients is poor, despite active treatment.

Vascular surgeons occasionally encounter heparin-induced thrombocytopenia, in which a patient on heparin develops progressive vessel thrombosis with a falling platelet count. Other

hypercoagulable conditions that may cause arterial thrombosis and result in acute limb ischemia are discussed in Chapter 40 (Disorders of Coagulation: Hypercoagulable States).

### Vasospasm

Primary Raynaud disease rarely, if ever, causes acute ischemia. Secondary Raynaud's, due to underlying connective tissue disorder, can be acute and may present with digital ischemia. Open revascularization is seldom possible, and the key to a successful outcome is prompt diagnosis and treatment with intravenous or intraarterial infusion of a vasodilator or prostanoïd. Digital ischemia can also follow intraarterial injection, most commonly as a result of inadvertent injection of illicit drugs. Ischemia may be profound and irreversible, particularly if particulate material is injected. Treatment consists of anticoagulation to prevent secondary thrombosis and infusion of thrombolytics, vasodilators, or prostanoïds, as appropriate.

### Aortic Dissection

Another condition that requires a high index of suspicion for diagnosis is aortic dissection, which may involve the aortic bifurcation and give the appearance of iliac artery thrombosis.<sup>9</sup> These patients typically have chest or back pain and may be hypertensive. Another clinical clue is renal failure if the dissection involves the renal arteries. Arterial dissection of other arteries supplying the lower extremity is uncommon but may follow trauma, or could be a sign of underlying fibrodysplasia.

### Bypass Graft Occlusion

Another significant cause of acute limb ischemia is the occlusion of an existing patent bypass graft. Clearly the rate depends on how many bypass grafts exist in a community.<sup>10,11</sup> In areas that are well supplied with vascular services, patients frequently present emergently with graft thrombosis. In the United Kingdom, a national survey in 1996 reported that graft or angioplasty occlusion was responsible for 15% of acute limb ischemia.<sup>12</sup> The diagnosis is usually easy, and the cause is more likely to be thrombosis than embolism. Assessment and treatment are similar to that for native vessel ischemia, but decisions about treatment can be much more difficult because of the variety of options available.

## CLINICAL PRESENTATION

The symptoms caused by vascular occlusion depend on the size of the artery occluded and whether collaterals have developed beforehand. Sudden occlusion of a proximal artery without existing collaterals leads to an acute white leg, whereas occlusion of the superficial femoral artery in the presence of well-established collaterals may be entirely asymptomatic. This is borne out by the number of individuals who are found to have occult femoropopliteal occlusive disease on population screening. Acute ischemia affects sensory nerves first; therefore loss of sensation is one of the earliest signs of acute leg ischemia. Motor nerves are affected next, causing muscle weakness; then skin and finally muscles are affected by the reduction in arterial



**Figure 103.5** Acute Ischemia, Class IIb – Immediately Threatened.

perfusion. This is why muscle tenderness is one of the end-stage signs of acute leg ischemia. Once ischemia is established, the skin's initial pallor becomes dusky blue as capillary venodilatation occurs. At this stage, pressure over the discolored skin leaves it white because the vessels are still empty (Fig. 103.5). The terminal stage of skin ischemia is caused by extravasation of blood owing to capillary disruption; digital pressure over the discolored skin produces no blush. At this stage, the skin is nonviable, and revascularization of necrotic tissue risks compartment syndrome and renal failure without salvaging the extremity (Fig. 103.6).

Historical series of patients with acute leg ischemia reveal a preponderance of embolic occlusion, usually secondary to valvular heart disease; however, this cause has essentially been eradicated owing to modern cardiovascular surgical expertise.<sup>1–3</sup> Today the usual cause of cardiac emboli is atrial fibrillation as a result of ischemic heart disease. This means that the affected population tends to be much older than it was 50 years ago, and patients often have established atherosclerotic disease of the arteries. This can produce the confusing picture of a patient with an embolus as well as peripheral arterial disease. Another effect is the gradual increase in the incidence of acute ischemia as the population ages.<sup>13,14</sup>

## CLINICAL ASSESSMENT

The initial assessment of acute critical ischemia involves an evaluation of both the limb and the patient as a whole.

### History

The initial symptoms depend on the severity of ischemia and can range from incapacitating pain to the sudden onset of mild claudication. Obviously, the more severe the ischemia, the faster the patient seeks medical attention. Severe acute ischemia is usually obvious, with extreme pain and loss of sensation and power in the limb. Less severe ischemia can be difficult to diagnose and may be confused with musculoskeletal pain, sciatica, and other causes of limb discomfort. The



**Figure 103.6** Acute Ischemia, Class III – Irreversible.

duration of symptoms is the most important part of the history; in patients with severe ischemia, irreversible muscle necrosis occurs within 6 to 8 hours if the condition is untreated. Patients with an acute white leg require urgent intervention. The symptoms of sensory loss and muscle pain are evidence of critical ischemia.

The history should include an attempt to define the cause of the ischemia. Historically, patients with emboli had valvular heart disease but no evidence of peripheral vascular disease or other atherosclerotic conditions; however, the presence of atherosclerosis no longer rules out embolism. Patients with acute-on-chronic thrombosis often give a history of prior intermittent claudication in the ipsilateral (or contralateral) leg. A full medical history is important because it may reveal other associated diseases such as diabetes mellitus. Risk factors for atherosclerotic disease should be sought, including smoking, hypertension, hyperlipidemia, and family history.

### Physical Findings

Thorough examination of the leg is fundamental and is used to define the severity of the ischemia. The well-known rule of Ps – pain, pallor, paralysis, pulse deficit, paresthesia, and perishing with cold – remains a good guide to both symptoms and signs. The color of the skin reflects its vascular supply. Marble-white skin is associated with acute total ischemia. Slow capillary refill is a sign that at least a small degree of distal flow is present and runoff vessels are probably patent. Sensation may be lost completely and the foot may be numb, but more often there is loss of fine touch and proprioception, which should be tested specifically. Muscle tenderness, particularly in the calf, is a sign of advanced ischemia. Acute ischemia is associated with the loss of peripheral pulses, which also helps define the level of the occlusion. Palpable normal pulses in the contralateral leg point toward embolism as the cause.

A full vascular examination reveals the level of the occlusion by the loss of arterial pulsation. A strong pulse can, however, mask an occlusion at that level because of the water-hammer effect. Other possible sources of embolization may become apparent, such as aortic or popliteal aneurysm, or cardiac abnormalities such as atrial fibrillation. Patients with acute leg

ischemia are often older adults with multiple comorbidities, and a full physical examination should be undertaken because the final outcome may depend as much on associated conditions as on the severity of the leg ischemia.

Handheld Doppler examination is also a basic part of the examination. Pedal arterial signals may be absent or reduced. The presence of normal biphasic signals excludes major proximal arterial occlusion. Soft monophasic signals are associated with patent distal vessels but proximal arterial occlusion. Absent Doppler signals in the ankle arteries is a poor prognostic sign. The arteries may be patent but with little flow, or they may be occluded with thrombus. In severe ischemia, ankle Doppler pressures are impossible to measure, partly owing to the lack of signal but also because of muscle tenderness. In less severe ischemia, an ankle pressure of 30 to 50 mm Hg can be expected, and an ankle–brachial index of about 0.3 is diagnostic of subcritical acute ischemia. Doppler can also be used to examine the extremity veins. In particular, a lack of a venous signal in the popliteal fossa suggests popliteal venous occlusion, which is a particularly poor prognostic sign in a patient with acute arterial ischemia.

## DIAGNOSIS

Following clinical assessment and classification, the anatomic location of the arterial occlusion can be diagnosed with a high degree of reliability.

### Aortic Occlusion

The diagnosis of an aortic occlusion is usually obvious. Paralysis of the legs is often the presenting feature; patients are unwell, with mottled skin discoloration that often extends above the groin onto the lower abdomen and no palpable extremity pulses. This is a particularly high-risk condition, and urgent treatment is indicated.<sup>15</sup> The kidneys are especially at risk, particularly if the aortic occlusion is due to an aortic dissection. The dissection or occlusion may already involve the renal arteries, in which case the patient presents in established renal failure. Successful revascularization restores the blood supply to a large muscle mass, and the effects of ischemia-reperfusion may cause further renal damage.

### Iliac Occlusion

The findings are similar to those for aortic occlusion, but unilateral. The femoral pulse is lost on the affected side, and mottling usually extends to groin level. Aortic dissection should be excluded if there is time for investigation or if symptoms are suggestive.

### Femoropopliteal Occlusion

Femoropopliteal occlusion is the most common situation in those with acute leg ischemia. The severity of the ischemia depends on whether the profunda femoris remains patent. The symptoms are more severe if the profunda is

involved. Although the femoral pulse may be strongly palpable (owing to the water-hammer effect), the artery may be occluded.

### Popliteal and Infrapopliteal Occlusion

In popliteal and infrapopliteal occlusion, the calf muscles are ischemic with a palpable femoral (and sometimes popliteal) pulse. In young patients, rare diagnoses include popliteal thrombosis due to muscular entrapment or cystic adventitial disease. The most sinister cause is popliteal aneurysm thrombosis or embolization. This diagnosis should be suspected if a generous popliteal pulse is palpable in either leg or there is a nonpulsatile mass in the popliteal fossa of the affected leg. The outcome of this condition is particularly poor, despite aggressive treatment.<sup>16</sup> Chronic embolization of thrombus from within the aneurysm gradually occludes the distal vessels and arterial outflow; the aneurysm then thromboses, leaving no distal arterial targets for revascularization. Tibial embolism is an infrequent diagnosis, because most emboli that produce symptoms are large and obstruct proximal arteries (Fig. 103.7). Very distal emboli can be challenging to treat because the embolectomy catheter is least effective in small distal vessels. Some authors recommend retrograde embolectomy of tibial emboli via pedal arteries.<sup>17</sup>

## CLASSIFICATION OF ACUTE LIMB ISCHEMIA

Acute limb ischemia used to be classified according to cause – thrombosis or embolism – because this had implications for treatment and prognosis. Patients with thrombosis tended to be younger but had a higher risk of major amputation. Patients with emboli tended to be older and had a higher risk of dying after treatment.<sup>18,19</sup> It has become clear that this is not a useful classification, because there is no way of proving definitively whether an occlusion is thrombus or embolus. A more valuable method of classification is based on the severity of the arterial



**Figure 103.7** Distal Ischemia Due to Occlusion of Small Vessels (Acute Blue Toe Syndrome).

ischemia, which is helpful in determining the urgency of intervention and has implications for outcome.<sup>20,21</sup>

The Society for Vascular Surgery and the International Society for Cardiovascular Surgery have published definitions of acute leg ischemia that are valuable for treatment and prognosis (Table 103.1).<sup>22,23</sup> These standards were modified in 2007 by a larger group – the Trans-Atlantic Inter-Society Consensus – which defined acute ischemia as any sudden decrease in limb perfusion causing a potential threat to limb viability.<sup>24</sup> They may be modified again in the future, but they have stood the test of time, and are unlikely to change significantly. The categories of ischemia are based on clinical findings and Doppler measurements, which can be performed at the bedside and are immediately available. In patients with class I ischemia (viable) or acute-onset claudication, intervention, particularly with thrombolysis, may be risky, and there is an argument for conservative treatment consisting of exercise and best medical therapy. In class III or irreversible ischemia, there is no indication to improve the blood supply, which may risk rhabdomyolysis, so the decision is between major amputation and palliative care.

Patients with class II ischemia require intervention, and the distinction between IIa (marginally threatened) and IIb (immediately threatened) is crucial. Any delay in treating the latter risks irreversible muscle necrosis, whereas in patients with IIa ischemia, there is time for investigation and semielective intervention. Class II ischemia encompasses the majority of patients with acute leg ischemia, and it may be helpful to think of class IIa as acute subcritical ischemia and class IIb as acute critical ischemia.<sup>21</sup> As outlined in Table 103.1, the three findings that best differentiate IIa from IIb ischemia are pain at rest, sensory loss, and muscle weakness.<sup>24</sup>

## PATHWAY OF CARE

It seems obvious to state that the outcome for a patient with acute limb ischemia is dependent on how they are treated, and where. The best results occur when patients are treated in a vascular center with 24/7 cover, and a full range of facilities. Recent European guidelines suggest that as soon as the diagnosis is made in a nonvascular center, the patient should be transferred to a vascular center for treatment, particularly if they have IIb acute critical ischemia, where transfer should be emergent.<sup>25</sup>

**TABLE 103.1** Classification of Acute Limb Ischemia

Category	Description/Prognosis	FINDINGS		DOPPLER SIGNALS	
		Sensory Loss	Muscle Weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
b. Immediately	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	Inaudible	Audible
III. Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

From Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg*. 1997;26:517–538.

## INVESTIGATION

Investigation may be valuable in confirming the clinical diagnosis and planning the appropriate treatment for patients with acute ischemia. However, when the limb is immediately threatened, there may be no time for investigation if direct operative intervention is required. It is possible to employ on-table angiography to assist in decision-making in the operating room. It is recommended that patients with acute limb ischemia are treated in a hybrid operating theater with access to the full range of open and endovascular procedures.<sup>25</sup> Time permitting, a number of methods can be used to definitively determine the site and nature of the arterial occlusion.

### Computed Tomographic Angiography

New-generation computed tomography (CT) scanners acquire images at very high speed and are available in most emergency suites. CT angiography has thus become the investigation of choice for urgent investigation of acute arterial ischemia. Intravenous contrast injection with current CT technology provides images that are similar in quality to intraarterial arteriography. The images sometimes require manipulation to produce the best results, but this is an acquired skill of many young vascular specialists. These images are particularly good for aortoiliac occlusions but give adequate information to plan treatment of infrainguinal occlusions. One concern is that the contrast material may have a deleterious effect on renal function, so intravenous fluids should be considered for prehydration at this stage.

### Ultrasound

Imaging with duplex ultrasonography is the mainstay of investigation for chronic arterial ischemia. It may not be available in all hospitals after hours, but it can be employed in cases of acute ischemia to define the level of the arterial occlusion and the patency of other vessels. Portable ultrasound machines may permit rapid, bedside imaging by vascular specialists trained in duplex imaging.

### Transfemoral Arteriography

Arteriography was the mainstay of investigation for acute leg ischemia, but has become redundant for diagnosis as a result



**Figure 103.8 Angiogram Showing Popliteal Embolus.** Note the meniscal-type cutoff, with no existing collaterals.

of the wide availability of CT angiography 24/7 in most hospitals. Its main use is to confirm the diagnosis at the start of an endovascular intervention. Brachial puncture can be used in the absence of femoral pulses. The angiogram confirms the level of occlusion and may provide further evidence of the cause. Thrombotic occlusion is likely if there are established collateral arteries and evidence of arterial atherosclerosis. Sometimes emboli can be seen in several vessels, establishing the diagnosis (Fig. 103.8). Following angiography, thrombolysis, percutaneous thrombectomy, angioplasty, or stenting can be employed.

### Magnetic Resonance Angiography

Magnetic resonance angiography with gadolinium enhancement is less useful than either CT or ultrasound in the context of acute limb ischemia. It is often unavailable out of hours, takes time for images to be acquired, and is generally inconvenient for sick patients.

### Echocardiography

Debate continues about the role of echocardiography. In practical terms, the investigation seldom alters management, because most patients are anticoagulated for life after successful treatment for acute ischemia. Some surgeons, however, regard the investigation as a vital part of the postoperative management. There are certainly some conditions that require

echocardiography to make a diagnosis, such as valvular disease (including vegetations), septal defect, and cardiac tumor. Problems associated with the routine application of echocardiography include the variability in results between transthoracic and transesophageal techniques and among different technicians, the inability to visualize the left atrial appendage, the fact that failure to visualize the source of an embolus does not rule out its existence, and the test's lack of influence on overall management.<sup>26</sup> A pragmatic view would be that echocardiography is indicated in young patients, after initial intervention for acute limb ischemia, and in those in whom a cardiac diagnosis is suspected, or when the results might affect decisions about long-term anticoagulation.<sup>27</sup>

## INITIAL MANAGEMENT

Once the diagnosis of acute ischemia has been established and its severity classified, a number of immediate interventions are possible. These are discussed briefly here and addressed in greater detail in Chapter 104 (Acute Limb Ischemia: Surgical and Endovascular Treatment).

### Anticoagulation

The threat to the limb escalates with secondary thrombosis of underperfused distal vessels, particularly in patients with emboli. Therefore, immediate anticoagulation with intravenous calcium heparin can stabilize the condition of the leg and prevent deterioration. Whereas low-molecular-weight heparin is a valuable therapy for many conditions, the potential for immediate reversal with protamine makes calcium heparin the drug of choice in this situation. Protocols using a weight-based bolus and infusion rates facilitate rapid therapeutic anticoagulation. If urgent operation is not undertaken, the infusion should be monitored using the activated partial thromboplastin time, aiming for a ratio of 2 to 3. It is vital not to assume that anticoagulation is being achieved while heparin is being administered; there is a wide variation in response to the drug, and careful monitoring by protocol is needed.

### Ancillary Supportive Measures

A number of other measures have been shown to be beneficial in patients with acute limb ischemia and are recommended in recent guidelines.<sup>25</sup> These include the use of oxygen delivered by facemask which in a small study improved skin perfusion, even in the ischemic limb.<sup>28</sup> Patients with acute ischemia are often dehydrated and at risk of renal dysfunction, so an intravenous infusion of fluid and monitoring of urine output is appropriate. Many radiologic maneuvers involve the use of contrast agents that can damage the kidneys, and adequate renal perfusion is important. As part of the diagnostic workup, a full blood screen for blood urea nitrogen and a full blood count are indicated. In patients with recurrent thrombosis, a thrombophilia screen should be performed at this stage, if indicated, because

therapeutic anticoagulation renders these investigations inaccurate.<sup>29,30</sup> These tests are indicated in patients with a strong family history of arterial and venous thrombosis or those with recurrent disease.<sup>31,32</sup> Patients are often in severe pain, and adequate analgesia is important. Intramuscular opiates are contraindicated in a patient who may receive thrombolysis, and patient-controlled intravenous analgesia is a good alternative.

## TREATMENT

### Options

Once the initial assessment is complete, a decision should be made about the intervention required and its timing. The following options are available: anticoagulation alone, operative intervention, and endovascular intervention via mechanical thrombectomy or thrombolysis.

#### Anticoagulation

Heparin anticoagulation has no direct thrombolytic effect; it is used to stabilize clot formation and prevent further secondary thrombosis. Use of anticoagulation alone as a treatment implies that the limb is likely to remain viable or that other therapeutic options are limited, perhaps by age or comorbidity. Before anticoagulants were available, treatment of acute leg ischemia was largely expectant, and historical series documented high morbidity and mortality rates, despite amputation.<sup>33</sup> Heparin and then warfarin made an immediate impact after their introduction.<sup>34,35</sup> Anticoagulation for stable class I ischemia, followed several weeks later by intervention (usually endovascular) if collaterals do not become established, is safe and effective. Anticoagulation has been shown to improve results after embolectomy.<sup>36</sup> In class III irreversible ischemia, anticoagulation is still indicated, since it allows stabilization of the limb, pending major amputation at a later date. Otherwise, anticoagulation may be a component, but does not constitute definitive treatment for acute leg ischemia.

#### Open Surgical Intervention

After Fogarty et al. described the embolectomy catheter for the remote removal of a clot via a groin incision in 1963, surgery became the main treatment for acute leg ischemia.<sup>37</sup> Over the years, the pattern of disease has changed, and emboli now occur in patients with ischemic heart disease, often in association with peripheral vascular disease. Thus the embolectomy procedure has become more complicated, and the results are inferior in patients who may have an acute thrombosis.<sup>38,39</sup> Increasingly, surgical bypass techniques are required in this situation, and a modern vascular surgeon should be able to offer a full range of bypass and endovascular procedures to patients with acute leg ischemia in a specialized environment to achieve optimal outcomes.<sup>40</sup>

#### Endovascular Intervention

Endovascular interventions offer an expanding range of alternative treatments for acute limb ischemia. Options include

mechanical thrombectomy with homemade (aspiration embolectomy) or commercially available custom-built devices. In expert hands, mechanical thrombectomy can yield good results in selected patients, particularly those with bypass graft occlusions. If unsuccessful, it can be followed promptly by surgical intervention or thrombolysis.<sup>41,42</sup>

Percutaneous thrombolysis is also an established intervention for all forms of acute arterial occlusion (see Ch. 38, Normal Coagulation). A potential advantage of thrombolysis is that unlike surgical embolectomy, which simply removes the thrombus from the large arteries, thrombolysis lyses clot in both large and small arteries and arteriolar and capillary beds.<sup>43</sup>

### Selection

The choice of intervention depends on the available expertise and the severity of the leg ischemia.<sup>44</sup> The most recent evidence summaries<sup>41,45,46</sup> and an updated Cochrane review<sup>47</sup> found little difference in outcomes to guide treatment selection between surgery and endovascular treatments, including thrombolysis. A recent review of the Swedvasc registry suggests a trend towards lower mortality after initial endovascular treatment with no adverse effect on the amputation rate.<sup>48</sup> There is a suggestion that endovascular first treatment may be more expensive overall.<sup>49</sup> Even in modern series, open vascular intervention for acute limb ischemia carries a significant risk of major morbidity (20%) or limb loss (22%).

Treatment should be guided by the severity of the limb ischemia. Patients with stable acute ischemia (Rutherford class I) who develop acute-onset claudication may be managed safely with anticoagulation alone, and intervention reserved for once the acute phase is over.<sup>50</sup> Patients with acute critical ischemia (class IIb) have most to gain from emergent treatment in a hybrid operating theatre, where a full range of open surgical or endovascular options should be available at a single setting.<sup>25</sup> If endovascular treatment is selected, there should be no delay. Percutaneous thrombectomy is a valuable option in cases where expertise exists. Low-dose intraarterial thrombolysis is contraindicated because it usually takes 12 to 24 hours to be effective. Accelerated thrombolysis may be an option in experienced units, using either high-dose bolus infusion techniques<sup>51</sup> or pulse spray thrombolysis.<sup>52</sup>

The treatment for stable (class IIa) acute ischemia should be individualized, given the number of options and the greater time available for deliberation. These decisions are often best made by multidisciplinary teams reflecting local expertise.<sup>51</sup> Obvious emboli may be treated most appropriately by embolectomy. With this exception, the primary alternative to surgery for class IIa ischemia is intraarterial thrombolysis, with or without adjunctive mechanical thrombectomy. There has been much debate about the advantages and disadvantages of thrombolysis versus a surgical approach, and a number of large randomized trials have compared the two modalities.<sup>53</sup> Whereas the NATALI prospective database reported good results from enthusiastic centers,<sup>54</sup> recent meta-analyses have failed to find systematic differences between therapies, and recent guidelines suggest surgical and

endovascular interventions are all reasonable options.<sup>25</sup> If a good surgical option exists, this may be best in a fit patient. Many patients with acute leg ischemia are in poor general health and at high risk of complications following operative intervention, particularly if general anesthesia is required. Thrombolysis is particularly indicated when the surgical options are poor and the runoff vessels in the leg appear occluded. Results of thrombolysis are poor if high risk patients are selected for treatment.<sup>55</sup>

## Prognosis

The medical state of a patient who presents with acute leg ischemia is a good prognostic index of survival.<sup>56</sup> In particular, patients with acute myocardial infarction or poor cardiac output have a high mortality rate.<sup>57,58</sup> Outcome can also be predicted from pretreatment POSSUM (Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity) physiology scores.<sup>59</sup> Despite active intervention, the outcome after treatment for acute limb ischemia is often poor. In some patients, limb ischemia is a manifestation of the end of life. Such agonal thrombosis may be recognized in the very elderly with multiple comorbidities, particularly in hospitalized patients,<sup>60</sup> and is an indication for palliative care rather than active intervention.<sup>61</sup> Another very high-risk group in whom palliation might be appropriate is patients with acute ischemia due to hypercoagulable blood as a consequence of advanced malignancy. Active intervention should not be denied as initial outcomes are reasonable, but prognosis is dependent on cancer stage, which is usually advanced; most of these patients succumb from their cancer within 6 months, even if treated actively.

## UPPER LIMB ISCHEMIA

A number of significant differences exist between acute ischemia of the arm and leg. Patients with acute arm ischemia tend to be, on average, about 4 years older than those with acute leg ischemia (mean age, 74). Arm ischemia seldom threatens the limb, and treatment decisions are less urgent.<sup>62,63</sup> The main reason for treating arm ischemia is to prevent late complications such as activity-induced arm fatigue and pain.<sup>64</sup> Most arm ischemia is due to cardiac embolism (Fig. 103.9); atherosclerosis is rare in upper limb arteries.

Patients often present with a cold feeling and numbness rather than pain in the arm. The diagnosis is clinical and can be confirmed by duplex imaging. Imaging is recommended unless the arm is immediately threatened and an axillary or brachial pulse is easily palpable (when urgent intervention is needed). In the stable situation, the arm often improves after initial anticoagulation, and decisions about whether to perform embolectomy can be difficult. Up to 50% of patients have late symptoms of arm pain if untreated. Intervention should be considered if the arm is threatened or if future limb function is important to quality of life, such as involvement of the dominant hand. Brachial embolectomy should usually be done under local anesthesia, but with an anesthetist present to monitor the patient's condition, and to administer analgesia or sedation, as required.<sup>64</sup> Endovascular options are now being



**Figure 103.9** Acute arm ischemia due to brachial embolus of cardiac origin (same patient as in Fig. 103.2).



**Figure 103.10** Failed embolectomy with wound dehiscence resulting in ischemic contracture.

offered to an increasing number of patients with upper limb ischemia.<sup>65</sup> A small number of patients present with class IIb critical ischemia and should undergo urgent intervention.<sup>63</sup> Failed surgery in this situation risks ischemic contracture (Fig. 103.10) or even arm amputation on occasion. The threat to the arm is generally low, but up to 20% of patients with acute arm ischemia do not survive the acute event, usually owing to cardiac complications.<sup>66</sup> Like acute leg ischemia, the attrition rate after successful treatment is high; only 60% of patients survived 3 to 5 years in one typical series.<sup>66</sup>

Rare causes of arm emboli include thoracic outlet syndrome and proximal subclavian artery aneurysm. Arteriovenous fistulae for dialysis may also cause a number of complications, including thrombosis and aneurysm formation.

## EFFECT OF THE COVID-19 PANDEMIC

The pandemic has changed how healthcare systems have functioned worldwide, but it is recognized that vascular thrombotic events are a feature of severe forms of the disease. A recent review suggests that the incidence of acute limb ischemia has not risen, but that management of the condition in patients with

COVID-19 may be more problematic. Younger patients may be affected, and outcomes appear inferior in infected patients. Standard methods of care remain relevant, but three additional measures are recommended for patients with acute limb ischemia and COVID-19: (1) CTA imaging before revascularization should include the entire aorta and iliac arteries; (2) there should be a high index of suspicion, early testing for COVID-19 infection, and protective measures are advised; and (3) there should be preferential use of local or locoregional anesthesia during revascularization. In addition, high-risk patients should receive thromboprophylaxis, which may reduce the rate of both arterial and venous thrombotic events.<sup>67</sup>

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# Acute Limb Ischemia: Surgical and Endovascular Treatment

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Acute limb ischemia (ALI) is an emergent vascular condition, wherein a rapid decrease in lower extremity arterial perfusion threatens limb viability.<sup>1</sup> Despite advances in the prompt diagnosis and surgical management of limb ischemia, the reported rates of limb loss with amputation approach 15% of hospitalized patients, with a 15%–20% mortality rate within one year of diagnosis.<sup>2,3</sup> The etiologies of ALI, initial clinical evaluation, and medical decision-making are reviewed at length in previous chapters. This chapter presents the open surgical and endovascular therapeutic options in management of acute limb ischemia, with a therapeutic algorithm provided to assist treatment selection.

## **INITIAL MANAGEMENT**

After establishing the diagnosis and classifying the severity of ischemic insult, several perioperative measures critical to patient outcomes are enacted. Systemic anticoagulation should be initiated immediately upon confirmation of ALI and considered earlier in the diagnostic work-up if a high clinical suspicion of limb ischemia exists. Subset analysis of a randomized trial examining use of antiplatelet agents in peripheral arterial disease illustrated several clinical risk factors associated with ALI.<sup>4</sup> The study noted previous revascularization ( $P < 0.01$ ), baseline atrial fibrillation ( $P = 0.03$ ), and baseline ankle–brachial

index lower than 0.6 ( $P < 0.01$ ) as clinical factors associated with higher risk of ALI. Anticoagulation maintains patency to distal vascular beds and helps reduce the risk of further arterial thromboembolic occlusion. An initial weight-based bolus of unfractionated heparin 70–100 units/kg is followed by a continuous intravenous infusion of 1000 units/h. If an emergent intervention is not planned, heparin dosing should be titrated with bolus as required to maintain either an activated partial thromboplastin time (aPTT) at two to three times above normal range or an anti-factor Xa level in therapeutic range. For patients with known heparin allergy, a direct thrombin inhibitor can be substituted as systemic anticoagulant with established protocols for both perioperative and intraoperative use.

Perioperative lab evaluation should include complete blood count, coagulation studies, basic or complete metabolic panel, baseline serum fibrinogen for patients with arterial thrombolysis as part of the treatment strategy, blood type and cross-matching. In patients with recurrent thromboembolic events or idiopathic arterial occlusion, a full hypercoagulability workup is warranted. Arterial blood gas for measurement of acid–base balance and a baseline creatine phosphokinase (CPK) level to monitor ischemic-reperfusion injury are also valuable adjuncts. Ongoing fluid resuscitation is key to mitigating secondary systemic organ insults as revascularization for ALI is associated with intravascular volume depletion

following the inflammatory response of ischemia–reperfusion injury, as well as myoglobinuria and contrast-induced acute kidney injury.

## TREATMENT SELECTION

### Therapeutic Algorithm

The acuity of symptom onset and clinical manifestation of limb ischemia guides treatment strategies. Reporting standards for ALI exist to guide timing and choice of intervention (see Table 103.1).<sup>5</sup> The reported success of open and endovascular therapies for each level of acute ischemia also allows for creation of a therapeutic algorithm (see [Chapter Algorithm](#), below for guidance).

Class I ischemia is a viable limb, wherein the arterial occlusion has not compromised sensorimotor function and distal perfusion is maintained via collateral pathways. As the limb is not immediately threatened a window of time does exist to allow for completion of diagnostic studies, medical optimization of comorbidities and appropriate risk stratification. If revascularization is elected, patient and anatomic candidacy for an endovascular-first approach should be assessed. Viable tissue beds are more likely to tolerate the delayed time to reperfusion inherent to endovascular therapies in this minimally ischemic class.

The category of class II ischemia represents threatened limbs, mandating timely revascularization for limb salvage. The class is subdivided into marginally (IIa) and immediately (IIb) threatened limbs based on severity of ischemic neurologic deficits, with prompt and accurate characterization key to guiding revascularization. In the marginally threatened limb (IIa), a less severe ischemic insult allows for greater consideration of an endovascular-first approach. Etiology of arterial occlusion, patient comorbidities, presence of an arterial bypass graft or intraluminal stent, physician competency with endovascular therapies, and emergent availability of operative suites and vascular surgeons for failed endovascular intervention should all be considered in decision making. With progression in extent of sensory and motor neurologic deficits, ALI is classified as immediately threatened (IIb) and requires emergent revascularization. At this level of ischemia salvage of neurologically intact viable tissue is time-sensitive, favoring traditional open revascularization. An endovascular approach with more rapid means of revascularization, including aspiration or pharmacomechanical thrombectomy devices, may be considered for the skilled operator. An endovascular-first attempt for class IIb ALI is best suited for a vascular surgeon with proficiency in open and endovascular techniques, performed in an operative hybrid suite where advanced diagnostic imaging and ability to immediately transition to an open revascularization increases technical success of the limb-salvage intervention.

In the most severe class of ALI (III), primary limb amputation should be elected as definitive therapy. The profound extent or duration of limb ischemia results in irreversible damage to nerve sensory and motor function, and muscle rigor with

limb paralysis. Revascularization in this class is most often unsuccessful in salvaging a neurologically functional limb, with the risks of systemic insults and morbidity after attempted revascularization far exceeding potential benefits.

## SURGICAL REVASCULARIZATION

Surgical revascularization remains an effective strategy for management of limb ischemia, regardless of ischemic class. Vascular surgeons should develop and maintain advanced skills in the open surgical techniques as they can be utilized as primary therapy for ALI, in salvage-type settings when endovascular therapy has failed or been incomplete, or in hybrid interventions with planned or staged open and endovascular segments.

### Operative Techniques

Surgical revascularization for limb ischemia may include one or more of the following: (1) catheter embolectomy or thrombectomy; (2) arterial bypass procedures; (3) arterial thromboendarterectomy; (4) hybrid vascular procedures with open and endovascular components.

#### Catheter Embolectomy or Thrombectomy

First reported nearly six decades ago, the Fogarty embolectomy catheter (Edwards Lifesciences; Irvine, CA) has been the *de facto* gold standard for surgical extraction of acute and chronic thromboembolic disease.<sup>6,7</sup> Fogarty catheters are available in a variety of usable lengths, catheter French (F) size, inflated balloon diameters, with options designed for over-the-wire, arterial, venous, and bypass graft thrombectomy use. Vascular arterial exposure and basics of surgical technique are covered in previous chapters. The site of surgical cutdown for arterial exposure is dependent on the anatomic location of obstruction. An iliac or femoral arterial obstruction may be best approached via exposure at the common femoral level, while patients with distal bypass graft or concomitant popliteal–tibial level thrombosis may also require exposure at the most distal extent of arterial blockage. Following arterial exposure with control of inflow and outflow branches, therapeutic anticoagulation is confirmed, and vascular occlusion performed. An arteriotomy is made either transverse just proximal to branch points, or longitudinal if needed for endarterectomy or bypass graft anastomotic revision. Balloon thrombectomy catheters are sequentially passed proximally and then into distal branches with standard technique until no visible thrombus is removed, and both pulsatile inflow and distal back-bleeding are restored. On-table angiogram should be performed to confirm patency of treated vessels. [Figure 104.1](#) shows the completion angiogram in a patient treated with catheter thrombectomy for acute limb ischemia. The patient had undergone emergent bedside percutaneous placement of cannula for extracorporeal membrane oxygenation (ECMO) one day prior to operative exploration and had developed clinical signs of ALI within 24-hours post-procedure. Operative exploration



**Figure 104.1** Preoperative CTA (A) demonstrating thrombosis of left superficial femoral artery (SFA) and popliteal artery (yellow arrows). Post-thrombectomy angiogram (B–D) showing patency from femoral to popliteal bifurcations.

revealed cannulation at the proximal superficial femoral artery (SFA) with focal dissection of calcific plaque at the level of the femoral bifurcation, and extensive acute thrombotic occlusion of SFA and above-knee popliteal artery. Revascularization required femoral exploration, femoral–popliteal antegrade balloon thrombectomy, focal femoral bifurcation endarterectomy with bovine pericardial patch angioplasty. Repair resulted in restoration of in-line arterial flow and palpable pedal level pulses, with angiogram confirming patency of vessels without residual thrombus.

### Arterial Bypass

Arterial bypass surgery for ALI is more commonly performed in the setting of failed or incomplete catheter thrombectomy, as secondary intervention after failure of an endovascular-first approach, or in patients with known peripheral arterial disease experiencing acute-on-chronic arterial thrombosis wherein bypass offers better long-term limb salvage.<sup>8</sup> The same tenets apply for bypass surgery for acute ischemia as in chronic disease. Preparation for bypass graft surgery should include the use of contrast-enhanced CT or conventional angiogram to identify proximal and distal anastomotic sites, ensuring adequate arterial inflow and outflow for bypass graft patency, and utilizing the best available conduit to maximize long-term patency. A review from the Vascular Study Group of New England sought to report the contemporary outcomes of bypass surgery for ALI.<sup>9</sup> Between 2003 and 2011 the group identified 5712 lower extremity bypass

procedures performed, with 323 (5.7%) for acute ischemia. This retrospective review of a prospective database did not allow for determination of embolic or thrombotic etiology, or if bypass performed after an attempt of arterial thrombolysis or surgical thrombectomy. Primary end points of 1-year bypass graft patency, major amputation, and mortality were analyzed with comparison of the bypass graft in ALI cohort versus bypass graft for all other indications. Patients with ALI were found to be less likely on aspirin (63% vs. 75%,  $P < 0.0001$ ) or statin (55% vs. 68%,  $P < 0.0001$ ) medications, more often current active smokers (49% vs. 39%,  $P < 0.0001$ ), and more likely to have had failed prior ipsilateral bypass (33% vs. 24%,  $P = 0.004$ ) or endovascular therapies (41% vs. 29%,  $P = 0.001$ ). Other statistically significant factors for bypass with ALI included longer procedure duration ( $P = 0.007$ ), greater blood loss ( $P < 0.0001$ ), greater use of prosthetic conduits ( $P = 0.003$ ), and increased rates of in-hospital major adverse cardiovascular events ( $P < 0.0001$ ). At 1 year, no difference in bypass graft patency was observed between cohorts (18.1% vs. 18.5%,  $P = 0.77$ ), but patients who underwent bypass for ALI did possess increased rates of major limb loss (22.4% vs. 9.7%,  $P < 0.0001$ ) and mortality (20.9% vs. 13.1%,  $P < 0.0001$ ). The study highlights the role of poor compliance with risk factor management as a contributing factor in limb ischemia requiring bypass, references the data supporting worse outcomes with decreased limb salvage rates when bypass is performed for failed endovascular therapy,<sup>10–12</sup> and that comparable bypass patency rates do not translate to improved limb salvage.<sup>13</sup>

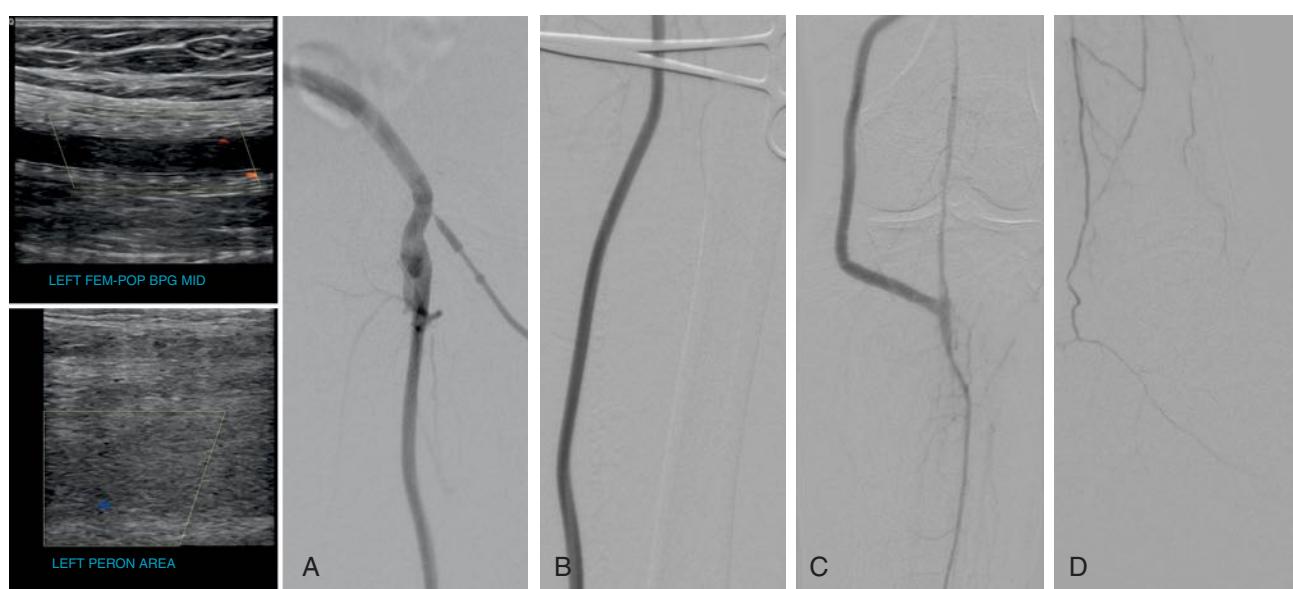
## Thromboendarterectomy and Hybrid Procedures

Arterial endarterectomy is rarely an isolated intervention for acute limb ischemia but may be the sole procedure required in cases of native common femoral artery acute *in situ* thrombosis or chronic atherosclerotic disease. Endarterectomy is often required in limb salvage cases to improve either arterial flow to collateral outflow tracts, or to improve bypass graft anastomotic proximal inflow or distal outflow. Figure 104.2 demonstrates management of acute bypass graft and native arterial thrombosis. The patient presented with clinical signs of acute limb-threatening ischemia with duplex demonstrating thrombosis of bypass graft, below-knee popliteal distal anastomotic site and the single-vessel peroneal runoff. Bypass graft patency was restored with traditional Fogarty balloon and novel graft thrombectomy catheters. Limb salvage required repeat common femoral endarterectomy to improve graft inflow, distal prosthetic graft interposition, popliteal and peroneal thrombectomy, with extended popliteal–tibioperoneal trunk endarterectomy with patch angioplasty to improve distal outflow. Completion angiogram illustrates technical success of multiple revascularization techniques in restoring flow through the peroneal outflow tract, with collateral reconstitution of posterior tibial artery at the level of the medial malleolus. Hybrid revascularizations, combining open and endovascular techniques, are useful for limb ischemia management when failure of an endovascular component accounts for at least part of the ischemic symptoms. Figure 104.3 illustrates a hybrid revascularization. The patient had undergone multiple interventions at an outside facility and was transferred to our institution with acute ischemic symptoms. Malposition of SFA stents across the origin of the profunda led to diminished flow and eventual thrombosis from chronic in-stent intimal hyperplasia, which then served as nidus for ipsilateral iliac artery outflow obstruction and subsequent

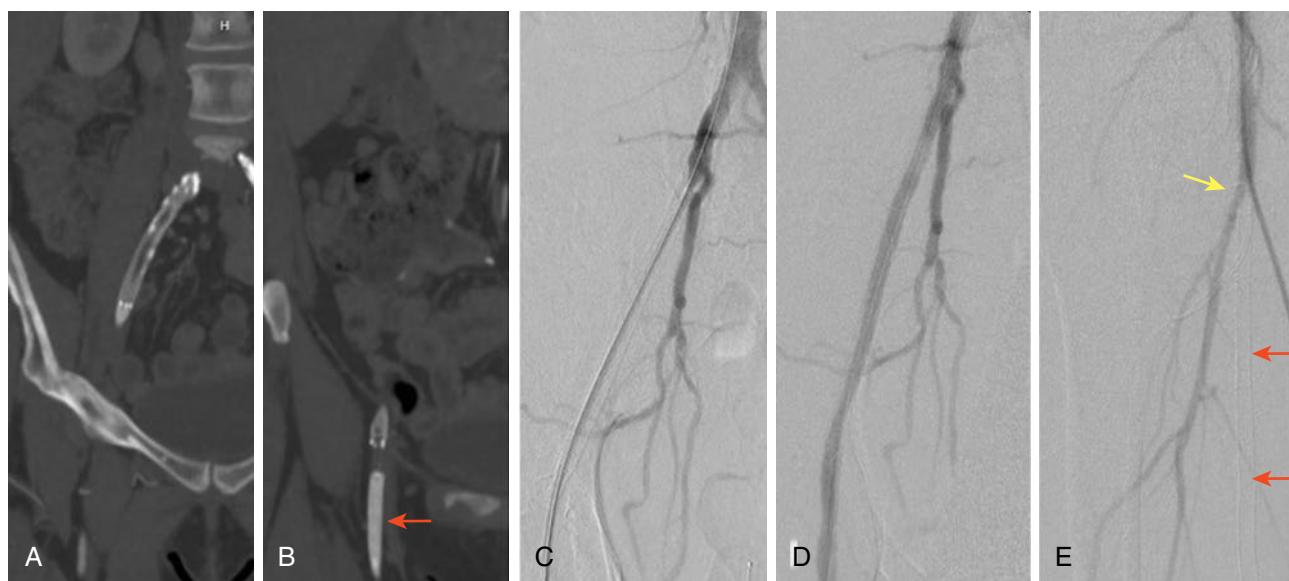
iliac stent thrombosis. Limb salvage utilized multiple surgical techniques including femoral–profunda endarterectomy with explant of the proximal SFA stent covering profunda origin, retrograde cannulation and catheterization of iliac arteries, attempt of over-the-wire thru-lumen thrombectomy catheter for iliac stent thrombosis, with repeat iliac artery stent placement. Angiogram confirmed brisk pulsatile flow in iliofemoral segment with restored patency of profunda providing robust collateral flow to lower leg popliteal and tibial outflow tracts.

## Results

Long-term outcomes for surgical revascularization of acute limb ischemia remain poor, even with advances in vascular diagnostic and therapeutic measures. As referenced earlier,<sup>9</sup> bypass surgery for ALI is associated with increased 1-year major limb loss (22.4%) and mortality (20.9%), as compared to bypass surgery for chronic occlusive disease. Single-center and population-based samples alike have reported similar heightened rates of morbidity and mortality. Kempe et al. published a 10-year experience with surgical management of ALI from arterial embolization, excluding arterial bypass or stent occlusions, with comparable rates of 90-day major limb loss (15%) and in-hospital or 30-day mortality (18%).<sup>14</sup> At 5 years, freedom from amputation was 80%, with an overall survival of only 41%. Severity of Rutherford class ischemia was directly associated with major limb amputation ( $P < 0.0001$ ) and mortality ( $P < 0.0286$ ). On a larger scale, a review of the National Inpatient Sample database from 1992 to 2000 identified 23,268 patients with discharge diagnosis of acute embolism and thrombosis of the lower extremities.<sup>15</sup> Nearly half (47.3%) of all patients underwent embolectomy for management of limb ischemia, with similar rates of major limb amputation (12.7%) and mortality (9.3%) reported of all treated. Maximal occurrence of both major



**Figure 104.2** Preoperative duplex (left) showing thrombosis of left femoral–popliteal bypass graft and peroneal artery outflow. Completion angiogram (A–D) demonstrating restoration of patency to bypass following graft thrombectomy and revision, with peroneal artery runoff and collateral reconstitution of posterior tibial artery.



**Figure 104.3** Preoperative CTA illustrating thrombosis of right iliac artery stents (A), and profunda origin occlusion from malposition SFA stent (B, red arrow). Re-canulation of iliac stents for attempt of over-wire thrombectomy (C), and patency restored with repeat stent placement (D). Angiogram confirmation (E) of restored patency to profunda (yellow arrow), and presence of residual thrombosed SFA stents (red arrows).

limb amputation and mortality were noted between 1993 and 1997, with rates of amputation (20%–25%) and death (10%–13%) comparable with large population-based studies.<sup>16–19</sup> The imperfect mortality and survival in management of patients with ALI is reflective of the challenges inherent to revascularization on patients with advanced cardiopulmonary comorbidities, and thus more susceptible to the end-organ physiologic stress with ischemia-reperfusion injury.

## ENDOVASCULAR THERAPIES

The refinement of endovascular technology has allowed for the development and application of therapies specific for limb ischemia. The primary goal of any endovascular intervention for ALI remains the same as in open surgical techniques, being the rapid clearance of clot burden for restoration of normal arterial perfusion. Endovascular therapies may include any one of the following core groups: (1) catheter-directed thrombolysis (CDT); (2) pharmacomechanical thrombectomy (PMT); or (3) mechanical thrombectomy (MT). The lower peri-procedural morbidity inherent to less invasive techniques may provide an alternative path to limb reperfusion in patients otherwise unable to safely undergo traditional surgical revascularization. With ALI from thrombosis of chronic atherosclerotic disease endovascular therapies can reveal the responsible lesion and allow for the performance of the most anatomically appropriate revascularization, be it endovascular or open surgical.

### Catheter-Directed Thrombolysis

Catheter-directed thrombolysis (CDT) remains a highly utilized therapy for management of viable (class I) and marginally threatened (class IIa) ALI. The procedure can be used for

acute embolism or thrombosis of native arterial atherosclerotic lesions, autogenous vein and prosthetic bypass grafts, as well as intraluminal stents. Thrombolysis is catheter-directed to minimize systemic effects, though contraindications do exist for use in patients at heightened risk of hemorrhagic complications from the systemic proteolysis inherent with treatment (Box 104.1).<sup>20–23</sup> Clinical judgment and operator experience must guide the use of thrombolytic agents to maximize benefits against risks, and minimize potential hemorrhagic complications. The technical aspects for arterial access, diagnostic imaging, and crossing occlusive lesions are similar for all endovascular therapies.

We prefer a retrograde contralateral femoral approach for initial access as it allows placement of diagnostic catheters in patent vessels proximal to thrombus. Antegrade access is acceptable, and at times anatomically required, though care must be taken to minimize entrance and disruption of thrombus while obtaining access. A micro-puncture access kit and ultrasound guidance should be mandated to ensure cannulation of the true common femoral artery, with hand-held injection of contrast via access sheath recommended to confirm cannulation site prior to sheath upsizing. The access system is upsized to a short 5-F sheath, and a diagnostic aortogram with selective lower extremity angiogram completed. Lower extremity runoff should be performed prior to crossing the occlusion to mark points of collateral reconstitution, potential distal anastomotic site if bypass is required, as well as to define tibial outflow patency. Once a decision is made to attempt endovascular therapy the patient is anticoagulated and a 45- or 55-cm 6-F delivery sheath is placed up and over the aortic bifurcation; delivery sheaths increase support for recanalization, and provide a more stable platform for indwelling lytic catheters. The basic combination of a 0.035-inch angled Glidewire

**BOX 104.1****Contraindications to Pharmacologic Thrombolytic Agents****Major Contraindications**

Active bleeding disorder  
Gastrointestinal bleeding within 10 days  
Cerebrovascular accident within 6 months  
Intracranial or spinal surgery within 3 months  
Head injury within 3 months

**Relative Major Contraindications**

Major surgery or trauma within 10 days  
Hypertension (systolic >180 mmHg or diastolic >110 mmHg)  
Cardiopulmonary resuscitation within 10 days  
Puncture of noncompressible vessel  
Intracranial tumor  
Pregnancy  
Diabetic hemorrhagic retinopathy  
Recent eye surgery  
Hepatic failure  
Bacterial endocarditis

(Terumo Interventional Systems, Somerset, NJ) with an angled or straight 4-F Glidécath catheter (Terumo Interventional Systems) is often adequate to cross an acute occlusion. The ease with which a guide wire passes through a thromboembolic occlusion (“guide wire traversal test”) does correlate with technical success of CDT.<sup>24</sup> We routinely use the 0.035-inch Glidewire Advantage (Terumo Interventional Systems) as the sole treatment wire as the distal 25-cm traditional Glidewire tip and remaining stiffer nitinol core with spiral PTFE coating provides a durable, steerable, support wire with exchange-length abilities. Catheter support can be improved with use of a 0.035-inch CXI support catheter (Cook Medical, Bloomington, IN) alone or coaxially with 0.018- or 0.014-inch systems (Cook Medical), or with use of Navicross support catheters (Terumo Interventional Systems). After crossing the occlusion aspiration of blood from the catheter suggests post-thrombus position, and a distal angiogram is performed to confirm true lumen and distal patency. The support catheter is then exchanged for an 0.035-inch compatible infusion catheter. Our preference is to use a Uni-Fuse Infusion Catheter (Angiodynamics, Latham, NY) as both 4-F and 5-F systems are available with multiple combinations of working and infusion lengths (Table 104.1). The multiple pressure-response outlet slits and occluding ball wire provides even lytic distribution throughout thrombus. Radiopaque markers help position the catheter just distal to thrombus endpoint, and just proximal to thrombus origin. The available thrombolytic agents and their mechanism of action are discussed in previous chapters. Recombinant tissue plasminogen activator (rtPA) (Alteplase, Genentech, Inc, South San Francisco, CA) is the lytic agent used in the United States. We utilize a low-dose regimen protocol with a 2- to 4-mg initial bolus, followed by a continuous infusion of 1 mg/h over a 10- to 12-hour period. Interval angiogram is performed the next day, or at any instance of clinical decline. Fibrinogen levels and coagulation parameters should be monitored every 4 hours

during lytic therapy, with a decrease in fibrinogen level guiding either rate reduction to 0.5 mg/h (fibrinogen <200 mg/dL) or therapy cessation (fibrinogen <100 mg/dL). Heparin infusion at a fixed rate of 500 units/h is instilled through the delivery sheath side port to prevent thrombosis. Figure 104.4 illustrates results of a Uni-Fuse catheter for limb salvage in a patient with acute thrombosis of a cryo-preserved vein bypass graft. Thrombolytic infusion restored patency to the bypass graft and tibial outflow tract.

**Results**

To date, five randomized controlled trials and several high-quality retrospective reviews have reported the technical success of CDT as compared to surgical thrombectomy.<sup>25–34</sup> In 1992, Nilsson et al. published the first randomized trial of CDT versus thrombectomy.<sup>25</sup> Twenty patients with ALI symptom onset between 1 and 14 days were randomized to surgery ( $N = 9$ ) or thrombolysis ( $N = 11$ ). Surgical thrombectomy was performed under epidural anesthesia, with thrombolysis patients receiving 30 mg rtPA via catheter infusion over a 3-hour period. Surgical thrombectomy was successful in five of nine patients, with CDT alone effective in four of eleven; additional procedures were required in patients of each treatment arm. No significant difference was noted in 30-day limb salvage rates, mortality, or hemorrhagic complications, with revascularization and limb salvage ultimately achieved in 19 of 20 patients. The Rochester trial (University of Rochester, NY) served as the first randomized trial in the United States, assigning 114 patients with ALI of less than 7 days’ duration to either CDT (urokinase,  $N = 57$ ) or operative intervention ( $N = 57$ ).<sup>26</sup> Successful CDT was achieved in 40 of 57 patients (70%), with the remaining 17 patients (30%) who failed thrombolysis undergoing operative revascularization ( $N = 15$ ) or primary amputation ( $N = 2$ ). At 12 months, limb salvage rates were equivalent (82% vs. 82%,  $P = \text{NS}$ ), though overall survival (58% vs. 84%,  $P = 0.01$ ) and amputation-free survival (52% vs. 75%,  $P = 0.02$ ) favored CDT. Increased perioperative mortality in the surgical arm was attributed to increased rates of cardiopulmonary complications (49% vs. 16%,  $P = 0.001$ ). Increased major hemorrhagic complications occurred more frequently with thrombolytic therapy (11% vs. 2%,  $P = 0.06$ ), with one lethal intracranial hemorrhage. The study highlights the utility of CDT as an initial though not definitive treatment option for limb reperfusion as 34 of 57 thrombolysis patients (59%) underwent open surgical revascularization based on culprit lesions revealed with thrombus clearance.

The STILE investigators (Surgery vs. Thrombolysis for Ischemia of the Lower Extremity) produced two randomized trials comparing CDT with open revascularization for non-embolic native arterial and bypass graft occlusion.<sup>27,28</sup> In the first report, 393 patients with less than 6 months of ischemia symptoms were randomized prospectively to either open surgery ( $N = 144$ ) or CDT with thrombolysis arm using either rtPA ( $N = 137$ ) or urokinase ( $N = 112$ ); no difference was noted in efficacy or incidence of hemorrhagic complications between lytic agents with the results pooled for comparative

**TABLE 104.1** Therapeutic Infusion Catheters

Company Name	Product Name	Sheath Compatibility (F)	Guidewire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
AngioDynamics	Pulse Spray	3, 4, 5 (catheter size)	0.018, 0.035	45, 90, 135 (catheter length); 2, 5, 10, 20, 30, 40, 50 (infusion pattern working length)	Patented pressure response outlet technology and occluding ball wire provides even distribution of lytic	Intended for use in the administration of fluids, including thrombolytic agents and contrast media, into the peripheral vasculature
AngioDynamics	SpeedLyser Infusion System	5 (catheter size)	0.018	15, 20, 25 (catheter length); 10, 15, 20 (infusion pattern working length)	Patented pressure response outlet technology and occluding system provides even distribution of lytic	Intended for use in the administration of fluids, including thrombolytic agents and contrast media, into the peripheral vasculature
AngioDynamics	Unifuse Infusion Catheter	4, 5 (catheter size)	0.035	45, 90, 135 (catheter length); 2, 5, 10, 15, 20, 30, 40, 50 (infusion pattern working length)	Patented pressure response outlet technology and occluding ball wire provides even distribution of lytic	Intended for use in the administration of fluids, including thrombolytic agents and contrast media, into the peripheral vasculature
Medtronic	Cragg-McNamara Valved Infusion Catheter	4, 5	0.035, 0.038	40, 65, 100, 135	Catheters with radiopaque markers proximal and distal to the infusion segments; Cragg-MicroValve at the distal tip provides endhole occlusion	Indicated for use in the controlled selective infusion of physician-specific pharmacological agents or radiopaque contrast media in the general vasculature
Medtronic	MicroMewi Infusion Catheter with multiple sideholes	2.9	0.018	150, 180	Catheters with radiopaque markers proximal and distal to the infusion segment; 5- and 10-cm infusion lengths for comprehensive infusion	Indicated for use in the controlled selective infusion of physician-specific pharmacological agents or radiopaque contrast media in the general vasculature
Medtronic	ProStream Infusion Wire		0.035	145, 175	Constructed with an integral core wire, stainless steel coil, and an outer Teflon layer for placement without a separate guide wire	Indicated for use in the controlled selective infusion of physician-specific pharmacological agents or radiopaque contrast media in the general vasculature
Merit Medical Systems, Inc.	Fountain Infusion Catheter with the Squirt Fluid Dispensing System	4,5		45, 90, 135	Fluid delivery system with consistent, forceful, pulsed injections for optimal thrombolysis procedures	Intended to administer infusions of various therapeutic solutions into the peripheral vasculature of a patient
Merit Medical Systems, Inc.	Fountain Infusion System	4, 5	0.035	45, 90, 135	—	Intended to administer infusions of various therapeutic solutions into the peripheral vasculature of a patient

**TABLE 104.1** Therapeutic Infusion Catheters—cont'd

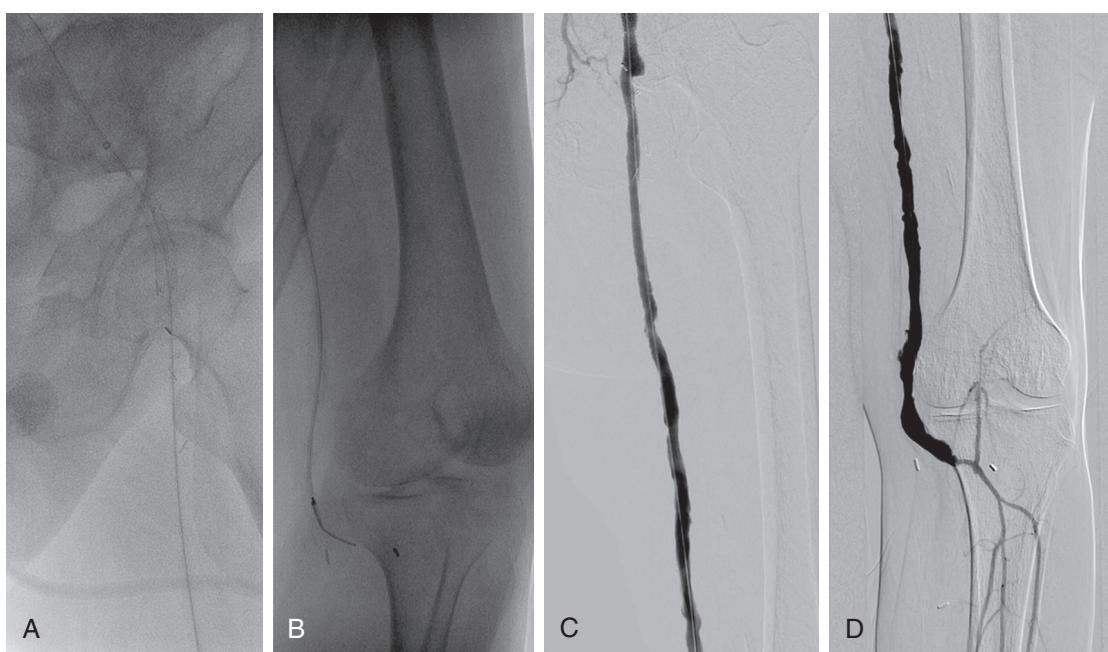
Company Name	Product Name	Sheath Compatibility (F)	Guidewire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Merit Medical Systems, Inc.	Fountain Infusion System: Catheter, occluding wire, and the AccessPLUS Hemostasis Valve	4, 5	0.035	45, 90, 135	–	Intended to administer infusions of various therapeutic solutions into the peripheral vasculature of a patient
Merit Medical Systems, Inc.	Fountain Occluding Wire	4, 5	–	45, 90, 135	Can be used for slow, continuous, or pulse infusion	Intended to administer infusions of various therapeutic solutions into the peripheral vasculature of a patient
Merit Medical Systems, Inc.	Mistique Infusion Catheter	5	0.035	45, 90, 135	Can be used for slow, continuous, or pulse infusion	Intended to administer infusions of various therapeutic solutions into the peripheral vasculature of a patient
ThermopeutiX, Inc.	TAPAS Targeted Adjustable Drug Delivery System	7	0.014	15–300 mm (adjustable)	Dual occlusive balloon technology to target, deliver, dwell, and aspirate any drug or therapeutic agent	Intended for use in peripheral arteries 1.8 mm for infusion of diagnostic or therapeutic agents
Translational Research Institute	ND Infusion Catheter	6	0.014	135	Expandable balloon to control blood flow during infusion through a multilumen spray tip	Intended to isolate a specific vascular treatment region from blood flow while allowing infusion of physician-specified fluids into the target region

U.S. FDA, United States Food and Drug Administration.

(From *Endovascular Today* 2019 Buyers Guide US Edition – US Device Guide – Therapeutic Infusion Systems.)

effect.<sup>27</sup> Primary endpoint was a composite clinical outcome of the occurrence within 30 days of at least one of the following: death; major amputation; ongoing/recurrent ischemia; major systemic morbidity. Thirty-day composite endpoint was less frequent with open surgery (36% vs. 61%,  $P < 0.001$ ) as a result of lower rates of ongoing ischemia (25.7% vs. 54%,  $P < 0.001$ ) and lower occurrence of life-threatening hemorrhage (0.7% vs. 5.6%,  $P = 0.014$ ). Randomization to CDT did result in a significant percent-reduction in the extent of revascularization required for over half of the thrombolysis arm (55.8% vs. 5.5,  $P < 0.001$ ). Duration of ischemic symptoms proved to have a direct effect on limb salvage (LS) and amputation-free survival (AFS) measured at 6 months. Acute ischemia (less than 14 days) favored thrombolysis for

lower rates of major amputation (11.1% vs. 30%,  $P = 0.02$ ), and improved AFS (15% vs. 37.5%,  $P = 0.01$ ). In contrast, symptoms of chronic ischemia (greater than 14 days) were best treated by open surgery with decreased major amputation (3% vs. 12%,  $P = 0.01$ ) and a trend toward improved AFS (9.9% vs. 17.8%,  $P = 0.08$ ). Subset analysis was performed of patients with native arterial occlusions of iliac–common femoral (IF,  $N = 69$ ) or superficial femoral–popliteal arteries ( $N = 168$ ); note, only 20% of patients analyzed had ischemia less than 14 days in duration.<sup>28</sup> Thrombolysis reduced the extent of surgery in both IF and FP occlusions. At 12 months, thrombolysis treatment was associated with greater risk of ongoing or recurrent ischemia (64% vs. 34.5%,  $P < 0.05$ ) and major amputation (10% vs. 0%,



**Figure 104.4** Placement of a Uni-Fuse thrombolytic catheter (Angiodynamics, Latham, NY) for acute thrombosis of cryo-preserved vein bypass graft (**A,B**). Post-thrombolysis patency of bypass graft with preservation of run-off (**C,D**).

$P < 0.05$ ). Poor lytic response was noted in patient with diabetes mellitus, FP occlusion, and critical ischemia. Thrombolysis for FP occlusion also was associated with increased risk of major amputation at 1 year (13.5% vs. 0%,  $P = 0.0013$ ). The results of the STILE trials helped frame our understanding of the increased benefit of thrombolysis for patients with acute ischemia of less than 2 weeks' duration, and the superior long-term freedom from recurrent ischemia and major amputation with surgical revascularization.

The last major randomized trial comparing thrombolysis to surgery for ALI is the two-part TOPAS trial (Thrombolysis or Peripheral Arterial Surgery).<sup>29,30</sup> Phase I examined the safety and efficacy of three doses of recombinant urokinase (2000–IU/min,  $N = 48$ ; 4000 IU/min,  $N = 52$ ; 6000 IU/min,  $N = 55$ ) versus surgery ( $N = 58$ ) for patients with less than 14 days of ALI.<sup>29</sup> The 4000 IU/min rUK dose proved the most efficacious with a higher rate of complete (>95%) lysis (71% vs. 66.7% at 2000 IU/min; vs. 60% at 6000 IU/min), and lower rates of hemorrhagic complications (2% vs. 13% at 2000 IU/min,  $P = 0.05$ ; vs. 16% at 6000 IU/min,  $P = 0.03$ ). Comparing rUK at 4000 IU/min against the surgical arm showed similar rates of both 1-year mortality (14% vs. 16%,  $P = \text{NS}$ ), and AFS (74.6% vs. 65.4,  $P = \text{NS}$ ). Phase II sought to compare the outcomes of rUK at 4000 IU/min alone ( $N = 272$ ) versus surgery ( $N = 272$ ) for patients with ALI of 14 days or less.<sup>30</sup> Based on available angiograms, CDT resulted in arterial recanalization in 79.7% of patients, with complete dissolution in 67.9%. Amputation-free survival was similar between rUK and surgery at both 6 months

(71.8% vs. 74.8%,  $P = 0.43$ ), and 1 year (65% vs. 69.9%,  $P = 0.23$ ). Similarly, no difference in mortality between CDT and surgery was noted at 6 months (16% vs. 12.3%,  $P = 0.22$ ) or 1 year (20% vs. 17%,  $P = 0.39$ ). The rate of major hemorrhagic complications was higher in the urokinase group (12.5% vs. 5.5%,  $P = 0.005$ ), with increased risk of bleeding in those receiving concomitant therapeutic heparin infusion ( $P = 0.02$ ).

### Pharmacomechanical Thrombectomy

Pharmacomechanical thrombectomy (PMT) combines thrombolytic therapy with mechanical clot extraction, with the advantages of decreasing total lytic dose and duration of thrombolysis. Procedural technique follows the same sequence as noted for CDT with ultrasound-guided arterial access, selective catheterization and sheath placement, and diagnostic angiogram prior to endovascular therapy.

The AngioJet Thrombectomy System (Boston Scientific, Marlborough, MA) combines mechanical thrombectomy via high-velocity saline injection with pulsatile delivery of intrathrombus lytic agent. A wide range of catheter treatment lengths and diameters are available to complement arterial and venous obstructions. A control system console monitors the system and energizes a pump, which delivers high-velocity saline towards the catheter tip. The pressurized saline jets create an incredibly low-pressure zone (Bernoulli principle) at the distal catheter facilitating thrombus disruption, aspiration and extraction. Clot extraction is enhanced

with use of a “power pulse-spray” (P-PS) mode. Common protocols use 10 mg of rtPA in 50 mL of saline, with the system pump delivering 0.6 mL of lytic solution per pedal pump/pulse. A single antegrade and retrograde pass in P-PS mode is recommended advancing the catheter slowly at 0.5 to 1.0 mm increments, with the console monitoring maximum run times. The concentrated pulsed lytic agent dwells for 15–20 minutes prior to returning the AngioJet system to thrombectomy mode for clot extraction with a single antegrade and retrograde pass, followed by angiography. Prior studies have demonstrated the utility of the AngioJet system with or without use of CDT in management of ALI.<sup>35–38</sup> The PEARL Registry (*P*ERipheral use of *A*ngiojet *R*heolytic thrombectomy with a variety of catheter *L*engths) reported the contemporary use of the AngioJet system in management of ALI, with a focus on defining patient and anatomic factors associated with procedural success.<sup>39</sup> The multicenter trial enrolled 283 patients with ALI symptoms within 2 weeks, with 147 (52%) treated with PMT and the remaining 136 (48%) receiving PMT plus CDT; propensity score-matched subsets were created to enhance analysis. Patients treated with AngioJet PMT alone had lower total lytic dose ( $P < 0.001$ ), shorter procedure lengths ( $P < 0.001$ ), and fewer treatment sessions ( $P < 0.001$ ). In matched cohorts, 1-year data showed PMT alone possessed greater procedural success (88% vs. 74%,  $P = 0.021$ ), amputation-free survival (87% vs. 72%,  $P = 0.020$ ), and freedom from amputation (96% vs. 81%,  $P = 0.012$ ). Poorer rates of amputation-free survival were noted with treatment of bypass grafts, infrapopliteal involvement, and increasing severity of Rutherford ischemia class. With the concern of delayed revascularization using endovascular therapies for ALI, the PEARL Registry shows the ability of AngioJet PMT to assist in rapid single-procedure revascularization. A large retrospective review sought to define contemporary results of AngioJet PMT and standard CDT (Uni-Fuse, Angiodynamics) for limb ischemia.<sup>40</sup> Authors treated 147 patients (154 limbs) via CDT and/or PMT for varying levels of ALI (Rutherford class I – 9.7%; IIa – 70.1%; IIb – 20.1%). Endovascular therapies included CDT alone ( $N = 83$ ), PMT alone ( $N = 15$ ), or combined CDT with PMT ( $N = 56$ ); PMT arm combined outcomes of single and dual therapy. The occurrence of a failed stent, bypass, or *in situ* thrombosis were similar across treatment groups. Overall, technical success was achieved in 83.8% of patients, with statistical significance in the PMT group (CDT 78.3% vs. PMT 90.1%,  $P = 0.047$ ). Duration of lytic therapy was equivalent between CDT and the 56 PMT patients requiring adjunct CDT (CDT, 25.5 h vs. PMT, 23.6 h,  $P = 0.445$ ). No significant difference was noted between CDT and PMT rates of 30-day mortality, or limb loss at 30 days or 12 months. Similarly, CDT and PMT did not differ in post-procedure primary patency ( $P = 0.524$ ), primary-assisted patency ( $P = 0.288$ ), secondary patency ( $P = 0.197$ ), or overall survival ( $P = 0.341$ ). On multivariable analysis, use of PMT was not

associated with increased risk of limb loss ( $P = 0.97$ ) or loss of primary patency ( $P = 0.525$ ). The presence of end-stage renal disease did confer increased risks of limb loss ( $P < 0.001$ ), as well as loss of primary ( $P < 0.001$ ) and secondary patency ( $P < 0.001$ ). Procedural technical success was predicted with use of PMT ( $P = 0.046$ ), as well as the presence of patent pedal outflow (1–3 patent pedal vessels, all  $P < 0.0125$ ).

An alternative PMT device is the EKOS catheter (Eko-Sonic Endovascular System, Boston Scientific, Marlborough, Massachusetts). The catheter is a 5.4-F multi-lumen catheter with channels for lysis delivery, a central lumen for the ultrasonic core wire, and an adjacent central coolant lumen. Catheter working lengths come in 106- and 135-cm options, with treatment zones ranging 6 to 50 cm. The ultrasonic core wire transducer elements are spaced 1 cm apart, with the ultrasound energy delivered simultaneously with infusions of lytic agent and coolant. Catheter temperature is monitored by the control unit, which can adjust ultrasound power to prevent overheating. The ultrasound waves propel lytic agent deeper into the thrombus and expose a greater surface area for thrombolysis. Studies have reported increased exposure of thrombus to rtPA with use of ultrasound, decreased procedure time and volume of lytic agent while increasing technical success.<sup>41–45</sup> The DUET trial reported the results of a Dutch randomized trial comparing outcomes of ultrasound-accelerated thrombolysis (UST) against standard catheter directed thrombolysis (ST) for ALI.<sup>46</sup> Sixty patients with Rutherford class I or IIa ischemia were randomized to either UST ( $N = 28$ ) delivered via the EKOS system, or ST ( $N = 32$ ) using a 5-F Uni-Fuse infusion catheter (Angiodynamics, Latham, NY). Thrombolysis with restoration of uninterrupted flow (>95% lysis) was faster in the UST than in ST group ( $17.7 \pm 2$  h vs.  $29.5 \pm 3.2$  h,  $P = 0.009$ ), and required less urokinase ( $P = 0.01$ ). No statistically significant difference was noted in technical success (UST 75% vs. ST 84%,  $P = 0.52$ ), increase in ankle-brachial index (UST 0.57 vs. ST 0.56,  $P = 0.88$ ), combined end-point of death and severe adverse events (UST 29% vs. ST 19%,  $P = 0.54$ ), severe bleeding (UST 11% vs. ST 6%,  $P = 0.66$ ), or 30-day patency rates (UST 71% vs. ST 82%,  $P = 0.35$ ). Ascher et al. conducted a retrospective review to compare the efficacy of a multi-hole infusion catheter (Uni-Fuse, Angiodynamics) against ultrasound accelerated thrombolysis (EKOS, Boston Scientific) in patients with ALI.<sup>47</sup> From 2006 to 2008, 91 patients underwent either CDT ( $N = 69$ ) or EKOS ( $N = 22$ ) therapy for ALI. Thrombolysis of prosthetic bypass graft utilized CDT in 32% and EKOS in 45% of cases treated. No significant difference was found in duration of thrombolysis (CDT 39.6 h vs. EKOS 45.6 h,  $P = 0.22$ ), volume of t-PA administered (CDT 44.6 mg vs. EKOS 48.2 mg,  $P = 0.6$ ), procedural success (CDT 72% vs. EKOS 86%,  $P = 0.31$ ), major bleeding (CDT  $N = 3$  vs. EKOS  $N = 0$ ,  $P = 1$ ), or 30-day mortality (CDT 4% vs. EKOS 4%,  $P = 0.97$ ). Clinical efficacy of ultrasound-accelerated thrombolysis and comparable outcomes to CDT have also been suggested by other recent single-center retrospective reviews.<sup>48,49</sup>

## Mechanical Thrombectomy

Mechanical thrombectomy uses aspiration, mechanical/rotational, or hydrodynamic forces to fragment and clear thrombus without infusion of a thrombolytic agent. A variety of devices within each class exist (Tables 104.2 and 104.3), each with defined indications for use in arterial, venous, or dialysis graft occlusions. Aspiration mechanical thrombectomy (AMT) catheters have gained popularity recently for the ability to remove fresh thrombus and emboli from peripheral

arterial and venous vessels across a wide range of diameters. The Indigo Aspiration Catheters (CAT, Penumbra, Inc, Alameda, CA) come in a range of catheter diameters and lengths to accommodate all arterial sizes. Arterial access and sheath positioning are performed as with other endovascular devices. The aspiration catheters engage the angiographically localized thrombus, with the Indigo Aspiration system providing continuous mechanical aspiration of thrombus.<sup>50</sup> Indigo Separators can be used in conjunction with corresponding catheter size to facilitate clearance of thrombus from the catheter tip.

**TABLE 104.2** Aspiration Catheters

Company Name	Product Name	Type	Maximum Tip Diameter (mm)	Minimum Guide Catheter Size (F)	Catheter Length (cm)
Control Medical Technology	Aspire Max 5 Mechanical Thrombectomy System	5-F braided large-lumen OTW	1.65	6	55, 135
Control Medical Technology	Aspire Max 6 Mechanical Thrombectomy System	6-F braided large-lumen OTW	1.91	7	55, 135
Control Medical Technology	Aspire RX-LP6 Mechanical Thrombectomy System	Rapid-exchange low-profile system	1.7	6	136
Getinge	Xpress-Way RX Extraction Catheter	6-F, low-profile tip, resistant shaft design, hydrophilic coating, preloaded stylet, short guide wire lumen for improved deliverability and performance	1.35	6	140
Getinge	Xpress-Way RX Extraction Catheter	7-F, kink-resistant shaft design, hydrophilic coating, preloaded stylet, short guide wire lumen for improved deliverability and performance	1.52	7	140
Medtronic	Diver CE Aspiration Catheter	Low-profile, rapid-exchange, hydrophilic coating with and without side holes	1.58	6	145
Medtronic	Export AP Catheter	Full-wall variable hub to tip braiding- hydrophilic coating; short, soft tip	1.73	6	140
Medtronic	Export Catheter	Guide catheter braid technology	1.73, 1.98	6, 7	145
Medtronic	Export XT Catheter	Full-wall variable hub to tip braiding – hydrophilic coating; short, soft tip	1.73	6	140
Medtronic	React 68 Catheter	Nitinol, coil + braid construction, beveled distal tip	0.068 inch	–	132
Medtronic	Riptide Aspiration System	Aspiration pump, collection canister, intermediate tubing, aspiration tubing	–	–	–
Merit Medical Systems, Inc.	ASAP Aspiration Catheter Kit	Manual aspiration catheter and kit	1.73	6 (guiding catheter ID, s 0.07 inch)	140
Merit Medical Systems, Inc.	ASAPLP Aspiration Catheter Kit	Low-profile manual aspiration catheter and kit	1.40	6 (guiding catheter ID, s 0.066 inch)	145
MicroVention Terumo	Sofia Flow Plus	Aspiration catheter	Distal OD: 2.1; ID: 0.070 inch	6	125, 131
Teleflex	Pronto .035 Extraction Catheter	Large-vessel thrombus aspiration catheter; full-length braided shaft; patented Silva tip	3.25	10 (sheath)	115

*Continued*

**TABLE 104.2** Aspiration Catheters—cont'd

Company Name	Product Name	Type	Maximum Tip Diameter (mm)	Minimum Guide Catheter Size (F)	Catheter Length (cm)
Teleflex	Pronto LP 5 F Extraction Catheter	Low-profile; hydrophilic coating; patented Silva tip; delivery stylet; 5-F guide catheter compatibility	1.35	5	138
Teleflex	Pronto LP Extraction Catheter	Low-profile; hydrophilic coating; patented Silva tip; round, braided shaft; delivery stylet	1.35	6	140
Teleflex	Pronto V3 Extraction Catheter	Full-length braided shaft; hydrophilic coating; patented Silva tip; maximized extraction lumen and force	1.65	6	140
Teleflex	Pronto V4 Extraction Catheter	Embedded longitudinal wire; hydrophilic coating; patented Silva tip; maximized extraction lumen and force; 5.5, 6, 7, 8 F	1.64–2.2	6, 7, 8	138
Terumo Interventional Systems	PriorityOne Aspiration Catheter	Fully braided stainless steel shaft with guide wire-style stylet for better deliverability	1.65, 1.9	6, 7	140

U.S. FDA, United States Food and Drug Administration.

(From *Endovascular Today* 2019 Buyers Guide US Edition – US Device Guide – Thrombus Aspiration Devices.)

Figure 104.5 illustrates use of Indigo CAT6 aspiration catheter for removal of cardiac embolic popliteal artery occlusion. Post-procedure angiogram demonstrates restored patency to popliteal and tibial runoff. Robust data is limited on the technical success of AMT for ALI. The Mayo Clinic has recently reported a retrospective experience with use of Indigo aspiration catheters (Penumbra, Inc) in management of limb ischemia.<sup>51</sup> From 2014 to 2017, 41 patients underwent 43 AMT procedures for limb ischemia resulting largely from embolism ( $N = 18$ ) or native arterial thrombosis ( $N = 13$ ). Aspiration thrombectomy was the main treatment in 29 cases and used adjunctively in 14, with a technical success of 52% when used as the sole therapy. There were no requirements for blood transfusion or severe bleeding with intervention, and a low rate of distal thromboembolism (2 of 43). Similar clinical efficacy of AMT using Indigo aspiration catheters has been reported in other single-center reports.<sup>52,53</sup> Recently, a 12-F catheter was introduced to improve the aspiration capacity in larger arteries and veins.

Mechanical and rotational thrombectomy devices rely on fragmentation and simultaneous aspiration of thrombus to restore arterial flow. Several on-market devices are available, though none are used with great frequency in management of acute limb ischemia.<sup>54–64</sup> Recently approved for use in the United States the Rotarex-S mechanical atherectomy plus thrombectomy device (Straub Medical AG, Wangs, Switzerland) provides a method of removing both acute thrombus and chronic atheroma. Available in 6- and 8-F systems, the device is designed to treat vessels ranging from 3 to 8 mm in diameter over an 0.018-inch guide wire. The catheter is composed of two metal cylinders, the inner connected to

the catheter shaft and the outer to the rotating helix. A motor and connected drive system rotate the helix and outer cylinder at 40,000 to 60,000 rpm, with mechanical disruption and aspiration of thrombus or atheroma burden. The Rotarex-S catheter has been reported in both retrospective and prospective studies for use in ALI.<sup>65,66</sup> In a retrospective review, 147 patients were treated with Rotarex-S for ALI with the device used as first-line therapy in 120 patients and as an adjunct after failed CDT in 27 patients.<sup>65</sup> All classes of ALI were represented (class I,  $N = 38$ ; IIa,  $N = 35$ ; IIb,  $N = 40$ ; IIb-III,  $N = 6$ ; Undetermined,  $N = 28$ ). Overall, the procedural revascularization success was 90.5%, with primary success achieved in 68.7% of cases and 21.8% when fibrinolysis added for outflow obstructions. Procedural complications included distal embolization in 4.8% of cases, and access-site hematomas in 4%. Overall, the review demonstrated device clinical success comparable with historical trials with an amputation rate of 2% ( $N = 3$ ), and 30-day mortality of only 0.7% ( $N = 1$ ). The Rotarex-S device was also included in a single-arm prospective trial to determine the efficacy of endovascular thrombus mechanical debulking as initial therapy in patients with acute and subacute limb ischemia (SLI).<sup>66</sup> Over a 6-year span the study enrolled 316 consecutive patients with either ALI ( $N = 202$ , 64%) or SLI ( $N = 114$ , 36%). The ALI cohort included 56 class IIa and 146 class IIb patients, with longer occlusion lengths (24.5- vs. 20-cm,  $P = 0.016$ ), more embolic occlusions ( $N = 50$  vs. 10,  $P < 0.001$ ), increased aortoiliac ( $N = 28$  vs. 7,  $P = 0.040$ ) and deep femoral occlusions ( $N = 26$  vs. 6,  $P = 0.033$ ), and infrapopliteal lesions ( $N = 138$  vs. 57,  $P = 0.002$ ). Technical success (defined as <50% residual

**TABLE 104.3** Mechanical Thrombectomy Catheters

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Argon Medical Devices, Inc.	Cleaner 15	7		65, 135	Battery-operated, handheld drive unit initiates the mechanical rotation of an atraumatic, wall-contacting, 15-mm sinusoidal vortex wire for effective thrombus maceration	Indicated for mechanical declotting and controlled and selective infusion of physician-specified fluids, including thrombolytics, in the peripheral vasculature; also indicated for mechanical declotting of native vessel dialysis fistulas and synthetic dialysis access grafts
Argon Medical Devices, Inc.	Cleaner XT	6		65, 135	Battery-operated, handheld drive unit initiates the mechanical rotation of an atraumatic, wall-contacting, 9-mm sinusoidal vortex wire for effective thrombus maceration	Indicated for mechanical declotting and controlled and selective infusion of physician-specified fluids, including thrombolytics, in the peripheral vasculature; also indicated for mechanical declotting of native vessel dialysis fistulas and synthetic dialysis access grafts
Boston Scientific Corporation	AngioJet AVX Thrombectomy Catheter	6	0.035	50	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from AV access conduits a 3-mm in diameter
Boston Scientific Corporation	AngioJet Solent Dista Thrombectomy Catheter	4	0.014	145	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from upper and lower extremity peripheral arteries 1.5 mm in diameter and for use with the Angiojet Ultra Power Pulse Kit for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system
Boston Scientific Corporation	AngioJet Solent Omni Thrombectomy Catheter	6	0.035	120	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from upper and lower extremity peripheral arteries, upper extremity peripheral veins, iliofemoral and lower extremity peripheral veins 3 mm in diameter, and for use with the Angiojet Ultra Power Pulse Kit for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system
Boston Scientific Corporation	AngioJet Solent Proxi Thrombectomy Catheter	6	0.035	90	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from upper and lower extremity peripheral arteries, upper extremity peripheral veins, iliofemoral and lower extremity peripheral veins 3 mm in diameter, and for use with the Angiojet Ultra Power Pulse Kit for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system
Boston Scientific Corporation	AngioJet PE Thrombectomy Catheter	6	0.035	120	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from upper and lower extremity peripheral veins, iliofemoral and lower extremity peripheral veins 2–6 mm in diameter, and for use with the Angiojet Ultra Power Pulse Kit for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system

*Continued*

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Boston Scientific Corporation	AngioJet Solent ZelanteDVT Thrombectomy Catheter	8	0.035	105	High-velocity water jets enclosed in catheter utilize the Bernoulli principle for capture, microfragmentation, and removal	Breaking apart and removing thrombus from upper and lower extremity peripheral veins, iliofemoral and lower extremity peripheral veins 2–6 mm in diameter, and for use with the AngioJet Ultra Power Pulse Kit for the control and selective infusion of physician-specified fluids, including thrombolytic agents, into the peripheral vascular system
Boston Scientific Corporation	EkoSonic Endovascular System	6	0.035	106 (treatment areas: 6, 12, 18, 24, 30, 40, 50); 135 (treatment areas: 12, 30, 40, 50)	The treatment offers a minimally invasive system for the acceleration of thrombus dissolution; the ultrasonic core generates a localized acoustic field that targets the entire thrombus; this greatly accelerates lytic dispersion by driving the drug deeper into the clot and unwinding the fibrin to expose plasminogen receptor sites	Indicated for the ultrasound-facilitated, controlled, and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism; the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature; and the infusion of solutions into the pulmonary arteries
Codman Neuro (Johnson & Johnson)	Revive PV Peripheral Vascular Thrombectomy Device	5 or larger		205	Mechanical thrombectomy with aspiration	The nonsurgical removal of emboli and thrombi from peripheral blood vessels
Control Medical Technology	Aspire Mechanical Thrombectomy Drive Unit				Mechanical thrombectomy drive unit, continuous and/or pulsed mechanical thrombectomy	A high-performance thrombectomy pump and drive unit to improve thrombectomy performance
ICHOR Vascular	ICHOR Aceso 12	12	0.035	45, 90, 150	Disobliteration using a compliant balloon as the primary mechanism of action with supportive aspiration to sweep thrombus, acute clot, or embolic material into the extraction funnel; the “control sheath” has an occlusion balloon to manage flow, maximize clot removal, while reducing distal embolization	Indicated for the nonsurgical removal of emboli and thrombi from blood vessels; intended for the peripheral vasculature, and is not intended for use in the coronary or neurovasculature
ICHOR Vascular	ICHOR Panacea 7	7	0.014	45, 90, 150	Disobliteration using a compliant balloon as the primary mechanism of action with supportive aspiration to sweep thrombus, acute clot, or embolic material into the extraction funnel; the “control sheath” has an occlusion balloon to manage flow, maximize clot removal, while reducing distal embolization	Indicated for the nonsurgical removal of emboli and thrombi from blood vessels; intended for the peripheral vasculature, and is not intended for use in the coronary or neurovasculature

Continued

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Inari Medical	ClotTriever Thrombectomy System	13	0.018, 0.035	74	Mechanical coring, collection, and retrieval of emboli and thrombi	The nonsurgical removal of soft emboli and thrombi from blood vessels; injection, infusion, and/or aspiration of contrast media and other fluids into or from a blood vessel; intended for use in the peripheral vasculature
Inari Medical	FlowTriever Retrieval/Aspiration System	20	0.035	95	Mechanical and aspirational disruption, fragmentation, maceration, and retrieval of emboli and thrombi	The nonsurgical removal of emboli and thrombi from blood vessels; injection, infusion, and/or aspiration of contrast media and other fluids into or from a blood vessel; intended for use in the peripheral vasculature and for the treatment of pulmonary embolism
Medtronic	Solitaire Platinum Revascularization Device 4 × 20, 4 × 40, 6 × 20	8, 9 (balloon guide)	0.014	180 (Solitaire push wire)	Designed to restore blood flow in patients experiencing ischemic stroke due to large intracranial vessel occlusion and for use in the neurovasculature, such as the internal carotid artery, M1 and M2 segments of the middle cerebral artery, basilar, and the vertebral arteries	Indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received IV tPA; endovascular therapy with the device should be started within 6 hours of symptom onset; indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset; patients who are ineligible for IV tPA or who fail IV tPA therapy are candidates for treatment
Medtronic	Solitaire X Revascularization Device (4 × 20; 4 × 40; 6 × 20; 6 × 24; 6 × 40 mm)		0.021	200		(1) Indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA)—endovascular therapy with the device should be started within 6 hours of symptom onset; (2) indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset—patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment; (3) indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (<70 cc by CTA or MRA; <25 cc by MR-DWI)—endovascular therapy with the device should start within 6–16 hours of time last seen well in patients who are ineligible for IV t-PA or who fail IV t-PA therapy

*Continued*

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Medtronic	Solitaire X-Pack (2 pack: 4 × 40 or 6 × 40 mm with Phenom 21 or 27)			200		(1) Indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV-t-PA)—endovascular therapy with the device should be started within 6 hours of symptom onset; (2) indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset—patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment; (3) indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (<70 cc by CTA or MRA; <25 cc by MR-DWI)—endovascular therapy with the device should start within 6–16 hours of time last seen well in patients who are ineligible for IV t-PA or who fail IV t-PA therapy
Medtronic	Solitaire X-Pack (3 pack: 4 × 40 or 6 × 40 mm with Phenom 21 or 27 or React 68 or 71)			200		(1) Indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA)—endovascular therapy with the device should be started within 6 hours of symptom onset; (2) indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset—patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment; (3) indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (<70 cc by CTA or MRA; <25 cc by MR-DWI)—endovascular therapy with the device should start within 6–16 hours of time last seen well in patients who are ineligible for IV t-PA or who fail IV t-PA therapy

*Continued*

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Penumbra, Inc. (Neuro)	3D Revascularization Device	6 (long sheath [Neuron MAX])	0.020	200 (delivery wire; compatible with Velocity Delivery microcatheter [160 cm] and 3 MAX Reperfusion catheter [160 cm])	Designed for use in combination with ACE Reperfusion catheters; the architecture enables maximum clot capture capability through four intraluminal chambers and is optimized for use with aspiration delivered by ACE catheters or the Penumbra JET 7 Reperfusion catheter	Part of the Penumbra System; indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments) within 8 hours of symptom onset; patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment
Penumbra, Inc. (Neuro)	Penumbra System Reperfusion Catheters: Penumbra JET 7, Penumbra JET D, ACE, and 5MAX require 8-F short sheath or 6-F long sheath	6 (Penumbra JET 7, Penumbra JET D, ACE, and 5MAX require 8-F short sheath or 6-F long sheath)	0.014–0.016	132–160	Direct aspiration clot removal with Penumbra Engine aspiration source	As part of the Penumbra System, the reperfusion catheters and separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment
Penumbra, Inc. (Neuro)	Penumbra System Separator and Separator Flex: 5MAX, 4MAX, 3 MAX, and 026			175–200 (Separator and Separator Flex length)	Separator-assisted clot debulking, if needed	As part of the Penumbra System, the Reperfusion catheters and separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset; patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment
Penumbra, Inc. (Peripheral Vascular)	Indigo System Catheters: CAT8, CATD, CAT6, CAT5, CAT3, and CAT RX	8 (CATD, CAT8), 6 (CAT6, CAT5), 5 (CAT3), 6-F guide catheter (CAT RX)	0.014–0.038	50–150	Separator-assisted mechanical extraction of thrombus/embolus with constant vacuum aspiration; available in a selection of sizes, the CAT family can provide access to distal peripheral vessels of the upper and lower extremities, including below the knee	Indicated for the removal of fresh, soft emboli and thrombi from vessels of the peripheral arterial and venous systems; as part of the Indigo Aspiration System, the Indigo CAT RX aspiration catheters and Indigo Separator 4 are indicated for the removal of fresh, soft emboli and thrombi from vessels in the coronary and peripheral vasculature
Penumbra, Inc. (Peripheral Vascular)	Indigo System Separators: SEP8, SEPD, SEP6, SEP5, SEP3, SEP4			90–200	The device is advanced and retracted through the CAT catheter at the proximal margin of the primary occlusion to facilitate the clearing of the thrombus from the catheter tip, as needed	Indicated for the removal of fresh, soft emboli and thrombi from vessels of the peripheral arterial and venous systems; as part of the Indigo Aspiration System, the Indigo CAT RX aspiration catheters and Indigo Separator 4 are indicated for the removal of fresh, soft emboli and thrombi from vessels in the coronary and peripheral vasculature

Continued

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Stryker	Trevo XP ProVue Retriever; 3 × 20 mm, 4 × 20 mm, 4 × 30 mm, 6 × 25 mm	8, 9 (balloon guide catheter)	0.014	190 for 3 × 20 mm, 180 for 4 × 20 mm, 4 × 30 mm, and 6 × 25 mm	Mechanical thrombectomy; 360° of consistently large cells, a soft distal tip and full-length radiopacity	Indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large-vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA); endovascular therapy with the device should start within 6 hours of symptom onset; intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke within 8 hours of symptom onset; patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment; indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large-vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA) – M1 segments with smaller-core infarcts (0–50 cc for age <80 years, 0–20 cc for age >80 years); endovascular therapy with the device should start within 6–24 hours of time last seen well in patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy
Teleflex	Arrow-Trerotola OTW PTD	7	0.025	65, 120	Battery-operated handheld unit rotates unique 9-mm fragmentation basket at 3000 rpm, macerating clot to <2 mm; basket can be deployed/withdrawn within catheter; deployed basket can be used to pull arterial plug	Permits mechanical declotting of native arteriovenous fistula synthetic dialysis grafts in conjunction with the Arrow Rotator Drive Unit (PT-03000-R)
Teleflex	Arrow-Trerotola PTD	5		65	Battery-operated handheld unit rotates unique 9-mm fragmentation basket at 3000 rpm, macerating clot to <2 mm; basket can be deployed/withdrawn within the catheter; deployed basket can be used to pull arterial plug	Permits mechanical declotting of native arteriovenous fistula and synthetic dialysis grafts in conjunction with the Arrow Rotator Drive Unit (PT-03000-R)

*Continued*

**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Thrombolex, Inc.	Bashir Endovascular Catheter	7	0.018	92.5	Designed to rapidly restore blood flow with the attendant endogenous lytics upon manually expanding a 12.5-cm long infusion basket; physician-specified fluids, including thrombolytics, can be pulse-sprayed or infused through 48 precision-drilled holes in the basket into the thrombus; the basket is opened by an actuator on the handle, and infusion fluids can be administered via a syringe or infusion pump	Indicated for the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature
Thrombolex, Inc.	Bashir S-B Endovascular Catheter	7	0.018	92.5	Designed to rapidly restore blood flow with the attendant endogenous lytics upon manually expanding a 10-cm long infusion basket; physician-specified fluids, including thrombolytics, can be pulse-sprayed or infused through 48 precision-drilled holes in the basket into the thrombus; the basket is opened by an actuator on the handle, and infusion fluids can be administered via a syringe or infusion pump	Intended for the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature
Thrombolex, Inc.	Bashir N-X Endovascular Catheter	7	0.018	92.5	Designed to rapidly restore blood flow by pulse-spraying or infusing physician-specified fluids, including thrombolytics, into the target area via 48 precision-drilled holes; the infusion fluids are administered via a syringe or infusion pump; may be used in the pulmonary arteries and peripheral vasculature; the patent center lumen of the device allows for pulmonary artery pressure measurements and mixed venous oxygen saturation during infusion	Intended for the controlled and selective infusion of physician-specified fluids into the peripheral and pulmonary artery vasculature

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**TABLE 104.3** Mechanical Thrombectomy Catheters—cont'd

Company Name	Product Name	Sheath Compatibility (F)	Guide Wire Compatibility (inch)	Working Length (cm)	Mode of Operation	U.S. FDA Indicated Use
Walk Vascular, LLC	Jeti-6 Fr	6	0.010–0.038 (OTW) or none	120	Internal saline jet just within the catheter tip breaks up thrombus and soft emboli while removing the thrombus through aspiration	For all peripheral venous and arterial vasculature
Walk Vascular, LLC	Jeti-8 Fr	8	0.010–0.038 (OTW) or none	100	Internal saline jet just within the catheter tip breaks up thrombus and soft emboli while removing the thrombus through aspiration	For all peripheral venous and arterial vasculature

U.S. FDA, United States Food and Drug Administration.  
(From *Endovascular Today* 2019 Buyers Guide US Edition – Mechanical Thrombectomy/Thrombolysis – Endovascular Today.)

stenosis post-Rotarex-S) was achieved in 232 of 316 patients (73.4%), with less than 30% residual stenosis in 140 (44%), and no residual stenosis in 52 patients (16.5%). With use of adjunct endovascular techniques, procedural success (<30% residual stenosis) was 100%. Infrapopliteal lesions treated at index procedure required CDT in only 9% of patients ( $N = 29$ ) due to resistance to mechanical debulking, with the combination of Rotarex-S and adjuncts significantly improving tibial patency ( $P < 0.001$ ). At 30 days, primary and secondary patency rates were 94.3% and 97.2%, respectively; open surgical revascularizations were not required in any patient. Amputation-free survival at 30 days was 94.9% overall, 93.6% in ALI and 97.4% in SLI patients. Follow-up data was available for 199 patients at 12 months, with an AFS of 87.4%. Re-intervention rate was 14.9% at 1 year, including both endovascular ( $N = 26$ ) and open surgical ( $N = 12$ ) revascularizations without a significant difference amongst etiology or severity subgroups. The study demonstrates the utility of the Rotarex-S catheter as initial therapy for patients with ALI and SLI regardless of Rutherford ischemic class, arterial anatomy, tibial runoff, or contraindications to surgery or thrombolysis.

## OUTCOMES

The expansion and refinement of catheter-based interventions for limb ischemia has allowed for a more patient-individualized approach to limb salvage regardless of ischemic class. A recent survey of the Vascular and Endovascular Surgery Society (VESS) membership revealed increased use of endovascular therapies for bypass graft occlusions with Rutherford class IIa ischemia, with preference for open revascularization for class IIb–III or in centers lacking hybrid operative suites.<sup>67</sup> Large retrospective reviews of the United States Medicare<sup>68</sup> and Veterans Affairs Health Systems<sup>69</sup> have also helped to define a several-decade trend in limb ischemia management and outcomes. The Medicare claims data reviewed (1998–2009) was notable for a decreased incidence in admission for ALI, though increased rates of intervention and a shift towards endovascular therapies for limb salvage. Despite the shift towards less-invasive techniques, risk-adjusted rates of mortality and amputation-free survival remained unimproved at both 30 days and one year. Authors attributed the decline in ALI incidence to improved primary and secondary prevention strategies of cardiovascular risk factors,<sup>70–72</sup> and an increased use of anticoagulants for atrial fibrillation<sup>73,74</sup> affecting rates of arterial embolic occlusion. The review highlights that, even in the modern endovascular era of vascular surgery, survival rates for ALI remain poor at one year post-procedure. A retrospective review of the Veterans Affairs Healthcare System reports a similar experience and trend in ALI diagnosis and management, with unimproved rates of mortality or major adverse events over the time-frame studies.<sup>69,75–80</sup> A survey of the Nationwide Inpatient Sample demonstrated a temporal increase in endovascular-first approach to ALI management from 2005 to 2014, though with an ever-increasing cost of care as compared to open surgery



**Figure 104.5** Pre-procedure duplex (left) with thromboembolic occlusion of left popliteal artery. Angiogram evidence of embolic occlusion to above-knee popliteal artery (**A,B**, red arrow). Restored patency of popliteal and tibial run-off following aspiration thrombectomy (**C,D**). (From Penumbra, Inc. Alameda, CA.)

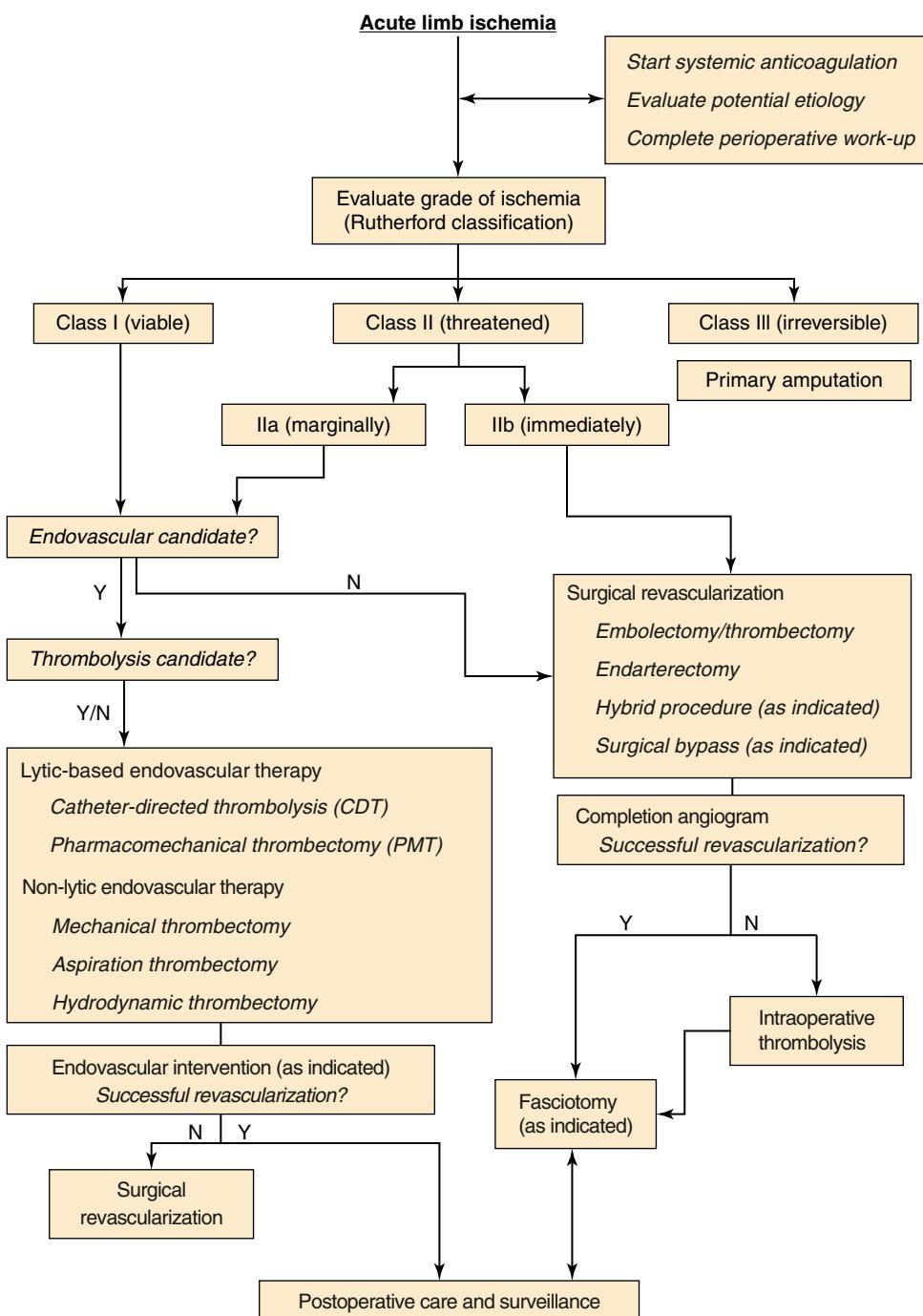
without improvements in limb salvage rates.<sup>81</sup> Recently published meta-analyses have further confirmed comparable rates of limb salvage for catheter-based and surgical revascularization.<sup>82</sup> The results of these large reviews and the suggestion of clinical equipoise in mortality and limb-salvage outcomes even in the endovascular-first era must be borne in mind as we select not only patient-specific, but durable and cost-efficient methods of care.

## POST-PROCEDURE CONSIDERATIONS

Operative management of acute limb ischemia is associated with significant systemic end-organ insults related to ischemia-reperfusion (I-R) injury. The pathophysiology of I-R injury is reviewed in previous chapters. With restored perfusion to tissue beds, rhabdomyolysis with myoglobinuria, as well as extremity compartment syndrome, must be monitored for. Lab evaluation should include baseline and surveillance creatine

phosphokinase (CPK) levels, surveillance lab evaluation for electrolyte abnormalities and acid-base status, as well as urinalysis for hemoglobinuria or myoglobinuria if oliguria or discolored urine noted. Lower extremity reperfusion edema can be quite profound with ALI, with decompressive fasciotomy often performed as prophylaxis against compartment syndrome in patients with prolonged preoperative ischemia time. Compartment syndrome and techniques for fasciotomy are discussed in prior chapters. Our practice is to perform prophylactic fasciotomy for all patients with greater than 6 hours of ischemia time, as well as for any patient presenting with neurologic motor deficit. Delayed fasciotomy in the setting of ALI is associated with significantly increased risk of major amputation within 30 days. Diagnosis and management of acute limb ischemia remains clinically challenging, with further randomized trials needed to help define best practice guidelines for thrombus clearance and revascularization utilizing available open and endovascular techniques.

## CHAPTER ALGORITHM



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# Compartment Syndrome and its Management

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## INTRODUCTION

Compartment syndrome is a surgical emergency and a recognized complication of several conditions treated by vascular surgeons. Failure to arrive at a timely diagnosis increases the risk of

short- and long-term morbidity, including limb loss or permanent disability. Conversely, appropriate recognition and management of a compartment syndrome will optimize the chances of a full recovery. This chapter addresses the pathogenesis,

diagnosis, and treatment of compartment syndrome of the lower leg and other less common anatomic sites. Abdominal compartment syndrome is discussed in Chapter 182 (Vascular Trauma: Abdominal).

## PATHOGENESIS OF COMPARTMENT SYNDROME

### Local Hemodynamics of Compartment Syndrome

The unifying feature of all compartment syndromes, regardless of etiology or anatomic location, is an increase in intracompartmental pressure (ICP) within an unyielding fascial envelope that impairs tissue perfusion.<sup>1</sup> The adverse consequence of elevated ICP on tissue perfusion may be understood by applying Poiseuille's law ( $F = \pi r^4 \Delta P / 8\eta L$ ) to capillary blood flow within a muscle compartment. In this equation,  $F$  represents capillary blood flow,  $r$  is the radius of the capillary to the fourth power, and  $\Delta P$  is the pressure gradient from the precapillary arteriole to the postcapillary venule. Increasing ICP alters two variables in this equation,  $\Delta P$  and  $r$ . As ICP rises, pressure is transmitted to the postcapillary venules, increasing the venous pressure and decreasing the arterial–venous pressure gradient ( $\Delta P$ ). Furthermore, increased ICP may collapse capillaries, decreasing their radius and further increasing resistance to flow.<sup>1,2</sup>

### Compartment Pressures

Several theories exploring the role of ICP in the development of compartment syndrome have been proposed. The concept of a critical closing pressure was one of the earliest concepts, whereas more recent research suggests that the dynamic ICP threshold more accurately predicts which muscle compartments will develop compartment syndrome.

#### Critical Closing Pressure

Matsen suggested that there is a "critical closing pressure" above which capillaries collapse from transmural pressure and blood flow is arrested.<sup>1</sup> The pressure at which capillary blood flow ceases has been debated over the decades. Using vital microscopy to observe the response of isolated rat cremasteric muscle to increased external pressure, Hartsock found that a pressure gradient between the ICP and mean arterial pressure (MAP) of  $25.5 \pm 14$  mm Hg arrested capillary blood flow. Hartsock saw no significant collapse of arterioles, capillaries, or venules.<sup>3</sup> This study and others disproved the "critical closing theory" proposed by Matsen, suggesting instead that the arterial–venous pressure gradient ( $\Delta P$ ) is the critical determinant of capillary blood flow.<sup>1,3,4</sup> This conclusion has direct implications for determining the threshold ICP that defines compartment syndrome.

#### Absolute intracompartmental pressure threshold

Defining the threshold ICP that produces tissue injury and cell death is an important step in determining the pressure at which

fasciotomy is advisable. Hargens found that an absolute ICP of 30 mm Hg for 8 hours universally produced muscle necrosis in normotensive dogs, whereas pressures less than 30 mm Hg produced no muscle necrosis.<sup>5</sup> Tissues differed in their susceptibility to increased ICPs. Early signs of endoneurial injury were observed at pressures of 30 mm Hg for 8 hours.<sup>6,7</sup> The differential susceptibility to injury between tissues may provide an explanation for those cases in which a delayed fasciotomy fails to restore full neurologic function despite viable muscle in the compartment.

#### Dynamic intracompartmental pressure threshold

Defining compartment syndrome based on an absolute pressure threshold is appealing in its simplicity but ignores the role of arterial blood pressure in affecting compartmental blood flow. Changes in arterial pressure affect the arterial–venous pressure gradient ( $\Delta P$ ), altering compartment blood flow. Some authors have proposed defining compartment syndrome using a pressure threshold relative to MAP or diastolic pressure. Heppenstall found that healthy muscle in dogs developed evidence of tissue ischemia on *P*-magnetic resonance spectroscopy when the difference between MAP and ICP (MAP – ICP) dropped below 30 mm Hg.<sup>8</sup> Injured muscle showed greater sensitivity to ischemia, as tissue ischemia became evident when the difference between MAP and ICP was less than 40 mm Hg ([MAP – ICP] <40 mm Hg).

Heppenstall found that a dynamic pressure threshold (MAP – ICP) <40 mm Hg, prevented unnecessary fasciotomy in a number of patients with absolute ICP exceeding 30 mm Hg.<sup>8</sup> Another study found that use of a dynamic ICP threshold of 30 mm Hg less than diastolic pressure prevented unnecessary fasciotomies in most patients.<sup>9</sup> Using the diastolic blood pressure as their reference point, Heckman observed a dramatic increase in tissue injury and necrosis when the difference between the diastolic blood pressure and ICP was less than 10 mm Hg in dogs.<sup>10</sup> These studies offer compelling evidence that a dynamic ICP threshold *relative to MAP or diastolic pressure* is more appropriate for selecting patients for fasciotomy.

## CLINICAL ETIOLOGIES

### Vascular Causes

ICP is elevated by conditions that either increase compartment volume or produce external compression on the compartment. The most common vascular etiologies for compartment syndrome are ischemia-reperfusion (IR) injury associated with acute ischemia, arterial and venous traumatic injuries, crush injuries, phlegmasia cerulea dolens, and hemorrhage within a compartment.

#### Ischemia-Reperfusion

The IR phenomenon, described in detail in Chapter 6 (Ischemia-Perfusion), plays a central role in the pathogenesis of compartment syndrome due to acute ischemia and crush injury. IR increases compartment volume by causing muscle tissue

injury, which leads to increased microvascular permeability with efflux of plasma proteins and progressive interstitial edema.<sup>11</sup> With reperfusion, oxygen radical generation exacerbates microvascular permeability and resulting interstitial edema.<sup>11</sup>

Orrapin identified several risk factors for compartment syndrome after acute limb ischemia, including inadequate backflow from the distal arteries, high serum creatinine kinase levels, positive fluid balance, and advanced-stage and prolonged limb ischemia.<sup>12</sup>

### Trauma

Both arterial and venous trauma may produce compartment syndrome. Occlusive arterial injuries result in distal ischemia that initiates the IR phenomenon, whereas venous injuries may compromise venous outflow. The impact of compromised venous outflow is discussed next (Venous Outflow Obstruction). Fasciotomy rates vary according to the type of vascular injury, ranging from 29.5% for isolated arterial injuries, 15.2% for isolated venous injuries, and 31.6% for combined arterial and venous injuries. Injuries to the popliteal artery are notorious for a higher risk of compartment syndrome (61% incidence), compared with injuries above the knee (19% incidence).<sup>13</sup>

### Venous Outflow Obstruction

Uncomplicated deep venous thrombosis (DVT) often increases ICP, depending on the extent of DVT.<sup>14</sup> Only when there is extensive, multilevel DVT with occlusion of venous collaterals is the venous outflow obstruction sufficient to increase ICP and produce compartment syndrome. With increased venous hypertension the arterial–venous pressure gradient ( $\Delta P$ ) is altered and capillary blood flow is impaired. With reduced capillary blood, muscle cell injury ensues, exacerbating tissue edema. This cycle continues until eventually the postcapillary venules thrombose and venous gangrene develops.

Two examples of situations that may result in venous outflow obstruction and compartment syndrome include deep vein harvest for use as an arterial conduit and extracorporeal membrane oxygenation (ECMO). In a minority of cases, especially when there is concurrent great saphenous vein harvest or IR in the same limb, harvesting deep vein can produce compartment swelling sufficient to necessitate fasciotomy.<sup>15</sup> ECMO may cause lower extremity compartment syndrome in 10.3% (7.3% to 14.5%) of patients. Compartment swelling during ECMO may be a result of venous outflow obstruction due to the presence of large bore cannula in the femoral vein and ischemia induced by a partially occlusive arterial cannula in the same extremity.<sup>16</sup>

### Hemorrhage

Hemorrhage may be a source of rapid increases in compartment pressure. Thigh compartment syndrome has been described as the presenting symptom for rupture of a popliteal artery aneurysm<sup>17</sup> or postoperative hemorrhage after joint replacement surgery in an anticoagulated patient.<sup>18</sup>

## Nonvascular Etiologies

### Fracture

Tibial or forearm fractures are the most common orthopedic causes of acute compartment syndrome. These fractures injure the surrounding muscles and cause bleeding within the compartment, elevating ICP. The incidence of compartment syndrome with fractures ranges from 1% to 29%.<sup>9,19–21</sup> The anterior compartment of the leg and the flexor compartment of the forearm are most prone to this phenomenon. Comminuted fractures are more likely to result in a compartment syndrome, owing to the greater energy absorbed in such injuries.<sup>20</sup>

### Crush Injury

Crush injuries are another form of trauma that may cause compartment syndrome. Reported mechanisms include crushing by equipment at industrial sites or large building structures during earthquakes and blunt trauma due to assault.<sup>22,23</sup> Compartment syndrome after crush injury results from a combination of direct muscle injury and IR due to direct compartment pressure with underlying muscle ischemia and subsequent reperfusion upon removal of the external compressive force. Large-volume crystalloid resuscitation can exacerbate the increase in ICP.<sup>22</sup>

### Iatrogenic

Iatrogenic causes of compartment syndrome include extravasation of large volumes of fluid within a muscle compartment, extravasation of caustic medications such as contrast agents, inadvertent arterial injections, and hemorrhage related to arterial or venous punctures in coagulopathic or anticoagulated patients.<sup>24–26</sup> Additional mechanisms include the compression injuries associated with prolonged intraoperative immobilization, as occurs in the dorsal lithotomy position, and cast immobilization for fractures.<sup>27–29</sup>

### Secondary Compartment Syndrome

Rarely a compartment syndrome develops in a trauma patient without overt evidence of extremity trauma. This phenomenon has been termed “secondary compartment syndrome” and is believed to be a consequence of diffuse microvascular permeability due to trauma-induced systemic inflammatory response syndrome in concert with massive fluid resuscitation.<sup>30</sup>

## CLINICAL PRESENTATION

### History and Examination

The diagnosis of an acute compartment syndrome begins with a high index of suspicion. Symptoms of a compartment syndrome include pain that is disproportionate to the magnitude of the injury and paresthesias in the distal extremity.<sup>31</sup> The pain is typically not relieved by immobilization or reduction of fractures and responds poorly to analgesic medications. Paresthesias represent an early symptom of ischemia of the nerves traversing the muscle compartment in question.

On examination, the most common findings are a tense, swollen compartment with pain elicited by passive movement of the muscles in that compartment. A careful neurologic examination should document sensory and motor function distal to the compartment, focusing especially on the nerves that traverse the compartment at risk. For example, a compartment syndrome afflicting the anterior compartment of the lower leg may be accompanied by dysfunction of the deep peroneal nerve, causing numbness at the first dorsal webspace of the foot or inability to extend the great toe. Loss of two-point discrimination is a relatively sensitive indicator of developing compartment syndrome.<sup>31</sup> The overall sensitivity of exam findings for compartment syndrome is dubious. In a meta-analysis of compartment syndromes related to tibial fractures, Ulmer found that the sensitivity of clinical findings for diagnosing compartment syndrome is low (13% to 19%). The positive predictive value is equally low (11% to 15%), and the negative predictive value is high (97% to 98%). Ulmer concluded that the “clinical features of compartment syndrome are more useful in their absence in excluding the diagnosis.”

## Measurement of Compartment Pressures

Measurements of ICP are not required to ascertain the diagnosis of a compartment syndrome in most cases. Pressure measurement should be reserved for equivocal cases, unconscious patients, and pediatric patients in whom a compartment syndrome is suspected. In cases in which the diagnosis is apparent from history or examination, measuring ICP is superfluous and risks delaying definitive therapy.

### Technique

Measuring ICP requires an instrument for measuring compartment pressures and a working knowledge of the muscle compartments. ICP has been measured using a host of techniques and instruments, including simple manometers, wick catheters, slit catheters, side-ported needles, and fiberoptic transducers. There are two components to each system: (1) a needle to access the compartment and (2) a pressure measurement system. The most commonly used ICP measuring systems are the arterial line manometer and handheld Stryker system. The arterial line manometer is ideally suited for use in the intensive care unit and operating room where pressure transducers and monitors are readily available. In the emergency room the handheld Stryker system is particularly convenient.

The choice of compartments for pressure measurement should be guided by clinical exam. The most symptomatic or turgid compartment should be interrogated first, remembering that the anterior compartment of the lower leg and the flexor compartment of the forearm are most prone to compartment syndrome. Ultimately it is advisable to obtain compartment pressures from all compartments at risk. If necessary, multiple readings may be obtained. McQueen et al. reported high sensitivity, specificity and negative predictive value when continuous compartment pressure monitoring was used.<sup>32</sup> However, another study found that continuous compartment pressure invasive monitoring did not have an impact on outcomes when

compared to clinical observation of alert patients with tibial fractures.<sup>33</sup> ICP, MAP, and diastolic pressure should be recorded for the medical record. The pressure criteria that define a compartment syndrome will be discussed later in this section. A normal compartment pressure is ≤10 to 12 mm Hg.

Near-infrared spectroscopy (NIRS) is the most common noninvasive method of measuring compartment pressure,<sup>34</sup> with NIRS values in at least one injured compartment 3% or more below the uninjured contralateral compartment. These findings require validation in future larger interventional studies.<sup>35</sup>

## Unusual Presentations for Compartment Syndrome

Compartment syndrome may affect any myofascial compartment. Although less common than the lower leg, compartment syndromes have been described in the upper extremity, hand, thigh, foot, and buttock. For any of these compartment syndromes, pain out of proportion to examination and swelling remain the hallmarks of their clinical presentation. In some cases, passive plantar- or dorsi-flexion may exacerbate the pain. The presence of neurologic symptoms is highly variable and is not required to secure the diagnosis.

Hand compartment syndromes are usually associated with crush injuries or fractures of the carpal bones. Hand compartment syndrome may affect any of the 10 compartments of the hand. The classic symptoms are pain and local paralysis at the intrinsic muscles.<sup>36</sup> Forearm compartment syndromes are typically associated with direct blows, crush injuries, or fractures.<sup>37</sup> Pain, swelling, and neurologic symptoms are the classic symptoms of increased ICP in the forearm, especially after trauma.<sup>38</sup>

Thigh compartment syndrome is usually caused by blunt trauma from motor vehicle accidents, contusion,<sup>33,39</sup> or crush injury.<sup>22</sup> Reperfusion injury rarely results in a compartment syndrome of the thigh. The anterior thigh compartment is most commonly involved and universally presents with pain on passive motion. Paresthesias and paralysis may also be present.<sup>33,39</sup>

Gluteal compartment syndrome has been associated with hypogastric artery ligation or embolization during aortic aneurysm repair, hip arthroplasty, and prolonged compression during operative procedures.<sup>40–43</sup> Gluteal compartment syndrome has been cited as a cause of rhabdomyolysis, renal failure, and sciatic nerve palsy.<sup>40</sup>

## ADJUNCTIVE MEASURES

### Prevention of Compartment Syndrome

A variety of adjuncts have been proposed to mitigate muscle swelling and prevent compartment syndrome. The most common approach has been pharmacologic therapy to blunt oxygen radical formation during reperfusion of an ischemic limb to minimize IR injury. Mannitol, allopurinol, superoxide dismutase, deferoxamine, thromboxane A<sub>2</sub>, and melatonin have shown promise in reducing oxygen radical formation and ICP

in animal models.<sup>44–49</sup> The use of these agents in humans has been limited to anecdotal reports.<sup>50,51</sup>

In cases of impending compartment syndrome, Mars<sup>52</sup> proposed a protocol of “first aid to hypoxic cells.” Mars’ protocol included: (1) maintaining normal blood pressure because hypotension reduces perfusion pressure; (2) removing any constricting bandages; (3) maintaining the limb at heart level (with no elevation) to avoid reducing the arterial–venous pressure gradient; and (4) supplemental oxygen to optimize oxygen saturation. A recent intersocietal guideline for prevention of leg compartment syndrome during lithotomy pelvic surgeries includes lowering the legs to below the heart level for 15 minutes every 4 hours intraoperatively if the surgery is longer than 4 hours.<sup>53</sup>

## Prevention of Systemic Sequelae

Myonecrosis associated with compartment syndrome may liberate intracellular potassium, phosphate, myoglobin, and creatine phosphokinase (CPK). Treatments designed to prevent systemic sequelae of compartment syndrome are aimed at preventing further complications related to the electrolyte disturbances or myoglobinuria that result from extensive myonecrosis.

### Hyperkalemia

Hyperkalemia with cardiac arrest has been described among patients with significant myonecrosis, especially among patients with crush injuries.<sup>22,23</sup> Aggressive pharmacologic interventions, even hemodialysis or continuous hemofiltration, may be required to control severe hyperkalemia.<sup>54</sup>

### Myoglobinuria

Myoglobinuria exerts its nephrotoxic effects by inducing renal vasoconstriction, tubular cast formation, and direct heme protein–induced cytotoxicity.<sup>55</sup> The management of myoglobinuria includes aggressive crystalloid infusion, forced diuresis with mannitol, and alkalinization of the urine with bicarbonate. The rationale for crystalloid and bicarbonate infusion is based on the observation that heme proteins have minimal nephrotoxicity in the absence of hypovolemia and aciduria.<sup>54</sup> Clinical data affirm that early resuscitation with crystalloid diminishes the risk of progression to acute renal failure.<sup>22,23,54</sup> The data in support of mannitol and bicarbonate are more circumstantial. In a review of 1771 patients with acute renal failure due to myoglobinuria, Brown and colleagues found no difference in the incidence of acute renal failure, need for dialysis, or mortality between patients receiving mannitol and bicarbonate, compared with those receiving crystalloid infusion alone.<sup>51</sup> Recommendations for the management of myoglobinuria include hydration with a goal urine pH of greater than 6.5, despite the fact that the use of sodium bicarbonate has not been shown to be superior to saline diuresis.<sup>54</sup>

Myoglobin is poorly cleared by conventional dialysis membranes due to its relatively large molecular weight (17,000 Da), so hemodialysis is not a useful adjunct in preventing renal injury due to myoglobinuria, although continuous venovenous

hemofiltration has shown promise in preliminary studies.<sup>55</sup> Renal replacement therapy is currently reserved for standard indications, including the management of severe hyperkalemia.<sup>54</sup>

## FASCIOTOMY

### Criteria for Fasciotomy

The decision to proceed to fasciotomy may be dictated on clinical grounds or by ICP measurements (Table 105.1).

#### Clinical Criteria

Clinical criteria for fasciotomy include a swollen, tense compartment, pain with passive motion of muscle groups traversing that compartment, and neurologic findings referable to the compartment. Not all of these criteria are required to proceed to fasciotomy. The presence of a turgid compartment with either of the other two criteria (pain with passive muscle movement, neurologic changes) is sufficient to warrant fasciotomy. Any neurologic finding referable to a tense compartment is an absolute indication for expeditious fasciotomy because nerve injury is ongoing. The presence of a tense compartment alone places the limb in an equivocal category for which fasciotomy or continued serial examinations are options. As patients who are obtunded or require other operations are poor candidates for serial examination, making fasciotomy is the best option. If serial examinations are pursued, they must be performed by an experienced surgeon. In equivocal cases, ICP measurement may assist in decision-making.

An important consideration is the likely evolution of muscle swelling over the next several hours. In an equivocal case in which additional muscle swelling is inevitable, a “prophylactic” fasciotomy may be prudent. Scenarios in which prophylactic fasciotomy may be reasonable include acute ischemia exceeding 6 hours, especially if there is inadequate collateral flow, and combined arterial and venous traumatic injuries.<sup>13,56–58</sup>

**TABLE 105.1** Indications for Fasciotomy

Absolute Indications	Potential Indications
<ul style="list-style-type: none"> <li>• Tense compartment <i>plus either:</i> <ul style="list-style-type: none"> <li>• Pain with passive motion of muscles traversing the same compartment <i>or</i></li> <li>• Paresis or paresthesias referable to the same compartment</li> </ul> </li> <li>• Tense compartment in a patient who cannot be examined serially due to obtundation or need for other operations</li> <li>• ICP minus mean blood pressure &lt;40 mm Hg</li> <li>• ICP minus diastolic blood pressure &lt;10 mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>• Acute ischemia &gt;6 h with few collaterals</li> <li>• Combined arterial and venous traumatic injuries</li> <li>• Phlegmasia cerulea dolens</li> <li>• Tense compartment after crush injury</li> <li>• Tense compartment after fracture</li> </ul>

ICP, intracompartmental pressure.

### Intracompartmental Pressure Measurements

The threshold ICP for the diagnosis of compartment syndrome remains controversial, but the data favor the use of a dynamic ICP threshold related to MAP or diastolic pressure.<sup>8–10</sup> Fasciotomy is warranted if the difference between the ICP and MAP falls to less than 40 mm Hg or the difference in ICP and diastolic pressure is less than 10 mm Hg.

### Contraindications to Fasciotomy

Fasciotomy is contraindicated when the extremity is nonviable, due to extensive traumatic or ischemic injury. Crush injuries, in particular, may result in life-threatening complications from reperfusion because of the magnitude of the electrolyte shifts that result from reperfusion of ischemic muscle after fasciotomy.<sup>22</sup>

## TECHNIQUE OF FASCIOTOMY

Fasciotomy is the only known treatment for acute compartment syndrome. Performing an adequate fasciotomy is critical to complete decompression of a compartment syndrome. Poor technique may lead to incomplete decompression or injury to anatomic structures within the compartment. Technical details and relevant anatomy for fasciotomy are outlined in this section.

### Lower Extremity Technique

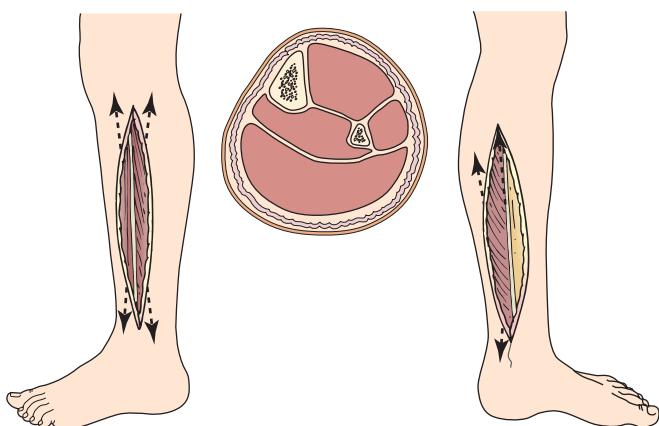
#### Lower Leg

##### Anatomic considerations

The lower leg is the most common site for compartment syndrome. The lower leg is subdivided into four anatomic compartments: anterior, lateral, superficial posterior, and deep posterior compartments. The most commonly injured nerve during a fasciotomy of the lower leg is the superficial peroneal nerve, which branches from the common peroneal nerve at or below the proximal fibular head and descends in the lateral compartment along the intermuscular septum separating the anterior and lateral compartments.<sup>59</sup>

##### Skin incisions

The length of the skin incisions is critical to ensuring that complete decompression of the compartments is achieved. Jensen et al. found that 12% of subcutaneous fasciotomies, using minimal incisions, had incomplete decompression requiring reoperation to extend the skin incision.<sup>31</sup> Jensen and Sandermann hypothesized that the skin itself could prevent adequate decompression of the compartment syndrome. Cohen noted that a skin incision of 8 cm decreased the mean ICP in the anterior compartment of the lower leg from 48 to 25 mm Hg; however, one-third of patients had compartment pressures that remained elevated. Full decompression of all compartments of the lower leg required incisions 12 to 20 cm in length.<sup>60</sup> Some authors have advocated using limited incisions when the muscle swelling is expected to be minimal, reserving extensive open incisions for cases in which the muscle



**Figure 105.1** Double-Incision Fasciotomy of the Lower Leg.

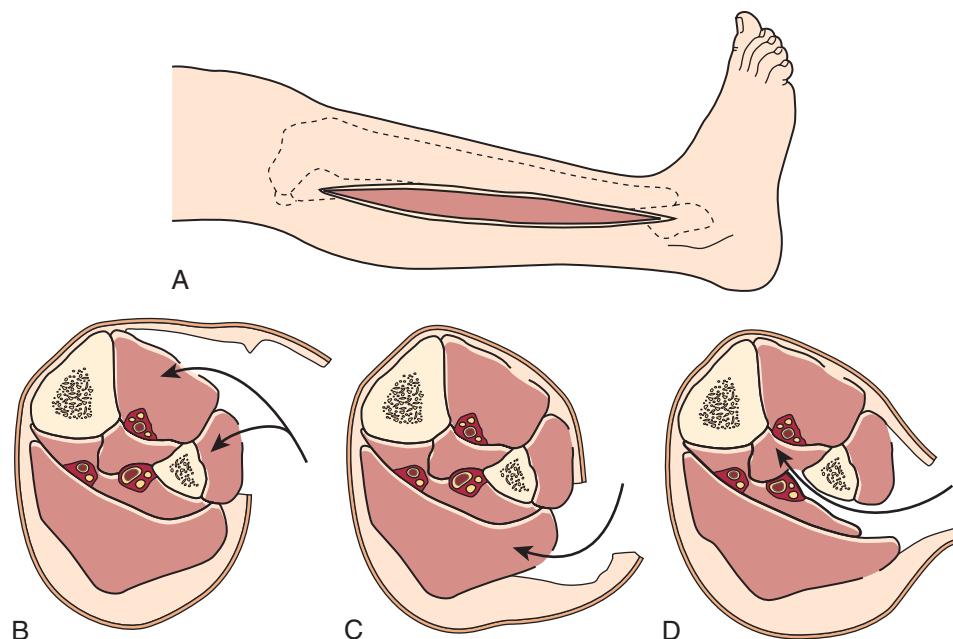
swelling is dramatic.<sup>61</sup> Unfortunately it is often difficult to predict the extent of postoperative swelling that will evolve postoperatively.

##### Double-incision technique

The double-incision technique (Fig. 105.1) for lower leg fasciotomy involves a generous longitudinal incision on the lateral aspect of the lower leg between the fibular shaft and the crest of the tibia. The incision is oriented directly over the intermuscular septum between the anterior and lateral compartments, approximately 4 cm lateral to the crest of the tibia. Pallister et al. explored the feasibility of handheld ultrasound for proper placement of skin incision immediately over the intermuscular septum.<sup>62</sup> Skin flaps are then raised medially and laterally to expose the fascia of the anterior and lateral compartments. The intermuscular septum between these compartments must be identified clearly to ensure that both compartments are thoroughly decompressed. The anterior and lateral compartments are opened via separate, parallel 12 to 20 cm fascial incisions using Metzenbaum or Cooley scissors, taking care to sufficiently elevate the posterior blade of the scissors off of the muscle to avoid injury to the common, superficial, and deep peroneal nerves. These nerves are most at risk of injury near the fibular head, so it is advisable to terminate the proximal extent of these fascial incisions 4 to 5 cm distal to the fibular head. A second incision is placed on the medial aspect of the leg 1 to 2 cm posterior to the tibia for decompression of the two posterior compartments. The saphenous vein and nerve should be avoided in the subcutaneous tissue. The superficial posterior compartment is decompressed via a longitudinal incision along the gastrocnemius fascia. The deep posterior compartment is decompressed by dividing the attachments of the soleus muscle to the tibia, exposing the fascia overlying the tibialis posterior and flexor muscles of the foot. This fascia is then incised longitudinally, avoiding injury to the posterior tibial artery. The advantage of the two-incision technique is its relative simplicity, allowing rapid decompression of the four compartments of the lower leg.<sup>63</sup>

##### Single-incision technique

The single-incision technique (Fig. 105.2) involves a lateral incision over the fibula from the fibular neck to 3 or 4 cm



**Figure 105.2** Single-Incision Fasciotomy of the Lower Leg. (A) Lateral skin incision from the fibular neck to 3–4 cm proximal to the lateral malleolus. (B) The skin is undermined anteriorly, and a fasciotomy of the anterior and lateral compartments is performed. (C) The skin is undermined posteriorly, and a fasciotomy of the superficial posterior compartment is performed. (D) An interval between the superficial posterior and lateral compartments is developed. The flexor hallucis longus muscle is dissected subperiosteally off the fibula and retracted posteromedially. The fascial attachment of the posterior tibial muscle to the fibula is incised to decompress the muscle. (From Davey JR, Rorabeck CH, Fowler PJ. The tibialis posterior muscle compartment: an unrecognized cause of exertional compartment syndrome. *Am J Sports Med.* 1984;12:391–397.)

above the lateral malleolus.<sup>64</sup> A subcutaneous flap is developed in an anterior direction to access the anterior and lateral compartments. These compartments are decompressed using the same technique outlined previously for these compartments (see Double-incision technique, above). A posterior subcutaneous flap is developed to access the superficial posterior compartment for a longitudinal fascial incision. The interval between the lateral and superficial posterior compartments is exposed. The flexor hallucis longus muscle is identified and dissected off of the fibula in a subperiosteal plane. The peroneal vessels should be displaced posteriorly to avoid injury to these structures during the subperiosteal dissection. The fascial attachment of the posterior tibial muscle to the fibula is incised to open the deep posterior compartment. Most surgeons no longer perform a fibulectomy. The primary advantage of the one-incision approach is the ability to decompress all four compartments through a single incision, but it is a relatively tedious approach to fasciotomy with a potential for injury to the peroneal artery and nerve. Most vascular surgeons now favor the double-incision technique.

### Thigh

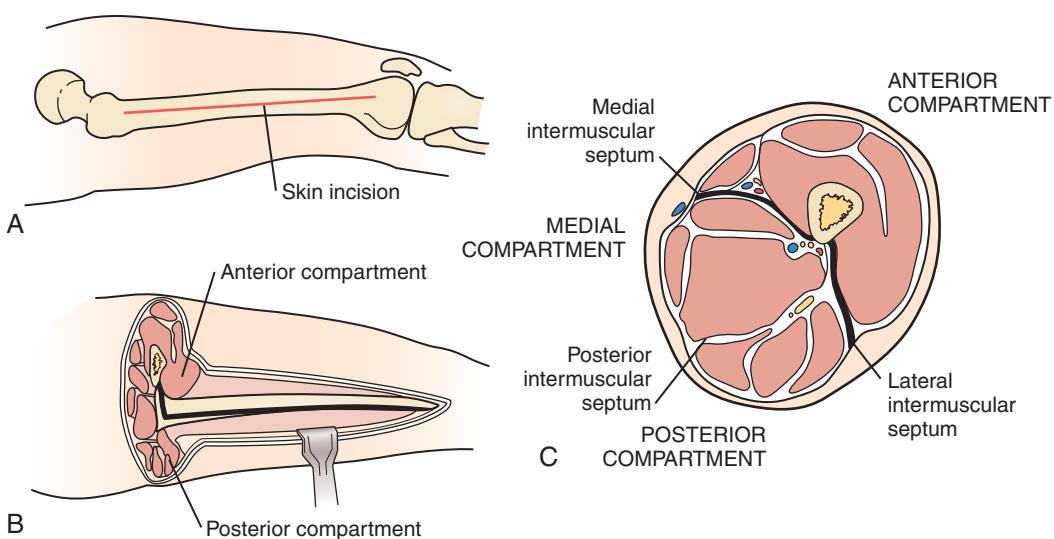
The thigh contains three compartments: anterior, posterior, and medial. The anterior compartment contains the sartorius and quadriceps muscles (rectus femoris, vastus lateralis, vastus intermedius, and vastus medialis). It receives its innervation from the femoral nerve. The posterior compartment contains

the biceps femoris, semimembranosus, and semitendinosus muscles. The sciatic nerve innervates this compartment. The medial compartment contains the pectineus, obturator externus, gracilis, and adductor muscles (longus, brevis, magnus, and minimus). The obturator nerve innervates the medial compartment.<sup>65</sup>

In most cases a single lateral incision may be used to decompress the posterior and anterior compartments (Fig. 105.3), whereas the medial compartment rarely requires decompression.<sup>66</sup> An incision is placed along the lateral thigh, beginning just distal to the intertrochanteric line and extending distally to the lateral epicondyle. The iliotibial band is exposed and incised longitudinally along the length of the skin incision to decompress the anterior compartment. The vastus lateralis is reflected medially to expose the lateral intermuscular septum. The intermuscular septum is incised over the length of the skin incision to release the posterior compartment. The medial compartment pressure should be measured. Decompression of the medial compartment is rarely necessary, although a separate incision over the adductor muscle group will decompress this compartment.

### Buttock

The buttock is composed of three major muscles, each with its own fascial compartment. There is no universally accepted standard incision for a buttock fasciotomy. However, a longitudinal incision is most frequently described in case



**Figure 105.3** Fasciotomy of the Thigh. (A) The incision extends from the intertrochanteric line to the lateral epicondyle. (B) The anterior compartment is opened by incising the fascia lata. The vastus lateralis is retracted medially to expose the lateral intermuscular septum, which is incised to decompress the posterior compartment. (C) Thigh compartments and appropriate incision. (A and B, redrawn from Tarlow SD, Achterman CA, Hayhurst J, et al. Acute compartment syndrome in the thigh complicating fracture of the femur: a report of three cases. *J Bone Joint Surg Am.* 1986;68:1439.)

series. Each of the muscle compartments requires decompression for a complete fasciotomy. Some authors have also recommended performing neurolysis of the sciatic nerve to prevent tension on the nerve from inflammatory adhesions.<sup>67</sup>

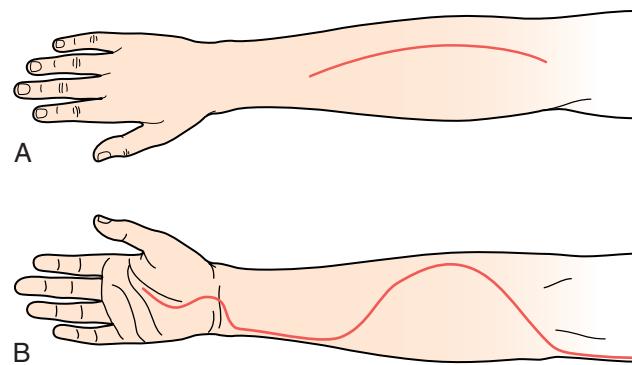
## Foot

Currently, there is variability to the number of compartments ascribed to the foot. The most frequently named compartments are medial, lateral, superficial, and calcaneal compartments, with an additional compartment corresponding to each interosseous muscle.<sup>68,69</sup> Decompression of the foot is required infrequently and most commonly associated with crush injuries.<sup>70</sup> Two longitudinal dorsal incisions are fashioned. The first incision is oriented along the medial aspect of the second metatarsal, and the second incision is placed at the lateral margin of the fourth metatarsal bone. A separate incision is required to decompress the calcaneal compartment. Through these incisions, each of the muscle compartments can be incised, typically with fine scissors. Care must be taken to avoid the medial and lateral plantar neurovascular bundles that traverse the longitudinal axis of the foot.<sup>70,71</sup>

## Upper Extremity

### Forearm

The forearm is the most frequent site of compartment syndrome in the upper extremity. Within the forearm, there are volar (flexor, superficial, and deep), lateral (mobile wad), and the extensor (dorsal, superficial, and deep) compartments. The volar, or Henry, fasciotomy (Fig. 105.4) uses a single incision to decompress both the lateral and volar compartments.<sup>30,72</sup>



**Figure 105.4** Fasciotomy of the Volar Forearm for Severe Volkmann's Contracture. (A) Extensive opening of the fascia of the dorsum of the forearm for dorsal compartment syndromes. (B) Incision used for anterior forearm compartment syndromes. The skin and underlying fascia are released completely throughout.

A curvilinear incision begins proximal to the antecubital fossa, medial to the biceps tendon, crosses the antecubital crease, and extends to the radial side of the forearm where it extends distally along the medial border of the brachioradialis muscle. From the distal forearm the incision extends across the carpal tunnel along the thenar crease. The fascia overlying the superficial flexor compartment is incised along the entire length of skin incision. The radial nerve and brachioradialis muscle are retracted to the radial side of the forearm, and the flexor carpi radialis and radial artery are retracted to the ulnar side. The fascia overlying each of the muscles of the deep flexor compartment are incised to complete the volar fasciotomy. If the dorsal ICP is elevated, a long incision from the lateral epicondyle to the wrist is used to perform a fasciotomy between the extensor carpi radialis brevis and the extensor

digitorum communis.<sup>30</sup> Carpal tunnel releases are controversial and may not be of benefit in isolated forearm compartment syndromes.<sup>72</sup>

### Hand

The hand is a rare location for compartment syndrome. There are 10 compartments of the hand: hypothenar, thenar, and adductor pollicis compartments; four dorsal interosseous compartments; and three volar interosseous compartments. The number of compartments in the hand complicates decision-making in performing a fasciotomy of the hand. The choice of fasciotomies for the hand should be tailored to symptoms.<sup>25</sup> All patients should have a carpal tunnel release, and most will require one to two dorsal interosseous fasciotomies. Many patients will also require thenar or hypothenar fasciotomy. All dorsal hand fasciotomies should be performed through longitudinal hand incisions.

## FASCIOTOMY WOUND MANAGEMENT

Fasciotomy may solve the problem of increased ICP, but resulting wounds may be a source of considerable short- and long-term morbidity.<sup>73,74</sup> The goal of wound care early after fasciotomy is preventing further muscle injury or necrosis until muscle swelling subsides sufficiently to permit closure. When muscle viability is questionable, periodic saline dressings permit caregivers the opportunity to inspect and debride the wound at regular intervals. Vacuum-assisted closure (VAC) therapy is an alternative means of wound coverage, although the wound should be inspected at frequent intervals early after fasciotomy. After tissue viability is ensured and wound swelling has subsided, the priority shifts to wound closure.

Fasciotomy wound closure has been attained through a variety of approaches. The options include delayed primary closure, closure by secondary intention, gradual dermal apposition, split-thickness skin grafting (STSG), and myocutaneous flap coverage. Each of these approaches has a role, depending on the clinical circumstances. Delayed primary closure offers the simplicity of direct closure but should be reserved for those cases in which muscle swelling is minimal or nonexistent. Wiger found that 7 of 12 fasciotomy wounds had increased ICP (>30 mm Hg) with attempted delayed primary closure on postoperative days 3 or 4, so early closure should be undertaken with caution.<sup>75</sup> Closure by secondary intention should be reserved for cases in which the patient is either medically or nutritionally ill-suited for any other option because this approach is the least expeditious in achieving wound closure. The addition of VAC therapy accelerates the process of closure by secondary intention and has been used with success for fasciotomy wounds.<sup>76,77</sup> To accelerate closure further, various forms of gradual dermal apposition have been advocated, including progressive closure with silastic vessel loops or cutaneous sutures placed at surgery or commercially available products.<sup>78–82</sup> Anecdotal reports have documented success with each

approach. Several authors have proposed closure of fasciotomy wounds using STSG.<sup>38,44,73,83</sup> In a randomized trial comparing VAC with shoelace technique, both methods were proven safe. VAC required a longer time to closure and was more expensive than the shoelace technique, especially in patients requiring later STSG.<sup>84</sup> Weaver demonstrated that if fasciotomy wounds could not be primarily closed during the first post-fasciotomy wash out, they are rarely closed through delayed primary technique, so early STSG of these wounds should be considered.<sup>85</sup> In contrast, pediatric fasciotomy wounds still have a high likelihood of being closed through delayed primary closure after serial surgical debridement.<sup>86</sup> Myocutaneous flap coverage is generally reserved for coverage of neurovascular structures or exposed bone in a limb that remains functional. Early closure may decrease the rate of wound complications associated with closure by secondary intention and truncate the length of hospital stay.<sup>73</sup>

## OUTCOMES

### Early Outcomes

The mortality rate for patients undergoing calf fasciotomy ranges from 11% to 15%.<sup>31,87,88</sup> Major amputations are required in 5% to 21% of limbs.<sup>31,87,88</sup> Wound complications occur in 4% to 38% of patients.<sup>73,74,87</sup> Wound complications are more frequent if fasciotomy is delayed more than 6 hours (37%), compared with early fasciotomy (25%).<sup>39,85,89</sup> Renal failure is a rare complication after compartment syndrome, unless there is considerable myonecrosis.<sup>54</sup> Neurologic deficits occur in 7% to 36% of limbs.<sup>87–89</sup> and are the most frequent early complications following a forearm fasciotomy.<sup>38</sup>

### Late Outcomes

The late outcomes for fasciotomy are determined largely by the functional status of the patient at hospital discharge. Neurologic deficits or amputation in the early postoperative period are harbingers of long-term disability. Even in the subset of patients discharged without amputation or neurologic deficits, a fasciotomy predisposes the limb to future problems. Fitzgerald and colleagues noted at late follow-up that 77% of fasciotomy sites were associated with impaired sensation at the margins of the wound, 7% had tethered tendons, and 13% had recurrent ulcerations at the fasciotomy site.<sup>90</sup> Bermudez and colleagues<sup>91</sup> found that a significant proportion of patients (47%) had clinical evidence of chronic venous insufficiency after lower leg fasciotomy due to impaired calf muscle pump function. A small subset (7.5%) of patients will require late amputation (between 30 days and 1 year).<sup>88,92</sup>

### Sequelae of Missed Compartment Syndrome

A delayed or missed compartment syndrome will have devastating consequences for the patient and the limb, increasing the risk of neurologic deficit, amputation, and renal failure.

Sheridan and colleagues found that the overall complication rate increased dramatically if fasciotomy was delayed more than 12 hours (54%), compared with early fasciotomies (4.5%).<sup>74</sup> Nearly half of the patients with delayed fasciotomies required amputation and 92% had a significant neuropathy.<sup>74</sup> Not surprisingly, delay of fasciotomy for more than 36 hours almost invariably results in amputation. After 3 to 4 days, compartment syndrome decompression is not indicated since the rate of infection and muscle necrosis is prohibitively high.

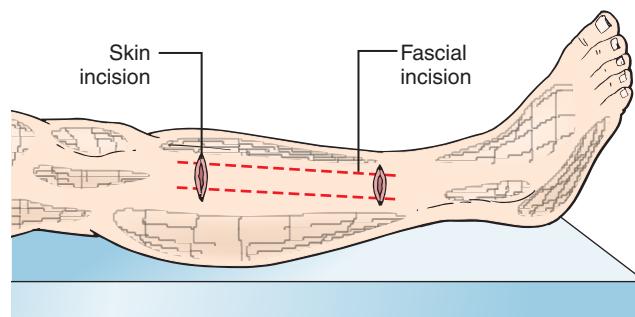
The classic late consequence of a missed compartment syndrome is a Volkmann contracture. In this state the ischemic muscle and nerve tissue are replaced by fibrosis, leaving the compartment firm, contracted, and dysfunctional.<sup>93</sup> Adjacent joints become stiff and immobile. Treatment consists of contracture and joint capsule release.<sup>94</sup> Orthopedic consultation for immediate- and long-term management is advisable.

## CHRONIC EXERTIONAL COMPARTMENT SYNDROME

### Clinical Presentation and Diagnosis

Chronic exertional compartment syndrome (CECS) is a syndrome of exercise-induced pain and tightness that usually affects the muscles of the lower leg, especially the anterior and lateral compartments, due to increased ICP and transient muscle ischemia.<sup>95–97</sup> The typical patient is a young (20- to 30-year-old), athletic patient who is a runner.<sup>95</sup> The syndrome is characterized by pain beginning 20 to 30 minutes after the onset of exercise, which abates with 15 to 30 minutes of rest. Paresthesias and muscle dysfunction often occur in the distribution of peripheral nerves traversing the compartment. Symptoms are bilateral in 82%. Physical examination often shows tenderness of the affected muscle compartment.

The differential diagnosis includes fascial hernias, medial tibial syndrome (for anterior compartment symptoms), and claudication due to popliteal entrapment syndrome (for calf symptoms). Although MRI and other tests may rule out other causes of leg pain, measurement of ICP is required to secure the diagnosis. Pedowitz and colleagues established pressure criteria for the diagnosis: (1) resting ICP >15 mm Hg; (2) ICP >30 mm Hg, 1 to 2 minutes after completion of exercise; or (3) ICP >20 mm Hg, 5 minutes after completion of exercise.<sup>98</sup> One or more of these criteria are sufficient for the diagnosis with the characteristic symptoms that are reproducible on exercise. Roscoe introduced modified criteria by measuring ICP continuously before, during, and after exercise on a treadmill, carrying a 15-kg load. Subjects with CECS had higher ICP immediately upon standing, and the diagnostic utility of ICP measurement was improved when measured continuously during exercise. Roscoe concluded that a threshold ICP of 105 mm Hg during phase 2 of his exercise protocol provides better diagnostic accuracy than the Pedowitz criteria.<sup>99</sup>



**Figure 105.5** Fasciotomy of the Anterior and Lateral Lower Leg Compartments for Chronic Exertional Compartment Syndrome.

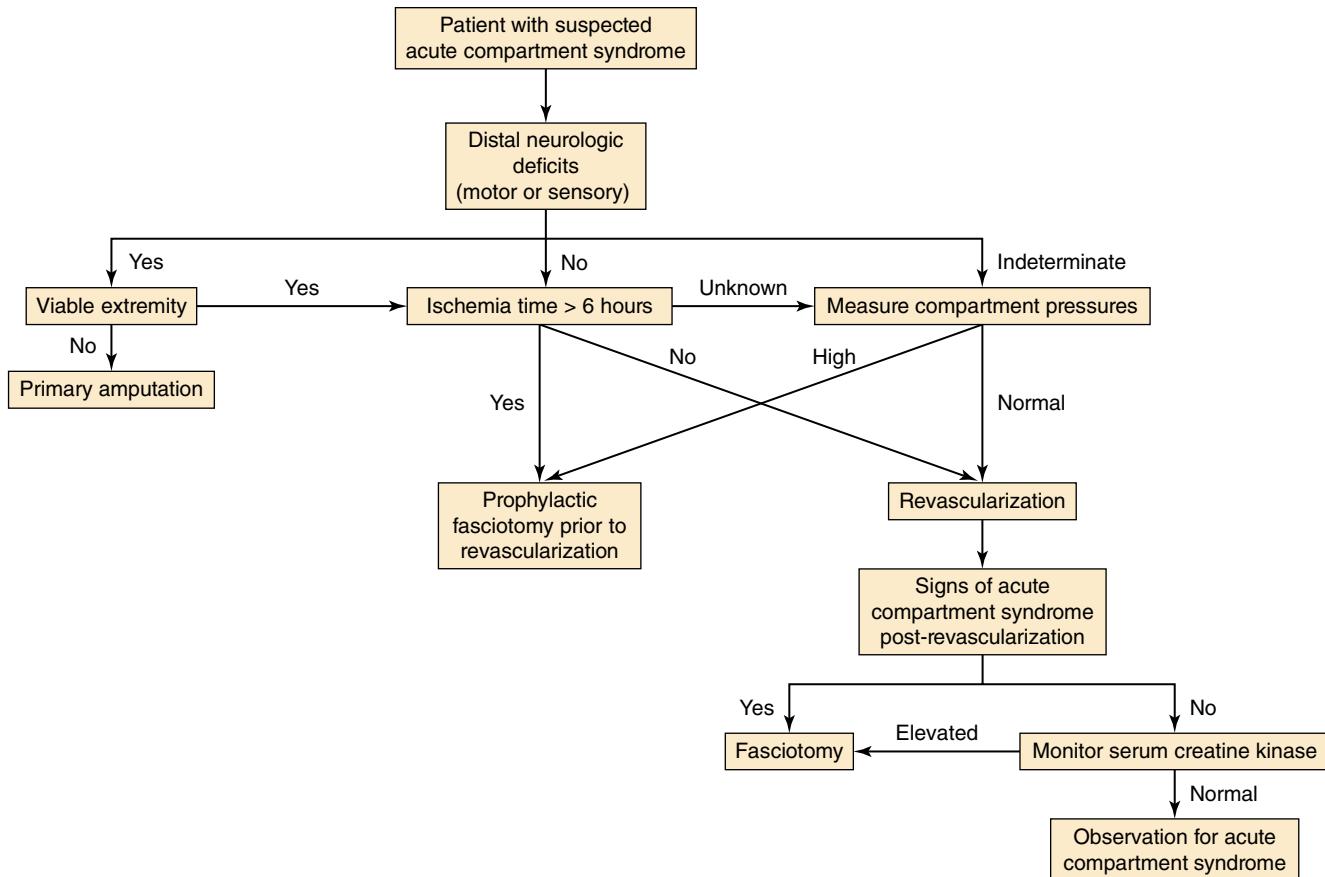
### Fasciotomy for Chronic Exertional Compartment Syndrome

Treatment for CECS is either avoidance of the precipitating exercises or surgical decompression of the affected compartment. Avoidance is poorly accepted by athletic patients, so fasciotomy is typically the treatment of choice. The approach to compartment decompression for CECS differs from treating acute compartment syndrome because only symptomatic compartments are decompressed. Both fasciotomy and fasciectomy have been proposed to decompress the symptomatic compartments. For subcutaneous fasciotomy (Fig. 105.5), two 2- to 4-cm transverse incisions are commonly used.<sup>100</sup> Both incisions are oriented over the intermuscular septum between the anterior and lateral compartments at the proximal and distal ends of the standard longitudinal fascial incisions of the anterior and lateral compartments. Two longitudinal fascial incisions are then performed between the two transverse skin incisions, akin to the fascial incisions used for a standard open fasciotomy (see Double-incision technique, earlier). For fasciectomy, a single longitudinal skin incision overlying the intermuscular septum between the anterior and lateral compartments is used. Two standard longitudinal fascial incisions are performed in the anterior and lateral compartments, followed by resection of a 2 × 6 cm ellipse of fascia. In his review of the treatment of 796 patients with CECS, Turnipseed advises fasciectomy as the treatment of choice in most cases of chronic compartment syndrome.<sup>101</sup>

### Outcomes

Long-term results appear promising in case series, which describe significant reduction in pain at 2 years following anterior compartment fasciotomy in 83% of subjects.<sup>100</sup> A recent large retrospective study also reported significant pain reduction and increased activity levels in CECS patients who underwent fasciotomy. The authors found ICP to be positively correlated with patient-reported pain.<sup>100</sup> In a group of 21 patients, self-reported outcomes of a staged unilateral and simultaneous bilateral fasciotomies were similar, but the patients who did not have all four compartments released reported worse outcomes.<sup>102</sup>

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A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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# Atheromatous Embolization and its Management

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Atheromatous embolization is a poorly recognized and under-diagnosed multisystem disorder associated with a high risk of all-cause and cardiovascular mortality.<sup>1</sup> There are a myriad of clinical manifestations that may occur across multiple organ systems, making differential diagnoses broad and diagnosis difficult. Further confounding diagnosis, atheromatous embolization is known by many different names: cholesterol embolization, cholesterol crystal embolization, blue toe syndrome, purple toe syndrome, atheroembolism, and pseudovasculitis. For the purposes of this chapter, these terms will be used interchangeably. After atheroembolism occurs, therapy involves three major strategies: treating the affected end organ, preventing further embolization from occurring, and preventing future cardiovascular morbidity and mortality by risk factor modification. Therefore, it is critical for clinicians to have a high index of suspicion and to recognize the clinical manifestations of this syndrome.

## INCIDENCE

The prevalence of atheroembolism ranges from 0.18% to 2.4%, based on series of unselected autopsy studies.<sup>2</sup> However, in older patients with more severe atherosclerosis, the incidence is much higher, from 8.6% to 12.3%.<sup>3,4</sup> Autopsy studies performed in patients with known advanced atherosclerosis who had undergone cardiac or vascular surgical procedures before their deaths found 22%–27% with evidence of atheroemboli.<sup>5,6</sup> Postmortem examination of patients who had abdominal aortic aneurysm resection found evidence of atheroembolism in 77% of this population.<sup>7</sup> In general, retrospective autopsy studies may overestimate the frequency of the disease due to detection of subclinical cases and selection bias inherent in obtaining information after necropsy. In contrast, clinically significant atheroembolic disease in clinical studies may be missed because of short-term follow-up. The prevalence

of atheroembolic disease in clinical studies has been estimated to be between 1% and 4%.<sup>8–12</sup> Changing demographics (i.e. an increasingly elderly population accompanied by more advanced atherosclerosis) portend an increased prevalence of atheromatous embolization, while surgical and endovascular technological advancements (i.e. better guide wires, catheters, and techniques) may counter these effects. There have been no recent studies on current prevalence rates.

## PATHOGENESIS

The first description of atheroembolism was published more than a century ago by the German pathologist, Panum. However, Flory<sup>13</sup> is credited for accurately describing the syndrome in 1945. Among 267 consecutive autopsies, he observed that the risk of atheroembolism is directly related to the severity of aortic atherosclerosis. There was no cholesterol crystal embolism when aortic ulceration was absent, 1.4% embolization with moderate aortic plaque erosion, and 12.8% with severe aortic plaque ulceration. The sources of atheroembolism are atherosclerotic plaques in large arteries such as the aorta, iliac, or carotid arteries which consist of a fibrous cap, under which are macrophages, necrotic debris, and cholesterol crystals. The vulnerable plaque, or the plaque at highest risk of rupture, is the one with a thin fibrous cap surrounding a large lipid-rich core.<sup>14</sup> Plaque rupture caused by either spontaneous, traumatic, or iatrogenic maneuvers leads to embolization of cholesterol crystals, platelets, fibrin, and other detritus into arteries or arterioles and results in local mechanical obstruction, as well as an inflammatory reaction that contributes to end-organ ischemia and necrosis.<sup>15</sup>

Cholesterol crystals are white and rhomboidal or rectangular in shape. They can also be elongated, biconvex, and needle shaped, and range in size from 250 µm to less than 10 µm in diameter.<sup>9</sup> Because they are lightweight and hydrophobic, they pass quickly through blood vessels until they are stopped by arterial bifurcations, a narrowing of the vessel lumen, or when reaching the terminal branches of the arterial circulation.<sup>9</sup> Cholesterol crystals that lodge in arterioles immediately incite an inflammatory response characterized by varying degrees of polymorphonuclear and eosinophilic infiltration.<sup>9,13,16,17</sup> By 2–4 weeks, a more chronic inflammatory infiltrate is seen

where cholesterol crystals become embedded in multinucleated giant cells and smooth muscle cells.<sup>16</sup> Endothelial proliferation and fibrous tissue can be found surrounding the crystals, ultimately leading to luminal obliteration.<sup>16,17</sup> At 1–2 months, crystals may extrude out of the vessel lumen and bury in the adventitia, or remain in the lumen, embedded within organized thrombus that may recanalize.<sup>16</sup> The crystals are resistant to breakdown by macrophages and have been shown to persist in tissue for up to 9 months.<sup>18,19</sup> Arterial lumina are eventually occluded by the accumulation of cells and fibrous material. These pathologic changes result in tissue effects distal to the cholesterol crystal emboli, including ischemia, and rarely, infarction, depending on the extent of organ involvement. This type of foreign body reaction explains the prolonged timeframe (weeks to months) for serum creatinine to rise in patients with atheroembolic renal disease and illustrates why renal function does not usually recover.<sup>18,20–22</sup>

## RISK FACTORS

The major risk factor for atheromatous embolization is atherosclerosis of the thoracic and abdominal aorta.<sup>23,24</sup> Other risk factors include age (>60 years), coronary artery disease, peripheral arterial disease, and abdominal aortic aneurysms.<sup>5,13,24</sup> Elevated serum low-density lipoprotein (LDL) to high-density lipoprotein (HDL) cholesterol ratios >2.23 have been associated with mobile and/or ulcerated aortic plaque in patients with ischemic embolic stroke of unknown source.<sup>25</sup> Patients with protruding mobile atheroma or aortic plaques greater than 4 mm in diameter have increased risk of embolic events.<sup>26,27</sup> Another feature that increases risk of atheroembolization is lack of plaque calcification.<sup>24</sup> It was hypothesized that non-calcified plaques are probably lipid-laden plaques with thin fibrous caps, which are unstable and prone to ulceration, rupture, and thrombosis.<sup>28</sup> Pedunculated, mobile plaques have also been associated with an increased risk of recurrent embolization (Table 106.1).<sup>29–31</sup>

Complex thoracic aortic plaques are not only valuable “markers” of severe widespread atherosclerosis<sup>24,32</sup> but also identify individuals at high-risk for cardiovascular disease such as peripheral arterial occlusive or coronary artery disease.<sup>33</sup> Although atheroembolism could occur spontaneously, it is

TABLE 106.1

Incidence of Events According to Plaque Thickness in the Aortic Arch Proximal to the Ostium of the Left Subclavian Artery

Plaque Thickness (mm)	RECURRENT BRAIN INFARCTION			ANY VASCULAR EVENT		
	Person-Years of Follow-Up	Number of Events	Incidence Per 100 Person-Years of Follow-Up	Person-Years of Follow-Up	Number of Events	Incidence Per 100 Person-Years of Follow-Up
<1	359.3	10	2.8	354	21	5.9
1–3.9	312.6	11	3.5	308.2	28	9.1
≥4	92.4	11	11.9	88.4	23	26

<sup>a</sup>Includes brain infarction, myocardial infarction, peripheral embolism, and death from vascular causes.

From The French Study of Aortic Plaques in Stroke Group: Atherosclerotic disease of the aortic arch as a risk factor for recurrent ischemic stroke. *N Engl J Med.* 1996;334:1216–1221.

usually precipitated by plaque dislodgement by mechanical trauma to the arterial wall during endovascular intervention or arterial clamping during cardiac/vascular surgeries.<sup>8,34–38</sup>

## Endovascular Procedures for Coronary and Peripheral Arterial Occlusive Disease

Endovascular intervention is now the most frequent precipitating cause of the atheromatous embolization syndrome.<sup>20,21,39–41</sup> Manipulation of the aorta with rigid catheters or guide wires and the force of contrast injection can cause mechanical trauma, consequently dislodging atheromatous material from the arterial wall.<sup>42</sup> Nevertheless, the most important risk factor remains the severity of atherosclerotic disease in the aorta. The reported incidence of atheromatous embolization from cardiac catheterization is from 0.15%–2%.<sup>11,21</sup> Clinically apparent cholesterol embolism, such as livedo pattern on the feet, blue toe syndrome, digital gangrene, or renal failure, was found in 1.4% of patients who underwent left heart catheterization.<sup>43</sup> As with coronary angiography, catheter manipulation of the aorta in endovascular procedures for noncoronary arterial occlusive disease is also a serious concern. Embolic protection devices used in both renal and carotid artery stenting procedures frequently retrieved visible atherosclerotic debris.<sup>44–51</sup> Piazza et al. analyzed embolic filter debris load in 278 patients undergoing carotid artery stenting for asymptomatic stenosis, and found that embolic debris was present in 74% of patients, with age >75 years, pre-existing ipsilateral cerebral ischemic lesions, hypoechoogenic plaque, and plaque length >15 mm as predictors of clinically significant embolic debris burden.<sup>52</sup> In one retrospective autopsy study, spontaneous cholesterol emboli were found in 27% of patients who underwent arteriography in their lifetime versus only 4.3% in those who had not.<sup>6</sup>

## Cardiac Surgery

Atheroembolization is a well-recognized complication of cardiac surgery and has profound medical and economic consequences. Doty et al.<sup>35</sup> retrospectively analyzed 18,402 patients who underwent cardiac surgery, finding evidence of atheroembolism in 0.2% of patients at autopsy. The clinical presentation of atheroembolism in this study was broad and included five distinct organ systems: heart, central nervous system, gastrointestinal (GI) tract, kidneys, and the lower extremities. In 21% of these cases, death was directly attributable to atheroembolism.<sup>35</sup> Kolh et al.<sup>53</sup> documented a significant increase in intensive care unit stay, overall hospital stay, and total hospital cost in patients with documented atheroembolism after cardiac surgery.

## Vascular Surgery

The effect of atheroembolism after major vascular surgery was first recognized by Thurlbeck and Castleman in 1957.<sup>7</sup> In their series, atheroembolism was present at autopsy in more than 75% of patients who died after aortic aneurysm surgery. Atheromatous embolization was either the cause of death or significantly contributed to nearly half of the mortalities in this series. Vessel

manipulation, cross-clamping, or incision may disrupt plaque during vascular surgeries including aortoiliac and aortofemoral bypass, carotid endarterectomy, and renal artery revascularization.<sup>11</sup> In a retrospective series of 1011 patients who underwent infrarenal aortic surgery or infrainguinal surgery, the diagnosis of cholesterol embolization was 2.9%.<sup>54</sup> In a study of 202 patients undergoing carotid endarterectomy or stenting evaluated with magnetic resonance imaging with diffusion weighted sequences preoperatively and within 24 hours postoperatively, procedure-related new embolic lesions were seen in 78% of stenting patients and 27% of endarterectomy patients. Shorter (<2 cm) and calcified lesions were associated with increased risk of microembolization with stenting, but not endarterectomy.<sup>55</sup> Due to the advent of better surgical techniques and mitigation of atheromatous embolization risk, this complication has become much less common than reported in older literature.<sup>56</sup>

## Anticoagulation

An increased risk of cholesterol embolization with anticoagulation and clinical improvement when anticoagulation was removed has been reported in case reports for nearly half a century.<sup>8,11</sup> One hypothesis is that anticoagulation may prevent thrombus formation over unstable atherosclerotic plaque, thus allowing exposed cholesterol crystals to embolize. Another hypothesis is that these agents may initiate disruption of complex plaques by causing intraplaque hemorrhage.<sup>57–60</sup> Based on these small case series and case reports, some investigators have recommended that warfarin be discontinued, when feasible, in patients with cholesterol embolization for which no other precipitant can be identified.

However, the data are not entirely clear in assessing anticoagulation safety in patients with a large aortic plaque burden. The assumption that anticoagulation precipitates cholesterol emboli syndrome was not confirmed by the SPAF-3 trial, in which patients with documented aortic plaque assigned to warfarin therapy had low annual rates of cholesterol embolization (0.7% per patient-year; 95% confidence interval, 0.1% to 5.3%).<sup>61</sup> Likewise, there was no report of cholesterol embolization in warfarin-treated patients with aortic arch plaque in The French Study of Aortic Plaques in Stroke Group.<sup>33</sup> Additionally, Dressler et al.<sup>31</sup> found that patients with mobile aortic atheroma not receiving warfarin had a higher incidence of vascular events than those who received warfarin treatment (27% had strokes vs. 0%). Whether anticoagulation is associated with a higher incidence of atheroemboli remains controversial, but anticoagulation has been advocated for patients with crescendo transient ischemic attacks (TIAs), a syndrome caused by atheromatous embolization to the eye or brain. Current literature suggests it is safe to continue anticoagulation therapy in patients with a compelling reason to do so, such as those with atrial fibrillation or venous thromboembolism.

## Thrombolysis

Atheromatous emboli have also been associated with thrombolytic therapy in case reports and small series,<sup>38,62</sup> but again this is controversial. Thrombolytic agents act by converting

**BOX 106.1****Clinical Manifestations of Atheromatous Embolization****Skin**

- Purple or blue toes
- Gangrenous digits
- Ischemic ulcerations
- Livedo reticularis
- Nodules

**Renal**

- Acute, subacute, and chronic renal failure
- Severe uncontrolled hypertension
- Renal infarction (rare)

**Neurologic**

- Transient ischemic attack
- Amaurosis fugax
- Stroke
- Altered mental status

**Eye**

- Hollenhorst plaque

**Cardiac**

- Myocardial infarction or ischemia

**Gastrointestinal**

- Abdominal pain
- Gastrointestinal bleeding
- Ischemic bowel
- Acute pancreatitis
- Liver function abnormalities
- Cholecystitis
- Splenic infarcts

**Constitutional Symptoms/Signs**

- Fever
- Weight loss
- Malaise
- Anorexia

Modified from Bartholomew JR, et al. Atheromatous embolization. In: Young JR, et al., eds. *Peripheral Vascular Diseases*. 2nd ed. St. Louis: C.V. Mosby; 1996.

plasminogen to plasmin; plasmin directly degrades fibrin. Theoretically, any therapy that causes the thrombus to undergo lysis may leave atherosclerotic plaque uncovered, placing the patient at risk for embolization. In one small prospective study, no relationship between the administration of thrombolytic therapy and cholesterol emboli syndrome was found.<sup>63</sup>

## CLINICAL FEATURES

Atheroembolism may not produce clinical symptoms or can present with a myriad of symptoms, including cardiovascular catastrophes such as myocardial infarction, stroke, acute renal failure, mesenteric ischemia, or peripheral arterial occlusive disease (Box 106.1).<sup>64–66</sup> In general, the organs affected by cholesterol embolism depend on the location of the embolic source. Atheroemboli from the ascending aorta and proximal aortic arch usually manifest with central nervous system or retinal pathology, whereas cholesterol crystal emboli originating from the descending thoracic or abdominal aortas affect the visceral organs and extremities. In general, bilateral lower extremity atheroembolism signifies a source proximal to the aortic bifurcation, whereas unilateral emboli may originate either proximally or in any artery distal to the aortic bifurcation. Patients with one or more large atheromatous plaques in the aorta may present with a catastrophic event, such as an acutely ischemic limb, or renal or mesenteric infarction.<sup>39,67</sup> Conversely, patients with microemboli may have milder localized signs or a clinical picture that suggests a systemic illness. There may be a temporal delay in clinical findings (especially for renal failure) after the inciting event of up to 8 weeks.<sup>65</sup>

### Cutaneous Manifestations

Skin manifestations are among the most common clinical manifestations of atheroembolism, and the common cutaneous

features are livedo reticularis and blue toes.<sup>68,69</sup> The appearance of cutaneous signs can be delayed, with 50% of patients in one series showing skin signs of atheroembolism >30 days after their procedure or other inciting event.<sup>68</sup>

#### *Livedo Reticularis*

Livedo reticularis is a blue-red mottling or discoloration of the skin that occurs in a netlike pattern, most commonly seen on the buttocks, thighs, or legs (Fig. 106.1A). A detailed skin examination performed in both the supine and upright posture is necessary because livedo reticularis is more readily demonstrable in the upright position.<sup>70</sup> Livedo reticularis is caused by obstruction of small arteries, capillaries, or venules in the deep dermis.<sup>11,21</sup> When the skin is biopsied in patients with atheromatous embolization, cholesterol crystals may be seen in the dermal blood vessels. However, livedo reticularis is not pathognomonic of atheroemboli and has an extensive differential diagnosis including, but not limited to, other causes of intravascular obstruction (i.e., antiphospholipid antibody syndrome, cryoglobulinemia, endocarditis, left atrial myxoma), vasculitis, or can be drug-induced (i.e., quinidine, quinine, amantadine, catecholamines).<sup>71</sup> Furthermore, there are also physiologic (cutis marmorata) and idiopathic (livedoid vasculitis) forms of livedo reticularis. Livedo can occur in young healthy women and appears to be related to abnormal sensitivity of the dermal blood vessels to cold (primary livedo reticularis); this pattern usually disappears on rewarming and such patients should be reassured there is no serious circulatory abnormality present.

#### *Blue Toe Syndrome*

In its classic presentation, the blue toe syndrome presents as the sudden appearance of a cool, cyanotic, and painful toe in the presence of palpable distal pulses (Fig. 106.1B).<sup>57–59,68</sup> Discoloration may also be seen on the sole of the foot. The



**Figure 106.1** Examples of Cutaneous Manifestations of Atheroembolism. Characteristic appearance of the foot in a patient with atheromatous embolization (A). There is a patchy distribution of livedo reticularis on the lateral aspect, plantar surface, and heel of the right foot (note the purple second toe). Typical appearance of blue or purple toes that may occur in atheromatous embolization (B). More severe cases may progress to gangrene (C).

discoloration may be patchy (see Fig. 106.1A), and asymmetric compared to the contralateral foot. These lesions may progress to ulceration, necrosis, and frank gangrene (Fig. 106.1C).<sup>11</sup> Accessory lesions may be present on the lateral and posterior aspects of the heels, which later develop into linear fissures with skin edge gangrene and a dark, necrotic base.

#### Other Skin Manifestations

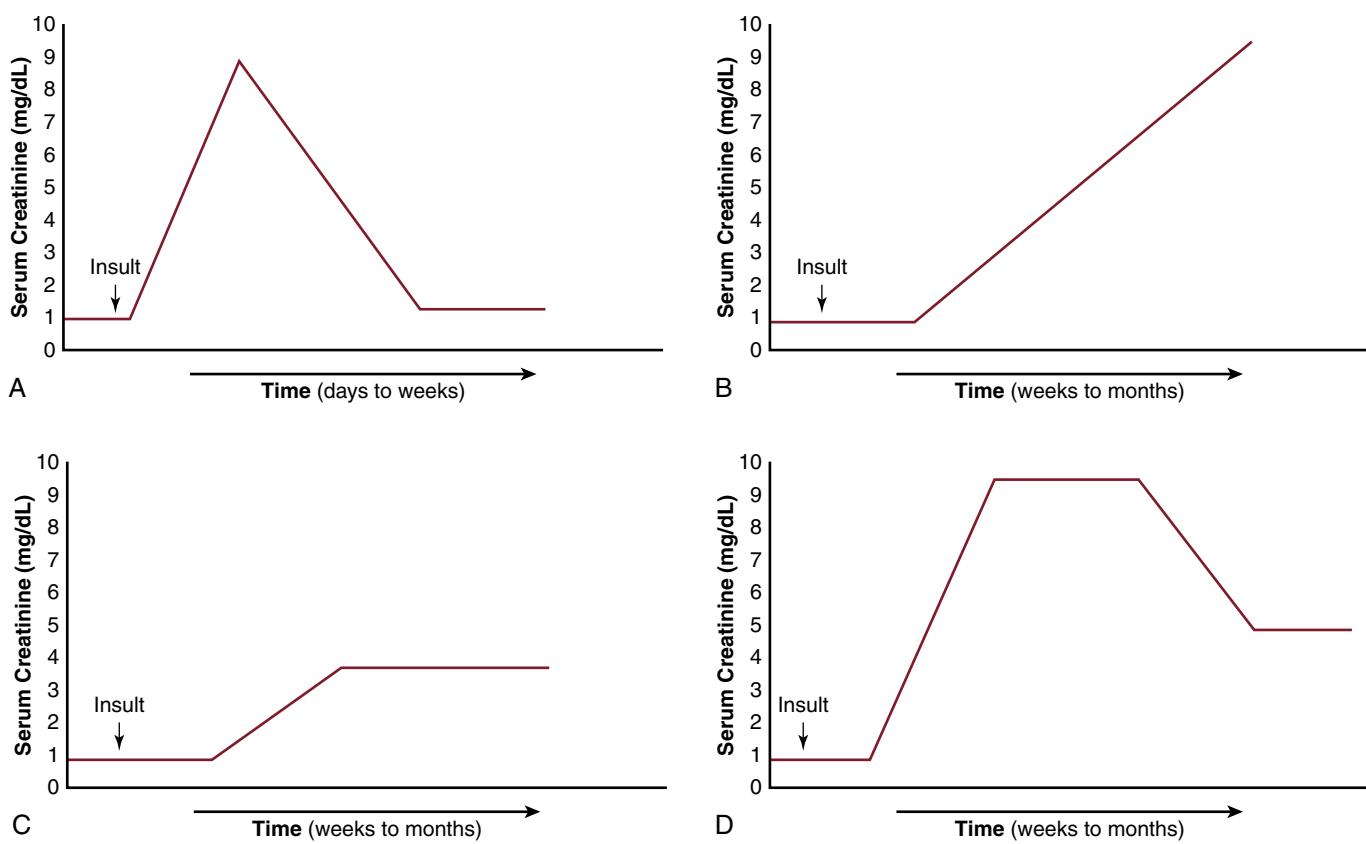
Other skin manifestations include splinter hemorrhages, petechiae, purpura, ulcers,<sup>72</sup> and raised nodules that appear due to subepidermal inflammation surrounding cholesterol crystals.<sup>11,68</sup> These nodules are painful, violaceous in appearance with a necrotic center, and may mimic a necrotizing vasculitis, such as polyarteritis nodosa or leukocytoclastic vasculitis. Ulceration of the penis and scrotum have also been described.<sup>73</sup>

#### Renal Involvement

The kidneys are the second most common target for cholesterol crystal embolization, due to the enormous blood flow through the kidney and close proximity of the proximal renal arteries to the plaque-bearing abdominal aorta.<sup>20–22</sup> Clinically detectable

atheroembolism may account for approximately 5%–10% of acute renal failure in inpatient encounters.<sup>10</sup> This condition is significantly underdiagnosed because of delayed presentation.<sup>1,20,22</sup> The cholesterol emboli cause occlusion of medium-sized arterioles (150 to 200 µm in diameter) and glomerular capillaries resulting in mechanical ischemia initially, followed by an inflammatory reaction within the arterioles. The inflammatory infiltration of PMNs, macrophages, and multinucleated giant cells leads to arteriolar thickening and fibrosis resulting in glomerular sclerosis, tubular atrophy, and interstitial fibrosis.<sup>20,65,74</sup>

It is important to recognize several different clinical presentations (Fig. 106.2)<sup>11,20–22</sup> of this disease, especially the differences between acute tubular necrosis (ATN) (see Fig. 106.2A) and atheroembolic renal disease (see Fig. 106.2B–D). Marked renal impairment with acute onset is the easiest form of atheroembolic renal disease to recognize. It has the closest temporal relationship to the inciting event and generally results from massive embolization, often causing catastrophic consequences. The subacute form of atheroembolic renal disease, the most frequently observed, is more insidious in onset, occurring a few weeks after the inciting event. Renal impairment may worsen over weeks to

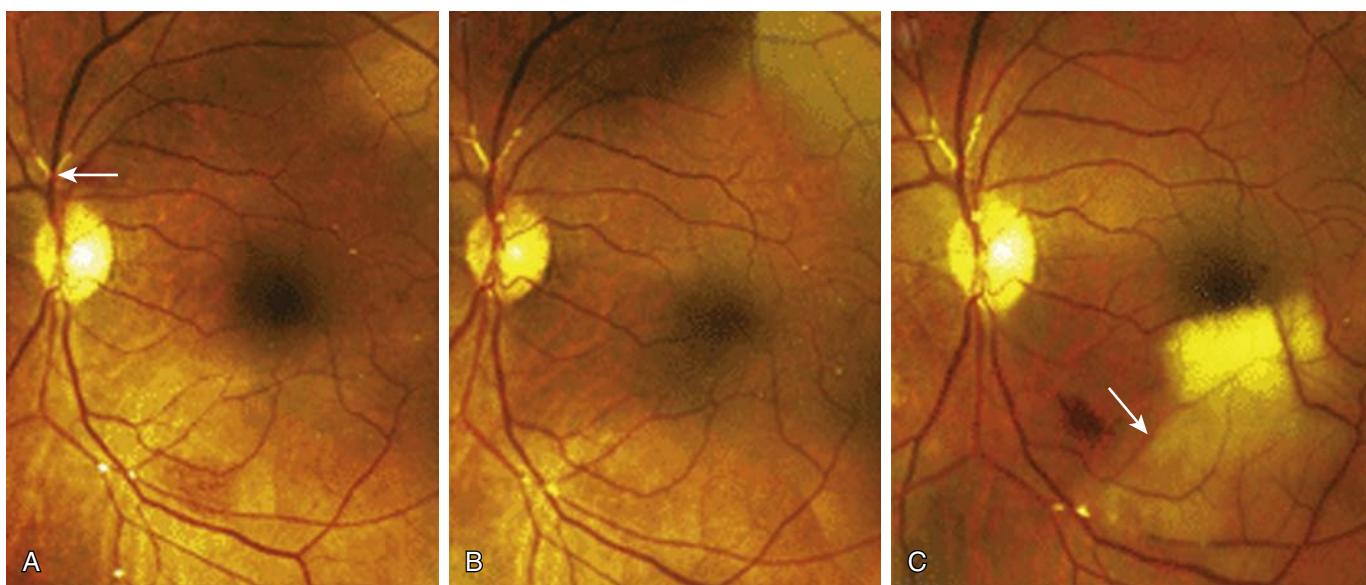


**Figure 106.2** Patterns of Renal Failure in Patients with Acute Tubular Necrosis (ATN) and Atheroembolic Renal Disease. In ATN, the serum creatinine rises within 24 hours of the inciting event and progresses to a peak over a period of days to weeks. Under most circumstances, the creatinine slowly returns to normal or near normal (A). In atheroembolic renal disease, there is a delay of 1 week to several weeks from the inciting event until the creatinine begins to rise. This may progress to end-stage renal disease over a period of weeks to months (B). Another presentation of atheroembolic renal injury is also a delay from the inciting event, followed by a rise in the serum creatinine over a period of weeks to months eventually leveling out and leaving the patient with chronic stable renal disease (C). There have been an increasing number of reports in which the patient requires renal replacement therapy and after a period of time, the renal function improves to the point where the patient no longer requires dialysis (D). (From Bartholomew JR, et al. Atheromatous embolization. In: Young JR, et al., eds. *Peripheral Vascular Diseases*. 2nd ed. St. Louis: C.V. Mosby Co.; 1996:266.)

months due to inflammation and foreign body reaction, or the cyclic occurrence of cholesterol crystal embolic showers (see Fig. 106.2B). In such circumstances, atheroembolic renal disease can be diagnosed only by performing a renal biopsy. Atheroembolic renal disease may also be present with chronic stable renal impairment (see Fig. 106.2C) in an asymptomatic patient. Clinical features tend to be similar to those of ischemic nephropathy and nephrosclerosis. Recovery of dialysis-dependent renal failure (see Fig. 106.2D) may occur in 21%–39% of patients initially requiring renal replacement therapy.<sup>22</sup> Atheroembolic renal disease is often associated with severe and poorly controlled hypertension due to ischemic atrophy of the renal parenchyma and activation of the renin–angiotensin–aldosterone system as glomerular filtration declines.<sup>59,65,75,76</sup> As a result, atheroembolic renal disease should be strongly considered in patients presenting with resistant hypertension.<sup>76,77</sup>

The renal outcome for patients with atheroembolic renal disease is quite variable. Early reports suggested a uniformly dismal outlook, with progression over weeks or months to end-stage renal failure.<sup>58,75</sup> However, more recently spontaneous recovery of

renal function in these patients has been reported, even after variable periods of dialytic support.<sup>8,78–80</sup> Recovery of renal function may be related to reversal of inflammation, resolution of ATN in ischemic areas, and hypertrophy of surviving nephrons.<sup>80</sup> Despite these promising case reports, most patients with atheroembolic renal disease continue to have either advanced chronic renal insufficiency or progress to end-stage renal disease requiring dialytic support. Scolari et al.<sup>21</sup> studied 354 patients followed for an average of 2 years, finding that 116 (32.7%) required dialysis therapy. Eighty-three patients remained on maintenance dialysis therapy, whereas 33 were able to discontinue dialysis. Five patients restarted dialysis within 2–6 months of stopping therapy. Cumulative renal survival probability was reduced by the presence of heart failure, baseline chronic kidney disease, age >70 years, iatrogenic atheromatous embolization, acute and/or subacute onset, and leg or GI involvement. Statin treatment was associated with protective effects initiated either before or after diagnosis. Multivariable analysis showed these same factors plus diabetes were associated with significantly increased risk for end-stage renal disease.



**Figure 106.3 Examples of Hollenhorst Plaques.** This 59-year-old man underwent stenting of the left internal carotid artery. Two months later, retinal examination of the left eye showed multiple, tiny refractile retinal arteriolar cholesterol emboli and a saddle embolus (A) superior to the optic nerve (arrow). Repeated examination showed an increase in the number of cholesterol emboli (B). Four weeks later, a sudden, painless loss of the left superior visual field occurred. Examination revealed whitening in the inferior macular region (C) (arrow), a finding that was consistent with an occlusion at the second major bifurcation of the inferior temporal branch of the retinal artery. (From Colucciello M. Images in clinical medicine. Retinal arteriolar cholesterol emboli. *N Engl J Med*. 2008;358:826.)

## Gastrointestinal Involvement

The GI tract is the third most common organ system involved according to autopsy findings, but is frequently overlooked and rarely diagnosed premortem.<sup>58,81,82</sup> Preferential involvement of the GI tract is probably a result of its rich vascular supply. Sites of GI involvement include the colon (involved in up to 42% of cases), small bowel (up to 33%), and stomach (in 12%).<sup>83</sup> Other areas reported include the pancreas, liver, gallbladder, and, less commonly, the spleen.<sup>84</sup> The pancreas and liver are frequent sites of cholesterol embolization, as indicated by autopsy reports, although clinically overt pancreatitis and hepatitis are an exceedingly rare presentation of cholesterol embolization.<sup>84</sup> In contrast, cholesterol embolization to the gallbladder, although even rarer, tends to be clinically significant when present, with a clinical presentation ranging from chronic acalculous cholecystitis to acute gangrenous cholecystitis.

The most common manifestations of GI tract involvement are abdominal pain, diarrhea, and GI bleeding. Abdominal pain may be caused by bowel ischemia with or without infarction, or by fibrous stricture with bowel obstruction as a consequence of tissue repair after repeated showers of atheroembolism.<sup>11</sup> The pathogenesis of diarrhea may be related to multiple mechanisms, including mucosal inflammation, accumulation of luminal blood, and malabsorption. GI bleeding is caused by superficial mucosal ulceration, erosions, and microinfarcts.<sup>83</sup>

The diagnosis of cholesterol embolism is rarely made by endoscopy alone because most endoscopic findings are nonspecific, including congestive or erythematous mucosa, erosions, ulcerations, necrosis, inflammatory polyps, or

strictures.<sup>2,8,83,84</sup> Mucosal punch biopsies from the stomach, duodenum, or colon may be helpful in making the diagnosis occasionally, demonstrating the typical appearance of cholesterol crystals.<sup>83</sup>

GI involvement commonly occurs in the context of multisystem cholesterol embolization syndrome, and prognosis tends to be poor with high overall mortality. In a retrospective review of 10 patients with histologically proven cholesterol crystal emboli diagnosed by endoscopic biopsy, death from atherosclerotic complications occurred in 5 patients (multisystem failure [3], stroke [1], and ruptured abdominal aortic aneurysm [1]) within 3 months of diagnosis. All patients also had cutaneous manifestations and end-stage renal disease.<sup>83</sup>

## Central Nervous System and Eye Involvement

Cholesterol embolization commonly occurs in the brain and eye and causes significant morbidity and mortality.<sup>2</sup>

### Retinal

The culprit atherosclerotic plaques are located in the ascending aorta, aortic arch, and/or carotid arteries.<sup>85,86</sup> Patients may develop visual disturbances such as amaurosis fugax or variable degrees of blindness caused by central or branch retinal artery occlusion.<sup>9</sup> Retinal cholesterol embolization is evident as yellow, highly refractile plaques (Hollenhorst plaques) at arterial bifurcations on ophthalmoscopic examination (Fig. 106.3).<sup>9,87</sup> From 2000 to 2005, 130 patients were analyzed with either Hollenhorst plaques or branch retinal artery occlusions.<sup>88</sup> This study found

a low rate of significant extracranial carotid artery disease among these patients (<30% in 68%, 30% to 60% in 22%, and >60% in 8%). Only six patients underwent carotid endarterectomy or stenting. With a median follow-up of 22 months, no stroke or TIA occurred, and overall survival was 94% in this cohort.<sup>88</sup> Among the 3654 survivors of the Blue Mountain Eye Study, the cumulative incidence of retinal emboli was only 2.9%.<sup>89</sup> The authors believed that this was an underestimation of the true incidence due to the transient nature of emboli and differential loss to follow-up. The same authors<sup>90</sup> assessed the relationship between retinal emboli and mortality in elderly patients. Of the 8384 patients with retinal photographs available, 2506 (30%) patients died over a 10- to 12-year time period. The cumulative mortality was higher in patients with than without emboli (all-cause mortality: 56% versus 30%; stroke-related mortality: 12% versus 4%; and cardiovascular mortality: 30% versus 16%).

### Cerebral

Cerebral cholesterol embolism may manifest as TIA, stroke, altered mental status, headache, dizziness, or organic brain syndrome.<sup>8,88,91</sup> In a retrospective review of 29 patients with autopsy-proven brain cholesterol emboli, encephalopathy was the predominant finding on neurologic examination.<sup>92</sup> This was most likely due to the diffuse and bihemispheric nature of cholesterol embolization. Involvement of the spinal cord artery, which can lead to lower extremity paralysis, has been rarely reported.<sup>64</sup> Recent history of a procedure involving the ascending thoracic aorta, acute renal failure, and encephalopathy in an elderly patient should raise suspicion for cholesterol emboli to the brain. Radiologic studies can be helpful by showing multiple small ischemic lesions or border zone infarcts.

### Other Areas

Cholesterol emboli can occur in virtually any organ. Cardiac manifestations include angina pectoris and myocardial infarction. The usual source in these circumstances is the aortic root or proximal coronary artery.<sup>93</sup> Pulmonary involvement has rarely been reported in the context of cholesterol embolism.<sup>94,95</sup> Hemoptysis and dyspnea are the most common respiratory symptoms described. The pathogenesis of pulmonary cholesterol embolism may involve direct atheroembolic deposition into the lungs<sup>96</sup> or *de novo* production of pulmonary lesions resulting from associated systemic inflammation.<sup>97</sup> Atherosomatous emboli have also been demonstrated in the spleen, bone marrow,<sup>98</sup> muscle, prostate, thyroid, and adrenals in autopsy studies.<sup>2,57,58,75</sup>

Nonspecific findings such as fever, weight loss, headaches, and myalgias have been reported and may suggest a multisystem illness (see Box 106.1).<sup>8,78</sup>

## DIAGNOSIS

The diagnosis of cholesterol embolization syndrome remains a significant challenge for physicians. The symptoms and signs are nonspecific and diverse, which is why this disease is sometimes referred to as the “great masquerader.”<sup>12</sup> For this reason,

a high index of suspicion and a thorough understanding of the various clinical manifestations are needed to correctly make the diagnosis ante mortem. The diagnosis can often be made on clinical grounds alone, without histologic evaluation, in a patient who has a precipitating event, characteristic end-organ symptoms, and evidence of peripheral embolization.<sup>8</sup>

### Laboratory Tests

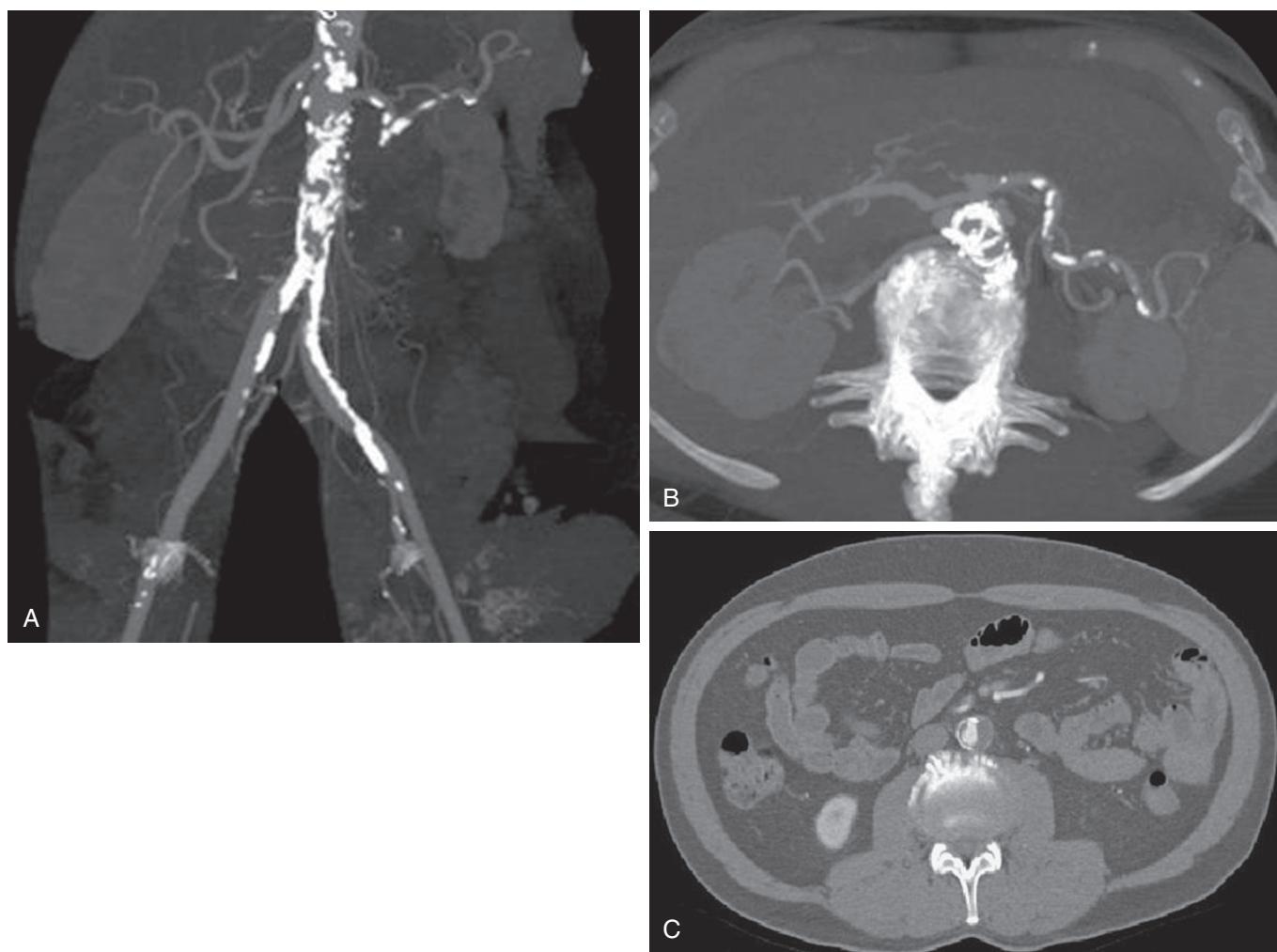
Other than laboratory data reflecting specific organ injury such as elevations in serum amylase, hepatic transaminases, blood urea nitrogen, creatinine, and creatinine phosphokinase which may be seen with involvement of the pancreas, liver, kidney, and muscles, respectively, there are no specific laboratory tests diagnostic for atheromatous embolization. Eosinophilia can be found in up to 80% of cases and is probably related to generation of complement C5, which has chemotactic properties for eosinophils.<sup>99</sup> However, eosinophilia tends to be transient and short lived.<sup>2,19</sup> Laboratory markers of inflammation, including C-reactive protein, fibrinogen, and the erythrocyte sedimentation rate, can also be elevated.<sup>58</sup> Other reported laboratory findings include leukocytosis, anemia, thrombocytopenia, and decreased complement levels.<sup>57,58,100</sup> Mild proteinuria, microhematuria, and hyaline or granular casts are the most common urinary findings in patients with confirmed cholesterol embolism.<sup>58</sup> Nephrotic range proteinuria, and eosinophiluria have been reported less commonly.<sup>18,101</sup>

### Imaging Modalities

Invasive vascular procedures requiring aortic instrumentation should be avoided as a diagnostic modality due to the potential risk for producing recurrent atheroembolism. Noninvasive imaging studies, such as multidetector CT angiography (Fig. 106.4), magnetic resonance angiography, and TEE (Fig. 106.5), can assist in confirming the diagnosis if a markedly irregular and shaggy aorta is demonstrated. In fact, one group developed a CTA “shagginess” score quantifying aortic luminal contour irregularity, which correlated with perioperative ischemic stroke after TEVAR.<sup>102</sup> It should be emphasized that these imaging modalities only demonstrate significant underlying atherosclerosis but cannot discern whether the atherosclerotic lesions are responsible for embolic events.

### Histologic Findings

In the absence of obvious clinical clues, definitive diagnosis may require biopsy. The highest yield for histologic confirmation is the skin in patients exhibiting livedo reticularis or an affected organ, such as an amputated extremity in a patient with gangrenous toes, the kidney in a patient with new-onset renal failure, or the GI tract in a patient with abdominal pain and GI bleeding. The cholesterol crystals dissolve in paraffin-fixed sections, leaving needlelike clefts (Fig. 106.6). Frozen or wet formalin-fixed sections reveal doubly refractile cholesterol crystals; with the Schultz histochemical stain, these crystals stain blue-green.<sup>103</sup>



**Figure 106.4** Multidetector computed tomography angiogram demonstrating marked calcified atherosclerotic disease in the infrarenal abdominal aorta in reformatted view (A) and axial view (B). Another example of infrarenal aorta with calcified plaque and extensive thrombus formation (C).

## DIFFERENTIAL DIAGNOSIS

Diseases that should be considered in the differential diagnosis include, but are not limited to, contrast nephropathy, ATN from ischemic injury, necrotizing vasculitis, leukocytoclastic vasculitis, thrombotic thrombocytopenic purpura, antiphospholipid antibody syndrome, and multiple myeloma. Thromboembolism from the heart or aneurysms, and other cardiac sources of emboli, such as an atrial myxoma, nonbacterial thrombotic endocarditis, and infective endocarditis,<sup>104</sup> should always be excluded.

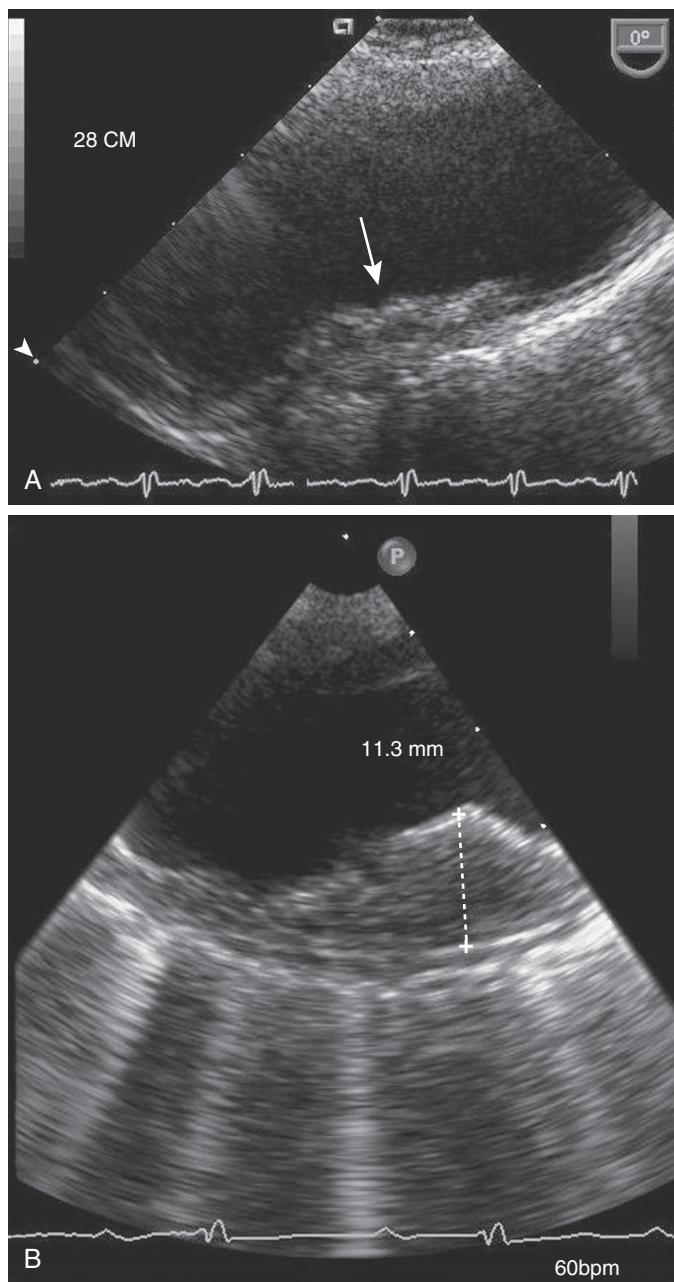
No laboratory test uniformly helps in the diagnosis of atheroembolic disease. The peripheral blood eosinophilia, hypocomplementemia, elevated sedimentation rate, and increased level of C-reactive protein seen in these patients are nonspecific findings that can also be found in patients with systemic or renal vasculitis.<sup>105</sup> Atheroembolic disease should be distinguished from vasculitis on the basis of other clinical findings and histology. The urine sediment in patients with atheroembolic renal disease is usually benign or shows only microhematuria. Rarely, eosinophiluria may be present.<sup>106</sup> In contrast, the urine sediment in patients with ATN often demonstrates pigmented casts (dirty

brown casts) and renal tubular cells. Atheroembolic renal disease is further differentiated from ATN or contrast nephropathy based on the time frame of renal impairment. In contrast nephropathy and ATN, renal failure occurs within 48–72 hours after the inciting event, whereas in patients with atheroembolic renal disease, the rise in creatinine is often delayed 7–10 days.<sup>20,21,64,65</sup> Additionally, full recovery of renal function is the rule for contrast nephropathy and ATN if the underlying precipitating factor is corrected, whereas it is the exception in atheroembolic renal disease.<sup>11,65</sup> However, there are examples of late recovery of renal function in patients with atheroemboli.<sup>107</sup> ATN is further characterized by normal blood pressure levels as opposed to the severe and refractory hypertension present in many patients with atheroembolic renal disease.

## TREATMENT

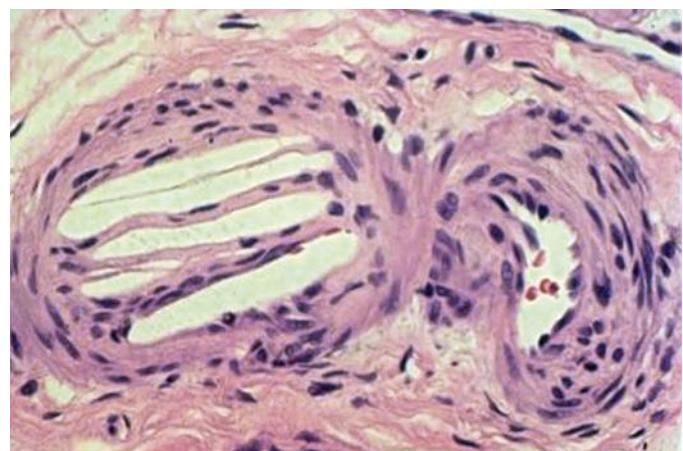
### Preventive Strategies

The most effective strategy for management of atheroemboli in vascular surgery is prevention. Imaging modalities such as



**Figure 106.5** Transesophageal echocardiogram demonstrating a large atheroma in the aortic arch (A) (arrowhead) and in the descending thoracic aorta (B). The descending thoracic aorta plaque measured 11.3 mm.

MRI/MRA, TEE, or CTA are excellent techniques to screen for high-risk patients by detecting the presence of aortic atherosclerosis preoperatively. When a severely atherosclerotic aorta is visualized, alternative surgical procedures should be considered to minimize aortic manipulation. For instance, use of epiaortic high-frequency ultrasound of the ascending aorta before manipulation during coronary artery bypass grafting has been associated with decreased stroke rates versus procedures without epiaortic scanning, as demonstrated in a recent propensity-matched analysis of 1320 patients (0.6% to 2.6%) and pooled estimates from systematic review and meta-analysis (0.6% vs. 1.9%).<sup>108</sup> Utilization of long guide wire exchanges is recommended, and back-bleeding from guiding catheters



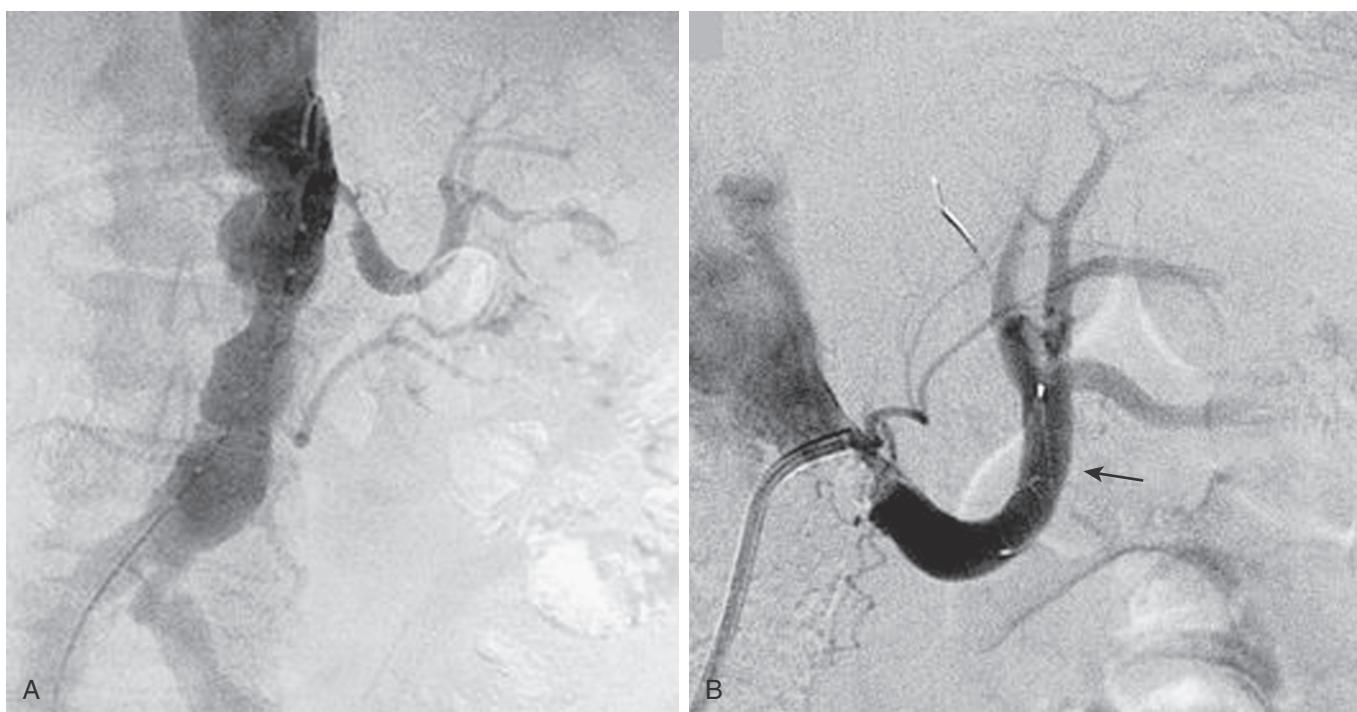
**Figure 106.6** Typical Appearance of the Cholesterol Clefts in a Specimen from a Kidney Biopsy. The convex-shaped crystals within the small arterioles of the kidney dissolve during the fixation process leaving the ghosts (left side), which is what is seen in the histopathology (hematoxylin and eosin stain,  $\times 200$  original magnification). Note the three red blood cells in the arteriole (right side).

allows for removal of debris. Advancement and removal of catheters should occur over a guide wire to straighten the catheter and minimize contact with the aortic wall. Brachial and radial access may minimize embolization from the abdominal aorta but not from the ascending aorta or arch. Proximal balloon occlusion and distal filters are both commonly used as protective devices during carotid artery stenting, with no significant difference seen between the two modalities in risk of stroke or 30-day mortality in a recent large meta-analysis<sup>109</sup> (Fig. 106.7).

## Medical Therapy

After atheromatous embolization has occurred, therapy is mostly supportive. Avoiding further inciting events (such as aortic manipulation), good control of hypertension and heart failure, dialytic support, and adequate nutrition are the mainstays of treatment.<sup>8,59</sup> Symptomatic care of the affected end organ and risk factor modification to prevent myocardial infarction, stroke, and the progression of atherosclerotic disease are important treatment goals.<sup>64,110</sup>

Pathologic descriptions of cholesterol embolism highlight the severe inflammatory reaction that contributes to vascular obstruction. Although the inflammatory process caused by cholesterol embolism may suggest a role for antiinflammatory agents,<sup>19</sup> the use of corticosteroids has had conflicting results. Some recent case reports described improvement in renal function in patients with suspected atheroembolism when corticosteroid therapy was used.<sup>111–116</sup> Corticosteroid administration has also been shown to be helpful in relieving symptoms related to mesenteric ischemia, such as abdominal pain and food intolerance, and for ischemic leg pain.<sup>8</sup> In contrast, in a series of 67 patients, of whom 18 were treated with corticosteroids, no survival benefit was attributed directly to this therapy.<sup>8</sup> Furthermore, in large retrospective series, Falanga et al.<sup>68</sup> found that corticosteroid use was associated with 100% mortality. Based upon the available literature, corticosteroid use cannot



**Figure 106.7** Catheter-based angiogram demonstrating a severely atherosclerotic aorta with a severe stenosis of the left renal artery and an occluded right renal artery. A selective angiogram of the left renal artery shows the severity of stenosis (A). There was a 7-mm Spider embolic protection device (arrow) (ev3 Endovascular, Inc., Plymouth, MN) placed before renal artery stenting (B).

be recommended on a routine basis for this patient population, although some authorities have recommended corticosteroids in patients with multisystem atheroembolic disease.<sup>22</sup>

Statins have shown benefit in the treatment of livedo reticularis caused by cholesterol embolization<sup>117</sup> and for treatment of atheroembolic renal disease.<sup>118</sup> Furthermore, in a retrospective analysis of 519 patients suffering stroke or peripheral embolism with severe thoracic aortic plaque visualized on TEE, multivariate analysis showed that statin use was independently protective against recurrent embolic events ( $P = 0.0001$ ).<sup>119</sup> The mechanism of the beneficial effects of statin therapy is most likely related to the plaque-stabilizing activity of these drugs.<sup>120</sup>

Iloprost (Schering AG, France), a prostacyclin analogue, has been reported to be beneficial for treatment of atheromatous embolization. It is a potent vasodilator that inhibits platelet aggregation and also has cytoprotective properties. It has been used to treat rest pain and nonhealing ulcers in patients with critical limb ischemia, as well as severe Raynaud phenomenon and thromboangiitis obliterans. In some reported individual cases or small series, patients who received iloprost infusions for ischemia of the distal extremities or kidneys reported a decrease in pain and improvement in their non-gangrenous skin lesions, as well as renal function.<sup>121–123</sup>

Low-density lipoprotein (LDL) apheresis with or without the addition of steroids was shown to be effective in improving skin manifestations. Hasegawa et al.<sup>124</sup> showed that combining corticosteroids and LDL apheresis improved atheroembolism related to blue toe syndrome. The mechanism is unknown, although it was postulated to improve blood viscosity by removing large molecular weight substances and

decreasing total and oxidized LDL, thus improving endothelial function and reducing circulating inflammatory cytokines and chemokines.<sup>124</sup>

Other forms of therapy that have been advocated include antiplatelet agents such as aspirin<sup>57,58</sup> and dipyridamole, low-molecular-weight dextran, intraarterial papaverine, and the use of platelet infusions to help stabilize the source of atheroemboli. However, no controlled trials have shown that any of these forms of therapy are beneficial. One recent randomized controlled trial showed that rivaroxaban was no better than low-dose aspirin for prevention of recurrent stroke after embolic stroke of undetermined source.<sup>125</sup> All patients should receive optimal risk factor modification with an antiplatelet agent (aspirin, clopidogrel, or both), a statin, and an angiotensin-converting enzyme inhibitor or angiotensin receptor blocking agent, all of which have been found to improve mortality in patients with underlying atherosclerotic disease.<sup>64,126–131</sup>

## Surgical and Endovascular Therapy

Surgical or endovascular treatment is a viable option when a source of cholesterol emboli can be identified, and the source is surgically or endovascularly accessible. However, it is often difficult to identify which of the many atherosclerotic plaques is the culprit lesion.

### Surgical Therapy

The aims of surgical therapy for atheroembolic disease are, first and foremost, elimination of the embolic source, and second,

arterial reconstruction of any hemodynamically significant proximal occlusive disease to encourage healing through improved end-arterial bed perfusion. Given the frequent instability of these lesions, surgical treatment has been perceived to be safer than endovascular approaches because the surgeon can clamp the artery proximal and distal to the lesion before manipulating the diseased vessel in an attempt to decrease the risk of recurrent embolization.<sup>132</sup> Thromboendarterectomy or resection and graft replacement have been the surgical approaches most commonly used.<sup>133</sup> Two prospective series reported favorable outcomes with vascular resection of atherosclerotic segments of large arteries identified as being the source of previous cholesterol crystal embolism.<sup>134,135</sup> However, when the suprarenal aorta was involved, greater mortality rates were observed, likely related to the risk for visceral and renal ischemia and/or atheroemboli.<sup>134</sup> Thus, according to some investigators, surgical elimination of the presumed source of cholesterol embolization should be reserved for patients with lower limb ischemia and an infrarenal source of embolization.<sup>11</sup> In patients who are too weak for a major surgical intervention, ligation of the external iliac arteries or common femoral arteries, followed by an extra-anatomic bypass (e.g., axillofemoral bypass) has been advocated.<sup>133,136</sup> The ligation prevents further embolization from reaching the legs, although embolization to the kidneys and intestines may still occur.

Finally, surgical treatment of thoracic aorta atherosclerosis may be considered. Surgical therapy cannot be recommended routinely for asymptomatic patients as the risks of such a complex procedure outweigh the benefits.<sup>137</sup> However, performing aortic arch endarterectomy or aortic resection along with planned cardiac procedures, if severe atheromatous disease is discovered, has been addressed. Stern et al.<sup>138</sup> reported a large increase in intraoperative stroke and mortality when surgery was performed to limit stroke risk after cardiopulmonary bypass. At this time, without randomized controlled trial evidence, surgical indications for aortic endarterectomy should be restricted to highly selected patients with multiple and documented embolic events despite optimal medical treatment, with low operative risk.<sup>30</sup>

### *Endovascular Therapy*

There are a few reports of intraarterial treatment of embolizing lesions, including thrombolytic administration,<sup>54,139</sup> percutaneous atherectomy,<sup>140,141</sup> balloon angioplasty,<sup>54,139</sup> and stent implantation.<sup>142,143</sup> Intraarterial thrombolytic administration in isolation is controversial with no current data to support or refute this practice. By destroying the platelet-fibrin thrombus that covers the atheromatous ulcerated plaques, thrombolysis may liberate cholesterol crystals into the arterial circulation with consequent microembolization.

In percutaneous transluminal angioplasty, the intima is fractured and remolded, which could increase the risk of distal embolization. However, anecdotal reports using this approach have shown symptomatic improvement in leg pain, reestablishment of peripheral pulses, and no evidence of recurrent embolization. Stent placement, in conjunction with angioplasty, may provide a protective scaffold to help secure these

lesions. However, a potential risk of recurrent atheroembolism may exist due to either plaque dislodgement or extrusion of atheromatous material through stent interstices during stent deployment.

The possibility of procedural-related distal embolization due to stent placement was highlighted in a recent study by Ohki et al.<sup>144</sup> that demonstrated a significant risk of distal embolization secondary to intraarterial stent placement in an *ex vivo* carotid endarterectomy model. In contrast, Matchett et al.,<sup>142</sup> in a retrospective report of 15 patients treated with stent placement for blue toe syndrome, found no procedure-related embolization and only one recurrent embolization during follow-up. Renshaw et al. reported successful angioplasty with stenting in eight patients with unilateral blue toe syndrome. Symptoms resolved in all eight patients over the ensuing month, with no recurrences during a mean follow-up of 18.5 months.<sup>145</sup>

The short-term results in studies using percutaneous atherectomy, in which plaque is shaved off the vessel wall and removed through a collection device, are similar to those of patients undergoing percutaneous transluminal angioplasty or surgery.<sup>140,141</sup>

The availability of covered stent grafts in recent years has raised their potential utility in the management of patients with distal atheroembolic lesions. Covered stents offer the added advantage of completely excluding the diseased segment, preventing the escape of thrombus or plaque debris. Kumins et al.<sup>146</sup> reported on the successful use of the Wallgraft endoprosthesis in two patients with distal microembolism from common iliac artery pathology.

Carroccio et al.<sup>147</sup> recently reported on endovascular stent-graft repair for abdominal aortic aneurysms in 16 patients with atheromatous embolization syndrome. The 30-day mortality was 0%, and the abdominal aortic aneurysms were successfully excluded in 88% of patients. Resolution of foot ischemia and prevention of further atheromatous embolization occurred in 89% of the patients still alive at 1 year. Six patients died during a mean follow-up of 26 months, further illustrating the very high mortality in this patient population.

Distal embolic protection devices, especially filters, were originally designed to minimize atheroembolism during percutaneous coronary or carotid interventions. An off-label use of these devices is to protect outflow arteries from atheroembolism during peripheral interventions. It would not be cost effective to use distal embolic protection for all peripheral interventions, and the arterial diameters compatible with these devices are limited. Nonetheless, distal embolic protection may be a useful adjunct for endovascular treatment of lesions deemed to be a high risk for periprocedural embolization. One group compared filter macroemboli burden for 508 patients that underwent lower extremity endovascular atherectomy and found chronic total occlusion, in-stent restenosis, thrombotic/calcific lesions >40 mm and atherosclerotic lesions >140 mm identified on angiography to be associated with greater embolic burden, supporting filter use for these indications during endovascular femoropopliteal atherectomy.<sup>148</sup>

Because of the limited studies available regarding the role of endovascular therapy for atheromatous embolization, its

**TABLE 106.2** Outcomes in Patients with Atheroembolic Renal Disease

Reference	N	Renal Failure Requiring Dialysis No. (%)	Recovery of Dialysis-Dependent Renal Failure No. (%)	Maintenance Dialysis (End of Follow-Up) No. (%)	1-Year Mortality No. (%)
Fine et al. <sup>58</sup>	221	62 (28)	13 (21)	0	179 (81)
Lye et al. <sup>75</sup>	129	52 (40)	13 (26)	0	83 (64)
Thadhani et al. <sup>18</sup>	52	23 (44)	7 (32)	0	45 (87)
Belenfant et al. <sup>8</sup>	67	41 (61)	16 (39)	23 (35)	9 (13)
Scolari et al. <sup>21</sup>	354	116 (33)	33 (28)	88 (25)	60 (17)

From Scolari F, Ravani P. Atheroembolic renal disease. *Lancet*. 2010;375:1650–1660.

clinical efficacy is difficult to compare with operative treatment strategies and further clinical evaluation is warranted.

### Pain Control

Pain control is critical in the management of peripheral cholesterol embolism. Pain associated with lower extremity ischemic and necrotic lesions secondary to cholesterol embolism is generally severe and disproportionate to the extent of tissue involved. Sympathectomy has received attention as a surgical measure for the palliation of atheroembolic lesions. Lee et al.<sup>149</sup> demonstrated that adjunctive sympathectomy resulted in improved healing of distal digital ischemic ulcers. Sympathectomy is easily performed during aortic procedures, or it can be achieved postoperatively through lumbar sympathetic block or laparoscopic techniques.

More recently, Ghilardi et al.<sup>150</sup> reported on two cases of inferior limb ischemia secondary to cholesterol embolism treated with the temporary surgical implantation of spinal cord stimulation devices. Spinal cord stimulation in this study was found to provide rapid and effective pain control and improvement in peripheral microcirculation manifested by the rapid resolution of necrotic lesions within 4–6 weeks.<sup>150</sup> These surgical techniques may not only be adjunctive to direct surgical treatment of the offending arterial segment, but also may be useful to control the pain of severe atheroembolic lower extremity lesions in patients who are not candidates for direct reconstruction of the embolic source. Pain specialists are often beneficial consultants in the management of severe pain that may occur in these patients.

### SUMMARY

Atheroembolism is a multisystem disease complicating advanced atherosclerosis. The clinical presentation varies from subtle to catastrophic manifestations. It is often under-recognized and requires a high clinical suspicion to diagnose. Treatment is mainly supportive with risk factor modification to prevent further insults. Removal of embolic sources is sometimes possible with surgical or endovascular intervention. In general, the prognosis of patients with atheroembolic disease is poor and most likely related to the severe and diffuse atherosclerosis present in this population. However, the course varies depending on clinical presentation. Patients with symptoms

limited to an extremity tend to have better prognoses compared with patients with disseminated cholesterol crystal embolization, particularly when there is evidence of visceral and renal involvement. The reported 1-year mortality in five different reports varied from 13% to 81% (Table 106.2),<sup>8,18,21,58,75</sup> with causes including cardiac, central nervous system, and GI ischemia.

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# Lower Extremity Arterial Occlusive Disease: Epidemiology and Natural History

MICHAEL S. CONTE

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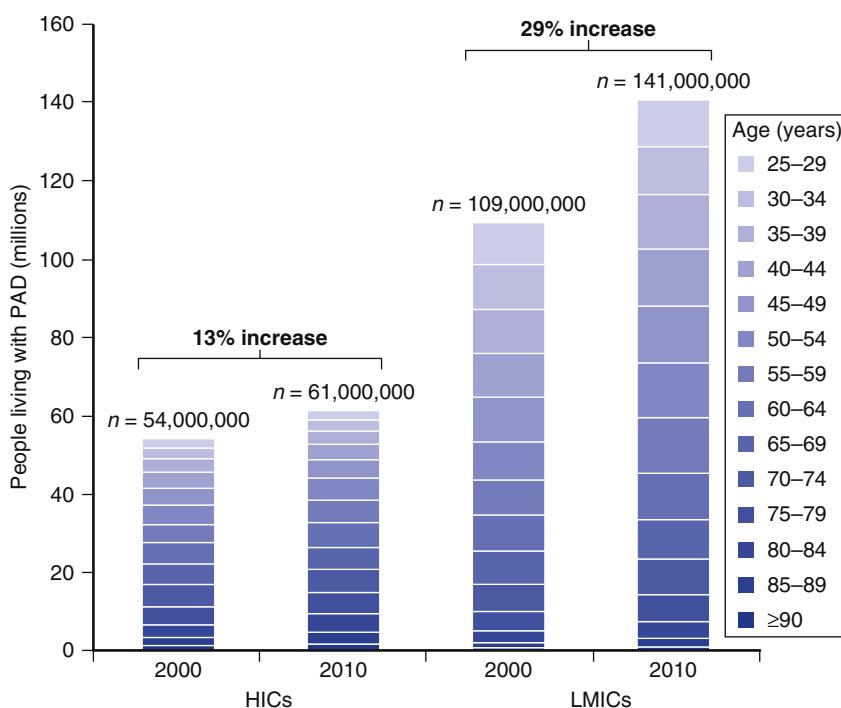
## EPIDEMIOLOGY OF PERIPHERAL ARTERIAL DISEASE

### Incidence and Prevalence

Peripheral arterial disease (PAD) is defined as chronic, atherosclerotic occlusive disease of the lower extremities. It has become a major global health problem, largely secondary to aging of the world's population, combined with the growing prevalence of risk factors such as diabetes, smoking, hypertension, and dyslipidemia. The increasing burden of PAD has resulted in mortality, morbidity, and escalating public health costs associated with care for the disease and its complications. Accurate information on PAD prevalence and incidence is limited because a large proportion of affected individuals have

preclinical disease or atypical symptoms, and PAD screening (e.g., ankle-brachial index [ABI] testing) is not routinely used. As a result, epidemiologic data have been drawn from isolated community screening studies, data on symptomatic states such as intermittent claudication (IC), and by extrapolation from other measured diseases (e.g., diabetes) and events (amputation) with known relationship to underlying PAD.

Epidemiologic studies have estimated that more than 200 million individuals are currently affected by PAD worldwide.<sup>1</sup> This prevalence rate has increased by approximately 25% over the preceding decade. The growth of PAD is evident in both high-income countries (HICs) and low- and middle-income countries (LMICs), with LMICs and the Pacific Rim/Southeast Asia region specifically demonstrating higher rates of growth (Fig. 107.1). Sex- and age-related prevalence of PAD

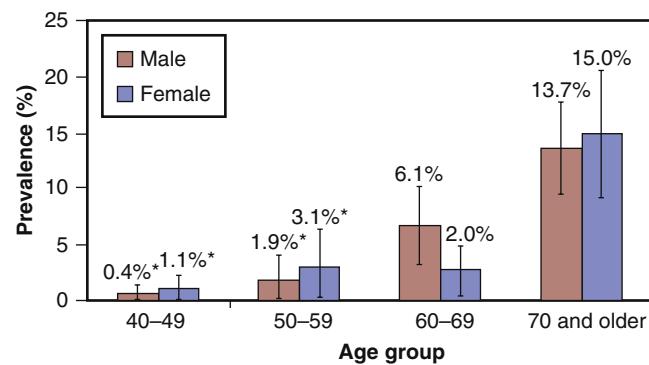


**Figure 107.1** Estimated global prevalence of peripheral arterial disease (PAD) by age in high-income countries (HICs) and low- and middle-income countries (LMICs) in 2000 and 2010. (From Fowkes FG, Aboyans V, Fowkes FJ, et al. Peripheral artery disease: epidemiology and global perspectives. *Nat Rev Cardiol.* 2017;14(3):156–170.)

differs somewhat around the globe. In **HICs**, men and women appear approximately equally affected and the prevalence rises from less than 5% younger than age 50 to approximately 20% in individuals older than 80 years. In **LMICs**, age-specific rates appear higher in women compared with men. Many studies have demonstrated that women have lower ABI than do men, although the reasons for this observation are unclear and not readily explained by differences in established risk factors for atherosclerosis. Data on PAD are sparse from many areas of the world and concerted public health efforts will be needed to develop more accurate models of incidence, prevalence, and outcomes. These efforts are justified by the economic impact of disability and health resource use that is engendered by PAD.

Data from the US population estimate that 8.5 million Americans are living with PAD.<sup>2</sup> There is a strong **age-dependent increase** in the United States, with a prevalence of greater than 20% in individuals older than 80 years (Fig. 107.2).<sup>3</sup> Nehler et al. estimated US incidence and prevalence of PAD over the years 2003 to 2008 using a broad capture of claims data from multiple insurers including Medicare, Medical, and commercial plans.<sup>4</sup> They reported an annual incidence rate of 2.35% and an overall prevalence of 10.69% among the enrollees.

Estimates of the prevalence of **IC** and **chronic limb-threatening ischemia (CLTI)** are fraught with similar **limitations** and are likely to be systematically **undervalued**. Estimates of IC prevalence have been derived from community questionnaire studies and, for CLTI, using administrative (billing) data on hospitalizations, procedures, and amputations. **IC** is estimated to affect up to 6% of individuals older than 65 years in Western countries.<sup>5</sup> It is recognized that many PAD patients describe **atypical leg pain syndromes** (non-calf pain or calf pain with nonclassic descriptors) that are not accurately captured.

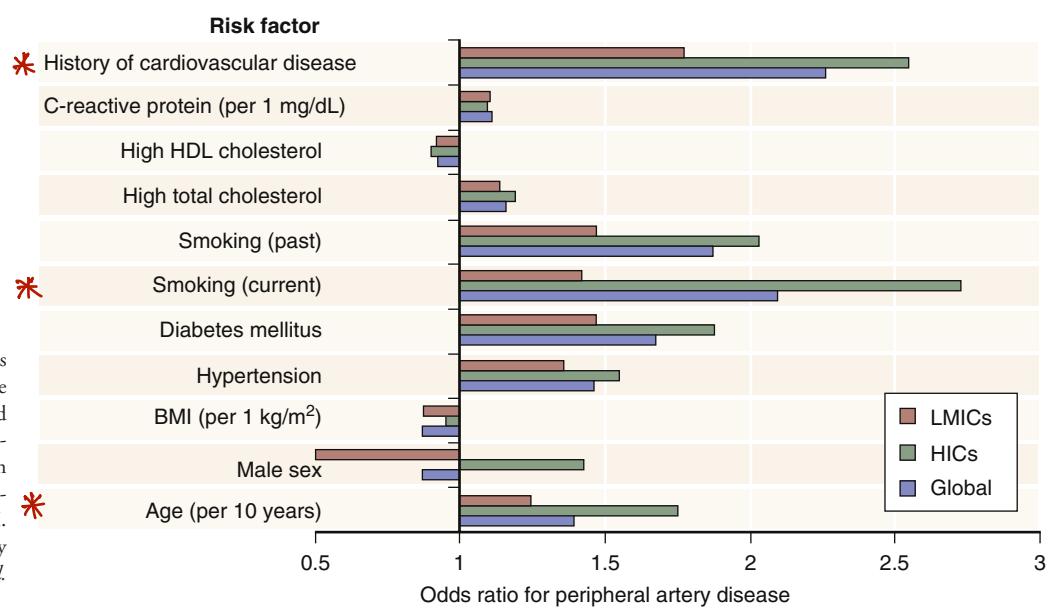


**Figure 107.2** Estimated age-specific prevalence of PAD in the United States from the National Health and Nutrition Examination Survey 1999–2000. \*Relative standard error >30%. (From Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999–2000. *Circulation.* 2004;110(6):738–743.)

Estimates of **CLTI** incidence and prevalence have ranged from 0.02% to 0.35% and 0.3% to 2% across studies of disparate adult populations.<sup>4,6–8</sup> This translates into approximately 2 million individuals in the United States.

## Risk Factors

PAD is a chronic manifestation of systemic atherosclerosis in the arteries of the lower extremities. As such, it shares many risk factors with other clinical atherosclerotic conditions such as coronary artery disease (CAD) and cerebrovascular disease (CVD). However, **differences in the profile of PAD, CAD, and CVD patients have been characterized**, and the strength of association of specific risk factors varies across the clinical syndromes, as well as across anatomic patterns (Fig. 107.3).



**Figure 107.3** Risk factors for PAD across the globe, in both low- and middle-income and high-income countries (LMICs and HICs, respectively). BMI, body mass index; HDL, high-density lipoprotein. (From Fowkes FG, Aboyans V, Fowkes FJ, McDermott MM, Sampson UK, Criqui MH. Peripheral artery disease: epidemiology and global perspectives. *Nat Rev Cardiol*. 2017;14(3):156–170.)

## Demographics

Age is the strongest risk factor for PAD. The disease is rare in individuals younger than 40 years, rises in prevalence in the sixth to eighth decades, and may affect 25% or more of individuals 80 years and older.<sup>3,9–12</sup> As mentioned previously, sex-related differences in PAD appear to be different around the globe, although the prevalence of more advanced, symptomatic stages of disease is consistently higher in men.

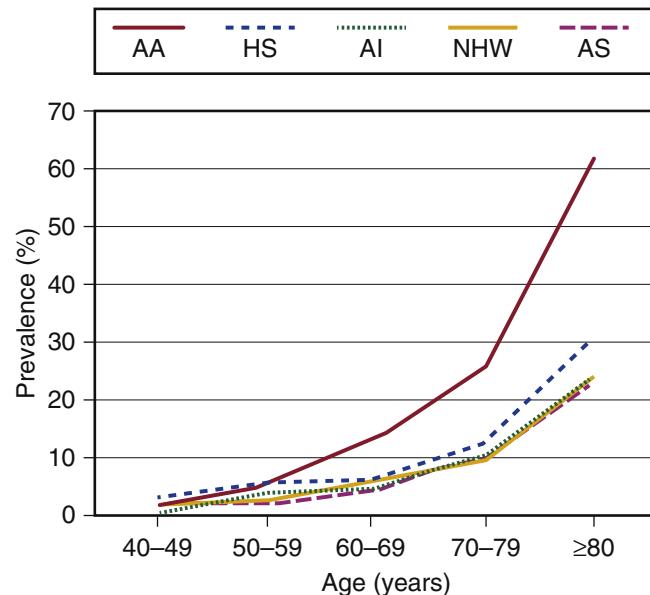
Several studies have demonstrated higher rates of PAD and poorer outcomes for black populations in comparison with non-Hispanic or Hispanic white populations (Fig. 107.4).<sup>2,3,13–16</sup> Reasons remain unclear because this disparity is not accounted for based on an imbalance of traditional risk factors such as age, smoking, diabetes, or hyperlipidemia.

## Smoking

Cigarette smoking is a strong and independent predictor of PAD across populations. Several studies have demonstrated odds ratios in the range of twofold to fourfold.<sup>3,11,17</sup> Second-hand smoke exposure appears to also carry increased risk for PAD, although data in this regard are limited.<sup>18,19</sup>

## Diabetes

Diabetes has been strongly associated with PAD prevalence and severity. Odds ratios reported for diabetes are similar to those for smoking, in the range of twofold to fourfold.<sup>3</sup> This association is modified by age and the duration of diabetes, such that older individuals with more than a decade of diabetes are at highest risk. The combination of diabetes and smoking is most insidious, portending a high risk for PAD severity, amputation, and mortality. Multiple studies have demonstrated that long-term outcomes of PAD are adversely influenced by the presence of diabetes, including reduced survival and a fivefold increased rate of limb loss.<sup>20</sup>



**Figure 107.4** Estimated United States prevalence of PAD by age and ethnicity. AA, African American; AI, American Indian; AS, Asian American; HS, Hispanic; NHW, non-Hispanic white. (From Allison MA, Ho E, Denenberg JO, et al. Ethnic-specific prevalence of peripheral arterial disease in the United States. *Am J Prev Med*. 2007;32(4):328–333.)

## Hypertension

Hypertension is common in the PAD population. The association is consistent across many epidemiologic studies, although less strong than that seen with smoking and diabetes. Because age is a common risk factor for both, the independent association between hypertension and PAD appears weaker on multivariable analyses.

## Dyslipidemia

Elevated total cholesterol (TC) and reduced high-density lipoprotein (HDL) levels have been associated with PAD in multiple studies. The ratio of TC/HDL was a strong predictor

in both the San Diego population study<sup>13</sup> and the Physician's Health Study.<sup>21</sup> Some studies have demonstrated a link between elevated triglyceride levels and PAD.<sup>22</sup> The relationship between PAD and low-density lipoprotein (LDL) levels appears less consistent, and no target LDL values for therapy have been developed specific to PAD.

### Obesity

Data specifically relating obesity to PAD are inconclusive. Some studies suggest a U-shaped relationship.<sup>23,24</sup> The distribution of body fat may be of greater relevance. Central obesity, more consistently linked to diabetes and to the “metabolic syndrome” (the cluster of central obesity, hypertension, elevated triglycerides, low HDL, elevated fasting blood glucose), appears of greater relevance to PAD than overall obesity.<sup>25,26</sup>

### Inflammation

Elevated biomarkers of systemic inflammation have been consistently associated with atherosclerosis in general and PAD specifically. Plasma levels of C-reactive protein and fibrinogen have shown consistent associations with PAD.<sup>3,27</sup> Both of these biomarkers have also been associated with PAD severity and with adverse outcomes in symptomatic patients. Indeed, CLTI patients appear to have the most pronounced proinflammatory phenotype across the spectrum of clinical atherosclerosis syndromes. Circulating cytokines such as interleukin-6 and adhesion molecules (soluble intercellular adhesion molecule-1, soluble vascular cell adhesion molecule-1) are also elevated in PAD patients.<sup>28</sup> The predictive value and clinical utility of these markers, as well as other candidate biomarkers such as D-dimer, β2-macroglobulin, asymmetric dimethylarginine, and cystatin C, remain undefined.<sup>29–31</sup>

### Homocysteine

Several studies have demonstrated a statistical relationship between elevated plasma levels of homocysteine and PAD.<sup>32</sup> However, the strength of the association is moderate when controlled for other risk factors.<sup>21</sup> In addition, homocysteine levels have not been clearly associated with progression or severity of PAD, and studies of folate supplementation (which reduces homocysteine) have shown no consistent effects on PAD.<sup>32</sup>

### Socioeconomic Status

PAD has been associated with lower socioeconomic status, including lower levels of income and education.<sup>33,34</sup> These associations span race/ethnicity and are only partly explained by traditional risk factors such as smoking. A recent analysis from the Atherosclerosis Risk in Communities (ARIC) study demonstrated that household income, educational attainment, and area-level deprivation index were strong predictors of hospitalization for advanced PAD.<sup>34</sup> These findings were attenuated but not eliminated after controlling for age, sex, race, risk factors, and access to healthcare. Mechanisms may include psychological stress, health literacy, and nutrition.

## ANATOMIC DISTRIBUTION OF DISEASE AND CLINICAL CORRELATIONS

A broad spectrum of anatomic lesion distribution and disease severity is encountered in the PAD population. Lower extremity arterial disease has been anatomically described by the levels (segments) affected – aortoiliac (AI), femoropopliteal (FP), and tibiopedal (TBP). These descriptors are both clinically useful and tend to be associated with patterns of risk factors across the spectrum of disease presentation. For example, smokers have a high frequency of AI and FP disease, whereas diabetes is more typically associated with TBP and FP involvement. There is also a clear relationship between disease pattern and clinical presentation. Patients with IC typically present with AI and/or FP disease, often with a single segment involved. In contrast, CLTI generally results from involvement of at least two arterial segments or severe TBP disease. This correlation is largely a reflection of the development of collateral pathways of blood flow circumventing single-level (especially proximal) occlusions.

Cohort studies including vascular imaging provide greater insight into anatomic distribution of lesions across subgroups of patients. Smoking tends to be more highly associated with AI and FP involvement, whereas diabetes is strongly linked to FP and TBP patterns of disease.<sup>20,35–37</sup> Diehm et al. examined angiograms from a series of 2659 patients who had undergone endovascular interventions for PAD. Proximal (AI) disease was associated with younger age, smoking, and male sex, whereas TBP disease was associated with diabetes and advanced age. Rueda et al. described patterns of disease among a cohort of 450 patients who had undergone angiography and revascularization for CLI at a single institution.<sup>38</sup> They found that more than half of such patients had occlusions in the popliteal or TBP segments, and another 30% had combined FP and TBP occlusions; these patterns were particularly common in patients with diabetes and/or end-stage renal disease (ESRD).

## CLINICAL SYNDROMES OF PERIPHERAL ARTERIAL DISEASE, STAGING AND NATURAL HISTORY

Individuals afflicted with PAD may be grouped by clinical presentation, with the largest proportion being asymptomatic. Atypical leg symptoms, classic IC, and CLTI signs or symptoms are frequent indications for referrals to vascular specialists for evaluation and treatment. We will consider each of these distinct subgroups and describe modes of presentation, staging, prognosis, and key disease modifiers. The reader is referred to other chapters in the text for detailed discussion of diagnostic testing modalities, medical therapies, and use of vascular interventions.

Classification schemes for PAD have used clinical descriptors and associated objective measures (Table 107.1). The Fontaine and Rutherford systems have been widely adopted for

Treadmill = 5min @ 2mph on 12% incline

**TABLE 107.1** Stages of Chronic Limb Ischemia

Fontaine Grade	Rutherford Category	Clinical Description	Objective Criteria
I	0	Asymptomatic	Normal treadmill or reactive hyperemia test
IIa <sup>a</sup> >200m	1	Mild claudication	Completes treadmill exercise <sup>b</sup> ; AP after exercise >50 mm Hg but at least 20 mm Hg lower than resting value
IIb <sup>a</sup> <200m	2	Moderate claudication	Between categories 1 and 3
	3	Severe claudication	Cannot complete standard treadmill exercise <sup>b</sup> ; AP after exercise <50 mm Hg
III <sup>a</sup>	4	Ischemic rest pain	Resting AP <30–50 mm Hg; ankle or metatarsal PVR flat or barely pulsatile; TP <30 mm Hg
IV	5	Nonhealing ulcer/focal gangrene <sup>c</sup>	Resting AP <50–70 mm Hg; ankle or metatarsal PVR flat or barely pulsatile; TP <40 mm Hg in nondiabetics, <50 mm Hg in diabetics; tcPO <sub>2</sub> <30 mm Hg
	6 above MTP <sup>d</sup> non salvageable foot	Major tissue loss <sup>d</sup>	Same as Rutherford 5 (Fontaine IV)

<sup>a</sup>Fontaine Grades III and IV, Rutherford categories 4–6 correspond to CLTI.<sup>b</sup>Five minutes at 2 miles per hour on a 12% incline.<sup>c</sup>Nonhealing ulcer or focal gangrene with diffuse pedal ischemia.<sup>d</sup>Extending above transmetatarsal level, or foot no longer salvageable.AP, ankle pressure; PVR, pulse volume recording; tcPO<sub>2</sub>, transcutaneous oxygen; TP, toe pressure.From Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg*. 1997;26(3):517–538; and Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg*. 2007;45:S34.

this purpose. They have been useful for developing treatment algorithms and prognosis across the broad spectrum of PAD. However, recent efforts to improve staging of limb-threatening disease may provide greater predictive value for endpoints such as amputation and are discussed later.

## Asymptomatic Disease

The majority of individuals with PAD detected by noninvasive testing are asymptomatic.<sup>39</sup> Reasons for the lack of symptoms may include lower severity/burden of disease, adequate collateral artery reserve, and limited levels of activity among older subjects or those with sedentary lifestyle or with other sources of disability.

Despite the lack of claudication or CLTI symptoms, asymptomatic PAD carries significant cardiovascular risk and mortality and is associated with functional decline (Fig. 107.5). Criqui demonstrated that individuals with asymptomatic PAD had an overall 2.7-fold greater risk of mortality and a 5.6-fold greater risk of CAD related death.<sup>40</sup> Thus the importance of diagnosing PAD in asymptomatic individuals relates to counseling and treatment of associated atherosclerosis risk factors. Notably, mortality and CV risk are strongly associated with both reduced ABI and with elevated ABI (>1.4) consistent with vessel calcification.<sup>41,42</sup> These data demonstrate an important relationship between the severity of PAD as determined by objective testing and long-term mortality, independent of symptoms.

Work from McDermott has highlighted that individuals with asymptomatic PAD have significant physical impairments and tend to decline further over time, leading to increased sedentariness.<sup>14,43,44</sup> Manifestations included reductions in daily physical activity, walking velocity, and

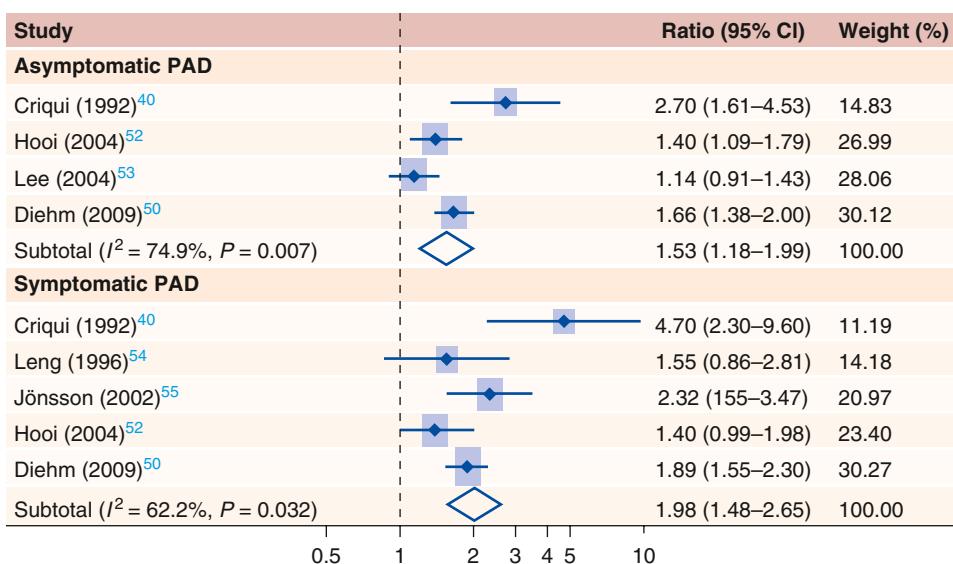
6-minute walk distance. These findings have been correlated to reduced calf muscle mass, increased calf muscle fat content, and impaired peripheral nerve function in asymptomatic subjects. The reversibility of these muscle and nerve changes remains unknown.<sup>45</sup>

The risk of progression from asymptomatic PAD to symptomatic states is not well defined. A meta-analysis estimated that 7% (4%–11%) of asymptomatic patients deteriorate to IC over a 5-year period.<sup>46</sup>

## Intermittent Claudication

IC is a clinical syndrome characterized by reproducible leg pain brought on by exercise and relieved by rest. Other causes of leg pain that must be considered in the differential diagnosis include neurogenic (e.g., spine disease), venous, joint, and other musculoskeletal disorders. Instruments such as the Rose and San Diego Claudication questionnaires have been used in clinical and epidemiologic studies to distinguish IC from other conditions.<sup>47,48</sup> In clinical practice a careful history, combined with a physical exam and simple noninvasive studies, readily establishes the diagnosis in the majority of patients. However, it is well recognized that atypical leg symptoms are common in PAD patients, including pain that may also occur while standing still or sitting and discomfort or fatigability with exercise that does not cause the individual to stop walking.

IC may affect proximal (buttock, hip, thigh) or distal (calf) muscles, although calf pain is by far the most common presentation. Symptom location reflects arterial disease proximal to that level. Thus AI disease frequently presents with proximal muscle symptoms (buttock, hip, or thigh), with or without associated calf pain, whereas FP disease will manifest as calf pain with exercise. An important corollary is that individuals with



ASx = 4–11% progress to IC c Syr  
 IC = 20% major CV event c Syr  
 = 10–15% MR c 5yr (20%)  
 = 20% limb deterioration c Syr (greatest in 1st yr)  
 = 1% /yr major amputation risk  
 CLTI = 22% (12–32%) 1yr MR  
 = 22% (2–42%) 1yr major amp.  
 = 50% Syr MR

**Figure 107.5** Estimated odds ratios for all-cause mortality for individuals with asymptomatic or symptomatic peripheral arterial disease (PAD). (From Fowkes FG, Aboyans V, Fowkes FJ, McDermott MM, Sampson UK, Criqui MH. Peripheral artery disease: epidemiology and global perspectives. *Nat Rev Cardiol.* 2017;14(3):156–170.)

isolated infrapopliteal (TBP) disease frequently do not have claudication symptoms, although foot claudication in plantar muscles has been described.

Severity of IC is generally described in terms of the initial claudication distance, based on walking in daily life or on a treadmill test. Patients with severe IC are generally unable to complete a standard 5-minute treadmill protocol (2 mph, 12% incline). These individuals often describe symptom onset within minutes of walking that forces them to stop, producing significant disability and impaired QoL. Functional testing of patients with IC demonstrates a broad range of impairment in lower limb strength, balance, and associated loss of mobility. Moreover, functional decline over time in IC is significant and is associated with the severity of PAD (e.g., ABI), as well as other factors such as age, race, and socioeconomic status.<sup>43,44,49</sup>

Numerous studies have associated IC with long-term risk for cardiovascular events and mortality, highlighting the importance of diagnosis, medical therapy, and surveillance in these patients.<sup>40,50,51</sup> Over 5 years, approximately 20% of patients with IC experience a major CV event and mortality ranges between 10% and 15%, (see Fig. 107.5). Data from large registries have demonstrated that symptomatic PAD is strongly associated with CV events and mortality, even more strongly than isolated CAD or CVD.<sup>52–54</sup> Despite this natural history, undertreatment of patients with symptomatic PAD has been a consistent finding across studies comparing the use of antithrombotic and lipid-lowering medications across PAD, CAD, and CVD populations.<sup>9,55</sup> These studies and others indicate that the delivery of guideline-based medical care remains suboptimal for patients with all stages of PAD.

The limb prognosis for patients with IC is generally considered as benign; however, a significant minority of patients will progress in the degree of disability and severity of limb threat.<sup>56,57</sup> In a recent systematic review, 21% of IC patients experienced deterioration of limb status over a 5-year period.<sup>46</sup> Symptomatic deterioration is greatest within the first year after diagnosis. Risk of major amputation has been estimated at less than 1% per year across a number of studies, although accurate

data are limited. Risk for progression from IC to CLTI is associated with similar underlying factors as for baseline PAD, although diabetes and continued smoking appear of heightened significance.

## Acute and Chronic Limb-Threatening Ischemia

Patients may present with limb-threatening ischemia in either an acute or subacute/chronic fashion. The differential diagnosis, natural history and treatment approaches are fairly disparate and thus these conditions have been separated on a clinical basis. Acute limb ischemia (ALI) is defined as a sudden decrease in arterial perfusion, with symptom duration of less than 2 weeks.<sup>58,59</sup> Thrombosis of pre-existing native artery disease (i.e., advanced PAD), or occlusion of prior bypass grafts or stents placed for PAD, comprise a portion of ALI cases. Other important causes include embolization (most frequently cardiac origin), traumatic injury, dissection and aneurysm disease. The ALI subgroup with thrombosis in the setting of extremity occlusive disease represents a small but important part of the spectrum of PAD. Recent clinical trials of antiplatelet and anticoagulant agents have focused on ALI as an important endpoint in a PAD population, demonstrating an incidence of 1–1.7%.<sup>60–62</sup> Factors associated with development of ALI include prior lower extremity revascularization, lower ankle brachial index (<0.6), and atrial fibrillation. ALI is associated with significant risk for major amputation (10%–15%) and 1 year mortality in the range of 15%–40%.<sup>58,59</sup>

The terms “critical limb ischemia” (CLI) and CLTI have been defined clinically as an advanced stage of PAD in which pain at rest in the foot or tissue necrosis (gangrene or non-healing ulceration) has been present for at least 2 weeks. These terms connote a severe impairment of limb perfusion insufficient to maintain baseline tissue requirements. Although this clinical presentation is easily distinguished from asymptomatic PAD and IC, it represents a very broad range of hemodynamic compromise and associated limb threat. Recent consensus efforts have supported the preferred terminology of “chronic

**TABLE 107.2**

**Summary of Risk Prediction Models for Patients with Chronic Limb-Threatening Ischemia Who Have Undergone Revascularization**

	Endpoints	Critical Factors	Reference
Taylor et al.	Mortality, ambulatory failure (median follow-up 2 years)	Age, race, ESRD, CAD, COPD, DM, dementia, baseline ambulatory status	Taylor et al. <sup>72</sup>
FINNVASC	Perioperative (30-day) mortality, limb loss	DM, CAD, gangrene, urgent operation	Biancari et al. <sup>73</sup>
PREVENT III	AFS (1 year)	ESRD, tissue loss, age >75, CAD, anemia	Schanzer et al. <sup>68</sup>
BASIL	Survival (2 years)	Age, CAD, smoking, tissue loss, BMI, Bollinger score, serum creatinine, ankle pressure (number measured and highest value), prior stroke/TIA	Bradbury et al. <sup>69</sup>
CRAB	Perioperative (30 day) mortality, morbidity	Age >75, prior amputation/revascularization, tissue loss, ESRD, recent MI/angina, emergency operation, functional dependence	Meltzer et al. <sup>70</sup>
Soga et al.	Survival (2 years)	Age, BMI, nonambulatory status, ESRD, cerebrovascular disease, tissue loss, left ventricular ejection fraction	Soga et al. <sup>71</sup>
VQI	Survival (2 years)	Age, CKD, ambulatory status, COPD, CAD, CHF, tissue loss, DM, beta-blocker use	Simons et al. <sup>67</sup>

AFS, amputation-free survival; BMI, body mass index; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; DM, diabetes mellitus; ESRD, end-stage renal disease; TIA, transient ischemic attack.

“limb-threatening ischemia” (CLTI) to be more broadly inclusive of the full spectrum of ischemia and neuropathy that are seen in these patients.<sup>63,64</sup> This subtle but important change implies that absolute threshold values for perfusion deficits that are “critical” are not readily defined across the population at risk and may vary in relation to the degree of tissue loss or infection that coexists in the limb. The “chronic” descriptor in CLTI also better distinguishes it from ALI as noted above.

Historically, hemodynamic criteria associated with the definitions of CLI have differed for rest pain versus tissue loss and vary by technique used (e.g., ankle pressure [AP], toe pressure [TP], ankle or toe index, tissue oximetry). Typical values associated with ischemic rest pain are an absolute AP less than 40 to 50 mm Hg and TP less than 30 mm Hg. With tissue loss, these defining values are typically increased to AP less than 50 to 70 mm Hg and TP less than 40 to 50 mm Hg, respectively. In the Fontaine and Rutherford schemes, rest pain and tissue loss are assigned different stages and Rutherford further discriminates “minor” (Rutherford 5) from “major” (Rutherford 6) tissue loss. The definition of Rutherford 6 used in the literature has ranged from a non-salvageable foot to necrosis extending anywhere proximal to the forefoot, leading to difficulty in analysis of treatment outcomes and prognosis of disease. All of these factors argue for a more consistent and comprehensive staging system for the threatened limb.

CLTI affects a minority of individuals with PAD, variably estimated at between 1% and 10%. The prevalence of CLTI has been estimated at 1.3% of an insured US adult population and 0.5% to 1.2% of Swedish adults older than 60 years.<sup>4,7</sup> A recent meta-analysis estimated the prevalence of CLTI at 0.8%.<sup>65</sup> Risk factors for CLTI include all of those relevant for PAD, with a notably higher preponderance of diabetes and renal disease. Many of these patients do not relate an antecedent history of classic IC, presenting with rest pain or tissue loss as the initial clinical manifestation of PAD. This may relate to the

(1) anatomic distribution of disease (e.g., predominantly infrapopliteal involvement), (2) coexistent peripheral neuropathy, (3) reduced mobility from comorbid factors, or (4) an acute inciting event such as trauma or foot infection. Careful examination of the limb and foot should evaluate for signs of ischemia, infection, skin breaks, and bony involvement and document the presence and quality of pulses and Doppler signals.

Numerous studies have documented the adverse systemic and limb prognosis associated with a diagnosis of CLTI. These patients have a greater burden of coexistent CAD and CVD and are at high risk for major CV events, mortality, and amputation. A recent systematic review examined the natural history of CLTI, summarizing data from 13 studies and 1527 patients who did not receive limb revascularization.<sup>66</sup> At 1 year, estimated mortality was 22% (12%–33%) and major amputation had occurred in 22% (2%–42%). However, these data are limited in generalizability because many patients with CLTI undergo revascularization.

Given the high cardiovascular risk and its importance for clinical decision-making in CLTI, multiple studies have sought to define prediction models for mortality and major amputation (Table 107.2).<sup>67–73</sup> Predictors have included advanced age (>75 or 80 years), renal failure, coronary heart disease, congestive heart failure, diabetes, CVD, tissue loss, chronic obstructive pulmonary disease, body mass index, dementia, and functional status. Frailty is a recently identified functional measure that is also of clear importance in this population.<sup>79,80</sup> All of these tools have been developed retrospectively using data from cohorts who have undergone revascularization, thereby excluding those who were managed conservatively or treated by primary amputation. None have been prospectively tested across the full spectrum of CLI/CLTI patients presenting for evaluation and treatment.

Limb prognosis in this patient population has a broad range consistent with the spectrum of presentation from rest

*WIFI in F<sub>3</sub>/F<sub>4</sub> + objective evidence of PAD*

pain through minor and major tissue loss, with or without infection. The need for improved staging to better define amputation risk and to appropriately compare treatment outcomes led to the recent development of the Society for Vascular Surgery Lower Extremity Threatened Limb

Classification System.<sup>64</sup> This system stratifies limb risk by grading three critical factors – Wound, Ischemia, and foot Infection (“WIFI”) – similar to a “TNM” system for malignancy (Table 107.3). The staging system applies to all patients with rest pain or tissue loss, combined with objective

**TABLE 107.3**

Society for Vascular Surgery Threatened Limb Classification System (WIFI) and Relationship to Amputation Risk

Component	Score	Description			
W (Wound)	0	No ulcer (ischemic rest pain)			
	1	Small, shallow ulcer on distal leg or foot without gangrene			
	2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes			
	3	Extensive deep ulcer, full-thickness heel ulcer ± calcaneal involvement ± extensive gangrene			
I (Ischemia)	ABI	Ankle pressure (mm Hg)	Toe pressure or $TcPO_2$		
	0	$\geq 0.80$	>100	$\geq 60$	
	1	0.60–0.79	70–100	40–59	
	2	0.40–0.59	50–70	30–39	
	3	<0.40	<50	<30	
fI (foot Infection)	0	No symptoms/signs of infection			
	1	Local infection involving only skin and subcutaneous tissue			
	2	Local infection involving deeper than skin/subcutaneous tissue			
	3	Systemic inflammatory response syndrome			

#### SVS WIFI Clinical Limb Stage (<https://apps.apple.com/us/app/svs-ipg/id1014644425>)

Based on Estimated Risk of Amputation at 1 Year

	Ischemia – 0			Ischemia – 1				Ischemia – 2				Ischemia – 3				
W-0	1	1	2	3	1	2	3	4	2	2	3	4	2	3	3	4
W-1	1	1	2	3	1	2	3	4	2	3	4	4	3	3	4	4
W-2	2	2	3	4	3	3	4	4	3	4	4	4	4	4	4	4
W-3	3	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	fl-0	fl-1	fl-2	fl-3	fl-0	fl-1	fl-2	fl-3	fl-0	fl-1	fl-2	fl-3	fl-0	fl-1	fl-2	fl-3

#### SVS WIFI Clinical Stage and 1-Year Rate of Major Amputations

Weighted Mean of Published Studies, N=2779 Patients<sup>a</sup>

Clinical Stage 1	Very low risk	0.75%	<u>WIFI correlates with</u>											
Clinical Stage 2	Low risk	5.9%	- amp risk											
Clinical Stage 3	Moderate risk	8.4%	- wound healing time											
Clinical Stage 4	High risk	25%	- need for revasc											

Clinical Stage 5 = Unsalvageable limb

- amp risk
- wound healing time
- need for revasc
- cost of care

[To more likely to need revasc.]

<sup>a</sup>Reference for composite data: Mills JL. The application of the society for vascular surgery wound, ischemia and foot infection (WIFI) classification to stratify amputation risk. *J Vasc Surg*. 2017;65:591–593.

Upper table demonstrates grading system for each component – wound, ischemia, foot infection. Lower table summarizes their integration into four stages of limb threat and published data on outcomes.

ABI, Ankle-brachial index; fl, foot infection; I, ischemia;  $TcPO_2$ , transcutaneous oxygen; W, wound.

Adapted from Aboyans V, Ricco JB, Bartelink MEL, et al; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J*. 2018;39(9):763–816.

evidence of PAD. Each of the three key factors is graded on a four-level scale, and the 64 combinations were assigned to four stages of clinical severity expected to correlate with amputation risk at 1 year. Multiple studies have been published demonstrating that WIfI staging is strongly associated with amputation and wound-healing outcomes.<sup>80–84</sup> These studies confirm that WIfI stage 1 is associated with very low amputation risk, whereas stages 3 and 4 are more likely to require revascularization and are at increased risk for limb loss. WIfI stage may also predict wound healing time<sup>74–78</sup> and has been correlated with costs of care.<sup>85</sup> Further efforts will be needed to prospectively validate and refine this system using large population-based registries.

## Screening for Peripheral Arterial Disease

The role of screening for PAD has been controversial. Given the strong association of PAD with mortality and CV events, some have advocated for ABI screening, which is noninvasive, simple, and inexpensive. However, the US Preventive Services Task Force found the evidence to support PAD screening as insufficient in terms of the balance of benefits and harms.<sup>86</sup> A recent systematic review concurred that the evidence to support PAD screening was lacking.<sup>87</sup> Current Society for Vascular Surgery guidelines recommend against population screening for PAD; however, they suggest that targeted screening may be reasonable among individuals at higher risk (e.g., age >70 years, diabetes) if it would improve risk stratification or influence medical therapy.<sup>88</sup> The 2016 AHA/ACC guidelines also recommend targeted ABI testing in asymptomatic individuals at increased risk for PAD, which they define as age older than 65 years, age 50 to 64 with risk factors for atherosclerosis or family history of PAD, age older than 50 with diabetes plus one additional risk factor, or any individual with established atherosclerosis in another vascular bed (e.g., coronary, cerebral).<sup>89</sup>

## Surveillance of Peripheral Arterial Disease Patients with Established Disease

The benefit of surveillance for patients with asymptomatic PAD is unclear. However, patients and their primary providers should be made aware of the presence of the disease and the signs and symptoms of its advancement. Those with diabetes or history of CLTI should have regular foot examinations and be counseled on preventive foot care. Symptomatic patients with objectively determined PAD are typically followed long-term to monitor for symptomatic worsening or disease progression. Many patients with mild-moderate IC are treated with smoking cessation, optimal medical management, and exercise. Others with disabling symptoms may require revascularization. The current SVS guideline recommends that all patients with IC be followed annually to assess for compliance with medical and lifestyle management, as well as for evidence of progression, with clinical exam and noninvasive testing (ABI).<sup>84</sup> The AHA guideline concurs with the need for long-term clinical follow-up.<sup>85</sup>

Patients with IC or CLTI who have undergone revascularization are monitored more closely, including surveillance of the vascular reconstruction. Although level 1 evidence is lacking, multiple cohort studies and the aforementioned guidelines support a benefit for duplex ultrasound surveillance of vein bypass grafts to promote long-term patency. It is less clear if surveillance of prosthetic bypass grafts or endovascular interventions is beneficial, although it is commonly used in clinical practice. Assessment of lower extremity functional performance, new or recurrent symptoms, and a complete foot examination should be a component of semiannual or annual visits in all patients following vascular interventions.

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A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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# Lower Extremity Arterial Disease: Decision Making and Medical Treatment

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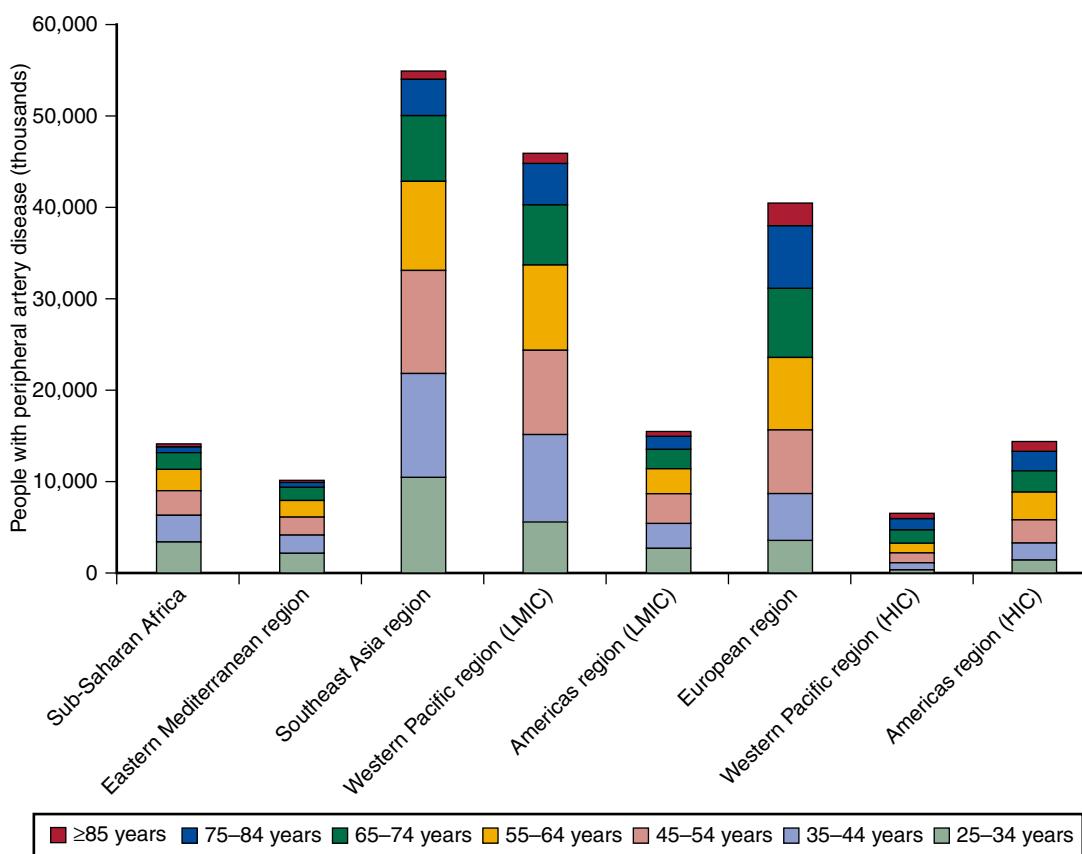
## CHAPTER ALGORITHM 1433

Lower extremity peripheral artery disease (PAD) encompasses a diverse and complex set of pathologies with multiple treatment options. As a result, shared decision making between the patient, their family/caregiver, and the provider is critical. Even the definition of PAD has been debated, since presentations can range from asymptomatic to gangrene. For the purposes of research and epidemiology, a commonly accepted modern definition is based on an ankle-brachial index of less than or equal to 0.9.<sup>1</sup> In 2013, Fowkes and colleagues reported that the global prevalence was 202 million people in 2010,<sup>2</sup> with a dramatic increase noted in low- and middle-income countries between 2000 and 2010 (Fig. 108.1). The prevalence of PAD is expected to increase in the United States and worldwide as the population ages, cigarette smoking persists, and the epidemics of diabetes mellitus, hypertension, and obesity continue.<sup>3</sup>

In accordance with the increasing prevalence of PAD, the number of lower extremity revascularization procedures has

been increasing; among US Medicare beneficiaries, the number of revascularizations has increased from 357 to 581 per 100,000 between 1996 and 2006.<sup>4</sup> Decisions regarding the management of lower extremity PAD pose a unique challenge owing to the complex interplay of factors that must be considered, including the underlying pathology and its natural history, degree of foot ischemia and infection, availability of conduit, comorbid conditions, functional status, ambulation potential, and suitability of anatomy for successful revascularization. Appropriate management of lower extremity PAD requires a firm understanding of these factors for good decision making.

Patients with lower extremity ischemia are typically divided into two groups – those with intermittent claudication (IC) and those with chronic limb-threatening ischemia (CLTI) – depending on symptoms at presentation. The term “chronic limb-threatening ischemia” is now preferred to describe the condition previously referred to as critical limb ischemia. It is



**Figure 108.1** Estimate of the number of cases, and contributing age groups, in eight WHO regions in the year 2010. LMIC, low- and middle-income countries. HIC, high-income countries. (Reprinted with permission from Elsevier. From Fowkes FGR, et al. Comparison of Global Estimates of Prevalence and Risk Factors for Peripheral Artery Disease in 2000 and 2010. *Lancet.* 2013;382:1329–1340.)

important to distinguish between IC and CLTI; they have very different natural histories in terms of limb outcomes, which makes the indications for treatment and expected risk–benefit tradeoff very dissimilar. The risk of major amputation is less than 5% over 5 years for claudicants, whereas the risk is approximately 30% in 1 year for those with CLTI.<sup>5</sup> Both groups have a high prevalence of comorbid cardiovascular conditions, with 5-year estimates of all-cause mortality as high as 20% and 50% for IC and CLTI, respectively.<sup>5</sup> Patients with CLTI often accept high-risk revascularization strategies because the risk of limb loss is so high, whereas the threshold to offer revascularization for IC should be far higher. That is, the indication to intervene for IC is lifestyle limitation, not limb loss; invasive measures should only be considered when other, lower-risk therapies have all failed. While the decision for revascularization is nuanced, it is clear that all patients with PAD require medical management of their cardiovascular disease.

## MEDICAL MANAGEMENT AND RISK FACTOR MODIFICATION

The most important element of treatment of patients with PAD is aimed at reducing their risk of death due to cardiovascular causes. PAD is an important indirect marker for systemic

atherosclerosis.<sup>6</sup> PAD patients are at significantly increased risk for premature cardiovascular events, including myocardial infarction (MI), stroke, and death.<sup>7,8</sup> Any patient older than 40 years who is found to have an ankle–brachial index (ABI) of less than 0.90 has significant PAD, even in the absence of symptoms.<sup>9</sup> Interestingly, more than 50% of patients with an abnormal ABI fail to show typical symptoms of claudication or CLTI, owing to the coexistence of other major comorbidities, a condition sometimes referred to as “chronic subclinical lower extremity ischemia.”<sup>10</sup> A systematic review of screening for PAD concluded that there was no evidence for revascularization in patients with asymptomatic PAD; instead, the value of screening may be in identifying a population in whom aggressive medical therapy may be warranted to prevent cardiovascular and cerebrovascular events.<sup>11</sup>

Several guidelines have been published<sup>10,12–14</sup> regarding the use of screening for PAD, including a clinical practice guideline from the Society for Vascular Surgery (SVS) Lower Extremity Guidelines Writing Group.<sup>15</sup> The authors recommend accepted preventive strategies for systemic atherosclerosis and comprehensive tobacco cessation interventions, as well as education on signs and symptoms of progression of PAD to the symptomatic state. Medical management for all PAD, regardless of symptom status, should include daily antiplatelet therapy and statin therapy to target a low-density lipoprotein (LDL) goal of

②

$< 2.6 \text{ mmol/L}$     $< 1.8 \text{ mmol/L}$

$< 100 \text{ mg/dL}$  or to  $< 70 \text{ mg/dL}$  in very high-risk individuals.<sup>15,16</sup> Other conditions associated with cardiovascular disease should also be optimized, including use of an angiotensin-converting enzyme inhibitor for hypertension and aggressive glucose control for diabetes.<sup>17</sup>

Medical management after revascularization greatly lacks standardization, with the evidence from the cardiology literature guiding much of these practices. While a comprehensive review is beyond the scope of this chapter, it should be noted that, in general, patients are prescribed single antiplatelet therapy at minimum after open or endovascular procedures. Other studies evaluating clopidogrel or dual anti-platelet therapy have had mixed results, specifically in terms of the trade-off between efficacy and bleeding risk. More recently, a large trial was conducted on the use of a direct oral anticoagulant (rivaroxaban); this was a randomized trial among patients who had undergone revascularization for PAD.<sup>18</sup> Their results suggest the use of low-dose rivaroxaban in addition to aspirin was superior to aspirin alone in terms of the composite end point of acute limb ischemia, major amputation, MI, ischemic stroke, and death from cardiovascular causes. Whether this practice will be widely adopted is yet to be determined.

## Exercise Therapy for Claudication

Multiple reports have clearly demonstrated improvements in pain-free ambulation and overall walking performance with structured exercise training.<sup>19–22</sup> Data from more than 20 randomized trials have confirmed that exercise therapy is the best initial treatment of intermittent claudication.<sup>22</sup> The benefits of exercise extend beyond improvement in the symptoms of claudication. Regular aerobic exercise reduces cardiovascular risk by lowering cholesterol and blood pressure and by improving glycemic control. In most patients, claudication initiates a downward spiral of cardiovascular deconditioning that can result in an annual mortality rate as high as 12%.<sup>22</sup>

The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines support supervised exercise for the treatment of intermittent claudication as a level IA recommendation.<sup>23</sup> The guidelines suggest that exercise training, in the form of walking, should be performed for a minimum of 30 to 45 minutes per session, 3 to 4 times per week, for a period not less than 12 weeks. During each session, the patient should be encouraged to walk until the limit of lower extremity pain tolerance is reached, followed by a short period of rest until pain relief is obtained, then a return to exercise. This cycle should be followed for the duration of the session. As the pain-free interval of ambulation increases, the level of exercise should be increased (Box 108.1).<sup>20</sup>

Although exercise therapy would appear easy to implement, effectiveness is often limited by poor patient compliance.<sup>24</sup> Studies have shown the superiority of clinic-based exercise programs over home-based programs,<sup>7,19</sup> but this can be overcome with the addition of behavioral change techniques.<sup>25</sup> Effective exercise training is not possible in up to 34% of patients because of comorbid medical conditions, and an additional 30% of patients simply refuse to participate in exercise training.<sup>10</sup> In

addition, while Medicare has recently begun covering supervised exercise training programs (for up to 12 weeks, 36 sessions), there are still barriers such as the need for transportation and an appointment with the facility. Therefore, even though exercise therapy in motivated patients offers proven benefits, its effectiveness is applicable to only approximately one-third of patients presenting with intermittent claudication. The use of either consumer-grade or research-grade activity trackers and other health technologies are areas of active investigation for overcoming some of these barriers. Along these lines, the SVS has recently partnered with a private telehealth company (CellEd, Palo Alto, CA) to pilot an app that leverages Apple Health-based mobility metrics to virtually prescribe and monitor progress along a supervised exercise therapy program.<sup>26</sup> In the future, technology-based at-home exercise therapy may have greater adherence rates, and therefore success, than other approaches.

## Pharmacologic Treatment of Claudication

Pharmacologic therapy for intermittent claudication has been the subject of intense research for more than 30 years. To date, only two drugs (pentoxifylline and cilostazol) have achieved FDA approval for the treatment of intermittent claudication in the United States; cilostazol is the only drug used in current practice. However, a number of other medications have been investigated, with varying degrees of evidence supporting their efficacy. These include several drugs and supplements with various reported mechanisms of action such as changes in tissue metabolism (naftidrofuryl, levocarnitine), enhanced nitric oxide production (L-arginine), and vasodilatory effects (statins, buflomedil, prostaglandins, angiotensin-converting enzyme inhibitors, K-134).

### Cilostazol

Cilostazol (Pletal) gained FDA approval in 1999 for the treatment of intermittent claudication. Oral administration of this phosphodiesterase III inhibitor increases cyclic adenosine monophosphate (cAMP) and results in a variety of physiologic effects, including the inhibition of smooth muscle cell contraction and platelet aggregation. Finally, cilostazol has a beneficial effect on plasma lipid concentrations, resulting in a decrease in serum triglycerides and an increase in HDL. Although the precise mechanism by which cilostazol improves the symptoms of intermittent claudication is unknown, it is likely a combination of these effects.

Several controlled clinical trials, including a meta-analysis, have confirmed the efficacy of cilostazol.<sup>27–29</sup> Results have shown increased maximal walking distances up to 50%, as well as significant improvements in health-related quality of life (QoL) measures.<sup>28</sup> There is also increasing evidence that cilostazol may modulate the synthesis of vascular endothelial growth factor (VEGF), potentially stimulating angiogenesis in patients with chronic lower extremity ischemia.<sup>30</sup>

The benefits of cilostazol in the treatment of intermittent claudication were compared with those of pentoxifylline in a randomized controlled trial performed by Dawson and associates.<sup>27</sup>

**BOX 108.1****Key Components of a Structured Exercise Program for Claudication****Role of the Primary Clinician**

- Establish the diagnosis of PAD using the ABI or other objective vascular laboratory evaluations.
- Determine that claudication is the major symptom limiting exercise.
- Discuss the risks and benefits of therapeutic alternatives, including pharmacologic, percutaneous, and surgical interventions.
- Initiate systemic atherosclerosis risk modification.
- Perform treadmill stress testing.
- Provide formal referral to a claudication exercise rehabilitation program.

**Exercise Guidelines for Claudication<sup>a</sup>**

- Include warm-up and cool-down periods of 5–10 min each.

**Types of Exercise**

- Treadmill or track walking is the most effective exercise for claudication.
- Resistance training may be beneficial for individuals with other forms of cardiovascular disease, and its use (as tolerated) for general fitness is complementary to but not a substitute for walking.

**Intensity**

- Initially, set the treadmill to a speed and grade that elicits claudication symptoms within 3–5 min.

<sup>a</sup>These general guidelines should be individualized and based on the results of treadmill stress testing and the patient's clinical status. A full discussion of the exercise precautions for persons with concomitant diseases can be found elsewhere for patients with diabetes (Ruderman N, Devlin JT, Schneider S, Kriska A. *Handbook of Exercise in Diabetes*. Alexandria, VA: American Diabetes Association; 2002); hypertension (ACSM's *Guidelines for Exercise Testing and Prescription*. In: Franklin BA, ed. Baltimore, MD: Lippincott, Williams & Wilkins; 2000); and coronary artery disease (*Guidelines for Cardiac Rehabilitation and Secondary Prevention/American Association of Cardiovascular and Pulmonary Rehabilitation*. Champaign, IL: Human Kinetics; 1999).

ABI, ankle-brachial index; PAD, peripheral artery disease.

From Stewart KJ, Hiatt WR, Regensteiner JG, et al. Exercise training for claudication. *N Engl J Med*. 2002;347:1941–1951.

- Patients walk at this workload until they experience claudication of moderate severity, at which point they take a brief rest period, either standing or sitting, to permit symptoms to resolve.

**Duration**

- The exercise–rest–exercise pattern should be repeated throughout the exercise session.
- The initial duration usually consists of 35 min of intermittent walking. This should be increased by 5 min each session until 50 min of intermittent walking can be accomplished.

**Frequency**

- Perform treadmill or track walking 3–5 times per week.

**Role of Direct Supervision**

- As walking ability improves, the exercise workload should be increased by modifying the treadmill grade or speed (or both) to ensure the stimulus of claudication pain during the workout.
- As walking ability improves, it is possible that cardiac signs and symptoms (e.g., dysrhythmia, angina, ST-segment depression) may appear. These events should prompt physician re-evaluation.

They found that cilostazol therapy significantly increased maximal walking distance by 107 m (54% increase), compared with a 64-m improvement in the pentoxifylline group (30% increase). There was no difference in maximal walking distance improvement between the pentoxifylline and placebo groups. Regarding the durability of the effect, a recent pooled analysis of nine randomized controlled trials demonstrated a significant benefit in maximal walking distance compared with placebo at 6 months.<sup>31</sup>

Cilostazol has a moderate but notable adverse effect profile that includes headache, diarrhea, and gastrointestinal discomfort. Its use is contraindicated in patients with congestive heart failure. High plasma drug levels may result when taken in combination with other medications metabolized by the liver via the cytochrome P-450 pathway.

system,<sup>10</sup> describe the extent of angiographic disease. Although they both can offer some guidance in the revascularization decision-making process (i.e., endovascular or open), other information must also be considered.

Caring for PAD patients requires a sophisticated understanding of multiple facets of the patient and the disease, as well as a robust command of procedural options and their relative risks and benefits. In many cases, it also requires the provider to communicate all of these complex competing risks to that patient and their family to help them make patient-centered decisions. Decision-making algorithms may be very different for patients with IC compared to those with CLTI since the goals are very different. In the case of IC, the goal is to reduce walking impairment and improve functional status and health-related quality of life. In CLTI, the goal is to reduce the risk of limb loss. Risk tolerance for procedural complications for the two conditions is therefore completely different. In addition, technical success does not always equate to clinical success. For patient-centered care to be delivered, “treatment success” must first be defined for each patient, followed by a comprehensive evaluation of the many facets described herein.

## DECISION MAKING FOR REVASCULARIZATION

Decision making in PAD is perhaps one of the most stimulating aspects of a vascular surgeon's work; there is almost never just one “right” answer. While it may seem that decision-making translates directly from the anatomic pattern of disease, this is only one facet. Anatomic classification systems, such as the Global Anatomic Staging System (GLASS),<sup>32</sup> and Trans-Atlantic Inter-Society Consensus (TASC) classification

### Defining Treatment Success

Although the general goal of any revascularization, whether for claudication or CLTI, is to increase the perfusion to the

**TABLE 108.1**

**Chronic Limb-Threatening Ischemia Endpoint Definitions and Event Rates** Reported by the Society for Vascular Surgery Working Group for the Development of Objective Performance Goals for Evaluating Catheter-Based Treatment<sup>a</sup>

Endpoint	Definition	Event Rate (%) (95% CI)
<b>Safety Outcomes (30 Day)</b>		
Major adverse cardiovascular event (MACE)	Myocardial infarction, stroke, or death (any cause).	6.2 (4.7–8.1)
Major adverse limb event (MALE)	Above-ankle amputation of the index limb or major re-intervention (new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis).	6.1 (4.6–7.9)
Amputation	Above-ankle amputation of the index limb.	1.9 (1.1–3.1)
<b>Efficacy Outcomes (1 Year; All Rates Are Freedom From Event)</b>		
Perioperative death or MALE	Perioperative death (30 days), or any MALE	76.9 (74.0–79.9)
Amputation-free survival (AFS)	Above-ankle amputation of the index limb or death (any cause).	76.5 (73.7–79.5)
Re-intervention or amputation or stenosis (RAS)	Any re-intervention, above-ankle amputation of the index limb, or stenosis	46.5 (42.3–51.2)
Re-intervention or amputation (RAO)	Any re-intervention or above-ankle amputation of the index limb.	61.3 (58.0–64.9)
Limb salvage	Freedom from above-ankle amputation	88.9 (86.7–91.1)
Survival	Freedom from death (any cause)	85.7 (83.3–88.1)

<sup>a</sup>As reported by the Society for Vascular Surgery Working Group for the development of objective performance goals for evaluating catheter-based treatment. CI, confidence interval.

Data are pooled from prospective trials of vein bypass surgery in CLTI.

From Conte MS, Geraghty PJ, Bradbury AW, et al. Suggested objective performance goals and clinical trial design for evaluating catheter-based treatment of critical limb ischemia. *J Vasc Surg*. 2009;50:1462–1473.

extremity as measured by physiologic testing, there are several other aspects that define treatment “success.” Optimal treatment starts with categorizing the disease state (IC versus CLTI) and communicating the associated prognosis to the patient.

### Limb- and Patient-Centered Outcomes

Traditional definitions of treatment success centered on technical outcomes such as graft/stent patency. However, graft patency may not correlate well with limb preservation; Simons et al. found that 10% of patients who underwent lower extremity bypass for CLTI failed to achieve clinical improvement despite having a patent graft at 1 year postoperatively.<sup>33</sup> Other outcome measures such as survival or amputation-free survival (AFS) have also been widely used. Some have questioned the appropriateness of these endpoints. In a critique of the Bypass Versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial,<sup>34</sup> Conte noted that lower extremity bypass is generally not offered as a life-saving therapy, and therefore survival is not an appropriate measure for comparisons between revascularization strategies.<sup>35</sup> In addition, Conte stressed the importance of limb- and patient-centered outcomes, such as freedom from re-intervention. This shift toward more patient-centered outcomes is reflected in the SVS objective performance goals (OPGs).<sup>36,37</sup> These guidelines were developed specifically for comparative evaluations of different treatments for CLTI, but the endpoints chosen are key components of treatment success for PAD, namely major adverse limb events, which included both freedom from major amputation as well as from

re-intervention. This approach shifts the focus of outcome measures from technical success rates such as primary and secondary patency to one that acknowledges a burden incurred by the patient with each intervention that is required to maintain that limb and function (Table 108.1).

### Outcomes Relevant to Claudication

For patients with claudication, surgeon-defined, procedural endpoints do not reflect the indication for intervention, which is walking impairment and health-related quality of life (QoL). If exercise therapy fails and revascularization is required, treatment success should be described in terms of physical function and QoL. Taylor and coworkers reported significant symptomatic improvement after intervention for claudication in nearly 80% of treated patients.<sup>38</sup> Revascularization in this series was exceedingly safe, with no early amputations and a 99% limb salvage rate at 5 years. This is critically important since the risk of limb loss without revascularization was also very low.

Although it is accepted that revascularization is not appropriate in every case, there is clear evidence that QoL is improved by revascularization in many instances.<sup>39–43</sup> Indeed, the need for patient-reported outcomes has recently been recognized by many key stakeholders. There are several survey instruments that measure patient-reported outcomes such as QoL; these include both general QoL and PAD-specific instruments.<sup>44</sup> While there is no consensus on the ideal questionnaire to use for the evaluation of patients with PAD, large registries in Europe have recently begun collecting patient-reported outcomes

using the VascuQoL-6<sup>45</sup> and EuroQoL-5D.<sup>46</sup> The PORTRAIT registry,<sup>47</sup> another large international registry, has used the Peripheral Artery Questionnaire in addition to the EuroQoL-5D.

### Outcomes Relevant to Chronic Limb-Threatening Ischemia

The simplest definition of treatment success for patients with CLTI is limb salvage. However, as previously described, the goals are more complex than that, and require a patient-specific approach. Taylor and colleagues studied 331 consecutive patients treated for Rutherford class 5 and 6 ischemia (tissue loss).<sup>48</sup> A bypass was deemed clinically successful if all four outcome criteria were met: (1) bypass patency until wound healing occurred; (2) limb salvage for at least 1 year; (3) maintenance of ambulatory status for at least 1 year; and (4) survival for at least 6 months. The authors found acceptable results when examining these components separately, including a graft patency rate of 72% and a limb salvage rate of 73% at 36 months. However, the clinical success rate, defined as the achievement of all four criteria, was only 44%. Furthermore, patients who presented with impaired ambulatory status, end-stage renal disease, gangrene, and infrainguinal disease (each independent statistical predictors) were especially prone to failure.<sup>48</sup> Prospects for a successful outcome became progressively dismal as the number of independent negative predictors increased. Patients harboring two of these independent predictors of failure experienced approximately a 33% probability of success; those with three predictors, a 10% probability of success; and those with all four independent predictors of failure, less than a 5% probability of success. This study illustrated the importance of patient-specific risk stratification and counseling on appropriate goals of care. For some patients, with a high risk of procedural morbidity and a low likelihood of limb salvage, the treatment goal may be reducing pain and the need for wound care; therefore “treatment success” may be best achieved with primary amputation.

## TREATMENT GUIDELINES ACCORDING TO PRESENTATION

### Claudication

The ACC/AHA guidelines suggest that the risk of major limb amputation for a patient with intermittent claudication is approximately 1% per year, whereas the risk of cardiac death is approximately 3% to 5% per year.<sup>10,23,49,50</sup> Treatment strategies have therefore stressed cardiovascular risk factor modification and medical therapy as the best initial treatment for patients with PAD symptoms limited to intermittent claudication. Medical treatment for intermittent claudication consists of smoking cessation, exercise training, and pharmacologic therapy, as already described. Revascularization is recommended only in cases of severe claudication and only after medical therapy has failed.

### Medical Therapy Versus Revascularization

The role of smoking cessation in treating the symptoms of claudication is unclear. Although studies have shown that smoking

cessation can improve walking distance in some cases, these findings are not universal.<sup>10</sup> However, the association between tobacco cessation and the reduction of subsequent cardiovascular events is undisputed. The rationale for smoking cessation is therefore based on reducing patient mortality and slowing the overall atherosclerotic disease process.

Currently available pharmacologic agents for claudication have already been discussed (see “Pharmacologic Treatment of Claudication”, above). The ACC/AHA guidelines recommend, in addition to routine antiplatelet therapy, a therapeutic trial of cilostazol (100 mg 2 times a day) as an effective method for increasing overall ambulation (class I recommendation).

When comparing medical to endovascular therapy, there are abundant data supporting the efficacy of medical therapy. For instance, the Edinburgh walking study consisted of a randomized trial to determine outcome differences in patients with intermittent claudication treated with angioplasty and stent versus medical management (daily low-dose aspirin, lifestyle modification) after 2 years. These investigators found no difference in maximal walking distance, treadmill distance until onset of claudication, and QoL measures between the two groups.<sup>51</sup> Supervised exercise therapy has also been compared with primary stenting for disabling claudication due to aortoiliac occlusive disease in the Claudication: Exercise Versus Endoluminal Revascularization (CLEVER) trial.<sup>52</sup> At 6-month follow-up, they reported that change in peak walking time was greatest for supervised exercise, intermediate for stenting, and least with pharmacologic therapy (mean change versus baseline,  $5.8 \pm 4.6$ ,  $3.7 \pm 4.9$ , and  $1.2 \pm 2.6$  minutes, respectively;  $P < 0.04$  for the comparison of supervised exercise versus stenting). QoL evaluation revealed significant improvements in both the supervised exercise and the stenting groups compared with pharmacologic therapy, but the benefit was greater in the stenting group than in the exercise group.

In summary, when weighing medical therapy versus revascularization for the treatment of intermittent claudication, the risk-to-benefit ratio favors initial medical therapy in most cases. However, medical therapy may be effective in as few as 30% of patients because of noncompliance and drug intolerance. When revascularization is chosen, modern approaches have become predominantly endovascular owing to its reduced procedural risks compared with open surgery. However, an analysis of practice patterns in New England between 2003 and 2009 demonstrated that an increasing proportion of lower extremity bypass procedures were performed for claudication in recent years (from 19% to 31%,  $P < 0.0001$ ). In addition, the percentage of patients with a history of previous endovascular intervention has steadily increased (from 13% to 23%,  $P = 0.02$ ).<sup>53</sup> The authors suggest that the high rates of prior endovascular intervention seen may reflect a “treatment trap”; after the decision has been made to intervene procedurally for claudication, surgeons may feel obliged to perform an open revascularization if a prior endovascular approach has failed to resolve symptoms. Of note, the 1-year incidence of major amputation after intervention on claudicants was 1.6% in this study; although this is low, it is a devastating outcome after a procedure for claudication. Clinical decision making

ultimately must incorporate not only the risks and benefits of various treatment strategies but also a discussion of realistic expectations as to the extent to which treatment will improve symptoms and improve QoL.

### Endovascular Treatment Versus Open Surgery

Ultimately, the selection of the best method of revascularization for an individual with claudication is based on a balance between the risks of the specific intervention and the degree and durability of improvement that can be expected from the intervention (see also Chs 109–113).<sup>10</sup> Because the natural history of vasculogenic claudication is relatively benign, that balance usually does not favor open surgery. In contrast, its relatively low morbidity and mortality make endovascular therapy particularly attractive,<sup>10</sup> and when it is anatomically feasible, endovascular therapy is often preferred to open surgery for most cases of claudication.<sup>51</sup> However, it is important to note that a growing body of evidence suggests that the concept that an endovascular option “does not burn any bridges” is false.<sup>54,55</sup>

Anatomy is one of several important considerations when selecting the best interventional modality for patients with claudication as well as those with CLTI. Prospective studies dating to the 1980s have characterized the arterial lesions and anatomy most conducive to long-term patency after angioplasty. Johnston and colleagues demonstrated in a prospective analysis that the arterial anatomy and clinical presentation most amenable to long-term patency and success using angioplasty were focal arterial lesions in large-diameter vessels with adequate outflow.<sup>56</sup> Outcomes were more favorable in nondiabetic patients presenting with claudication than in those with CLTI. The arterial segment best managed with percutaneous transluminal angioplasty is thus the common iliac artery, a vessel with all the favorable anatomic characteristics identified by Johnston's study. Atherosclerotic lesions in this segment are usually focal and possess good outflow. Angioplasty patency rates at 5 years generally exceed 70%.<sup>38</sup> Conversely, long-segment arterial disease, such as a long superficial femoral artery occlusion, is probably best treated with open bypass from the standpoint of durability of the revascularization. Diffuse multisegmental disease, more common with CLTI, can present a therapeutic dilemma.

### Chronic Limb-Threatening Ischemia

Although far fewer patients present with CLTI than with intermittent claudication, CLTI patients consume the vast majority of treatment resources. Since the prognosis for CLTI is considerably worse than for intermittent claudication, with as many as 25% of CLTI patients progressing to major limb amputation within 1 year, revascularization is always considered, rather than medical therapy and exercise. However, it is important to also note that 25% die of cardiovascular complications within 1 year of presentation; much of the additional complexity of decision making arises from this.

### Medical Therapy Versus Revascularization

The best information regarding the natural history of nonrevascularized limbs in patients with CLTI comes from the placebo

arms of pharmacotherapy trials of patients with unreconstructable vascular disease. Results suggest that this subgroup has a dismal prognosis, with nearly 40% of limbs progressing to amputation at 6 months.<sup>57</sup> Therefore, in functional patients, some type of revascularization is almost always preferable to medical therapy.

However, medical therapy for CLTI is not without some noteworthy successes. Indeed, wound care centers have become common adjuncts to many vascular surgical practices (see Ch. 118, Wound Care). Ischemic ulcer healing rates of 55% have been reported from dedicated centers using modern wound care methods such as negative-pressure wound therapy, intense debridement, and antibiotic therapy.<sup>10</sup> However, wound healing in such situations is often slow, laborious, and unpredictable. To date, pharmacotherapy for CLTI has failed to yield any major breakthroughs. The routine use of prostaglandins, vasodilators, antiplatelet agents, and even hyperbaric oxygen for the treatment of ischemic ulcers remains of unproven benefit.<sup>10</sup>

In summary, revascularization is an essential component in the relief of CLTI. Although medical adjuncts geared at risk factor modification may be important to slow the progression of systemic atherosclerotic disease, they play a secondary role in the treatment of the severely ischemic limb. In those rare cases in which vascular disease is truly unreconstructable, a trial of intensive wound care, preferably at a dedicated wound care center, may yield satisfactory healing rates for motivated patients with superficial ulcerations, or it may avoid major limb amputation in high-risk patients who are approaching the end of life.

### Limb Amputation Versus Revascularization

For the overwhelming majority of patients with CLTI, revascularization is the interventional treatment of choice. However, primary limb amputation continues to be required in 10% to 40% of CLTI patients, owing to overwhelming infection or unreconstructable vascular disease.<sup>10</sup> Unreconstructable vascular disease accounts for nearly 60% of patients requiring secondary amputation.<sup>10</sup> In many of these cases, revascularization has failed due to disease progression, recurrent ischemia, or persistent infection or necrosis despite a patent revascularization.

Although counterintuitive, limb amputation and prosthetic rehabilitation can be an excellent option, offering an expedient return to a reasonable QoL in selected cases. Maintenance of ambulation can exceed 70%, and maintenance of independence can exceed 90% in young, good-risk patients after below-knee amputation.<sup>58</sup> Clearly, amputation should be considered a tool capable of extending functionality and not a failure of treatment in these cases. Diamond and colleagues developed a prediction model designed to help forecast the likelihood of ambulation one year after major amputation.<sup>59</sup> This is an area that requires further study, since it would considerably augment the patient counseling process.

The use of an immediate postoperative prosthesis (IPOP) may aid in expediting a patient's recovery following below-knee amputation. This technique, first described in the 1960s, gained favor following a publication, the Prosthetic Research

Study, by Burgess and colleagues.<sup>60</sup> They reported that the use of a rigid cast placed intraoperatively facilitated faster healing and return to ambulation. Folsom and colleagues studied this technique in a population where the indication for amputation was not trauma, but rather severe infection or unreconstructable PAD.<sup>61</sup> Of 65 patients, 86% returned to independent ambulation, with an average time to ambulation of 15.2 days following below-knee ambulation. A more recent comparative analysis of IPOP compared with traditional soft dressings demonstrated no difference in complication rates, and a lower incidence of revision (soft dressings 27.6% vs. IPOP 5.4%,  $P = 0.021$ ).<sup>62</sup>

Patients with major tissue loss who are too sick or infirm to realize the benefit of limb revascularization should undergo palliative primary above-knee amputation. However, judging patients “too sick or infirm” can be difficult. Obviously, a non-ambulatory, elderly, nursing-home patient with knee contractures and neuropathic heel ulcers would qualify for a palliative above-knee amputation. For patients who are minimally ambulatory, with multiple comorbidities, the decision is less clear-cut. An individualized judgment is required to determine whether these patients will be better served by primary amputation or limb revascularization. In a single-institution study of 1000 consecutive revascularizations for CLTI, preoperative functional performance status was the most important predictor of postoperative functional outcome – even more important than limb salvage itself.<sup>63</sup> This finding strongly suggests that there is a definite subset of patients who are too sick or debilitated to realize the functional benefits of revascularization. Although more work is needed to better define such patients, this cohort is likely best suited for primary amputation.

### Endovascular Treatment Versus Open Surgery

For many years, the classic treatment approach for CLTI has been open surgery (see also Chs 109–113). CLTI is usually associated with multilevel arterial disease that is not ideally suited to percutaneous intervention. Diffuse, extensive PAD causing CLTI in both aortoiliac and femoropopliteal locations is best treated by surgical bypass according to TASC.<sup>10</sup> However, the primacy of surgical bypass for CLTI management has been challenged in recent years and has become the subject of intense debate. Those who favor open surgery for the treatment of CLTI often cite superior reconstruction patency and increased durability.<sup>64–66</sup> However, open surgery is usually associated with higher perioperative morbidity and longer hospitalization.<sup>67</sup> In addition, long-term postoperative graft surveillance is necessary to maintain a patent infrapopliteal bypass, as has been shown in well-performed studies from both Europe and North America suggesting that such surveillance is economically justified by preventing vein graft occlusion and late amputation.<sup>68,69</sup> A re-intervention rate of 20% to 30% to treat failing grafts due to intrinsic vein graft stenoses is usually necessary to maintain the increased durability attributed to open surgery.<sup>68,70</sup> Last, successful surgery depends on the presence of a suitable venous conduit for bypass.<sup>71,72</sup> Those who favor interventional treatment cite the low morbidity and mortality associated with a procedure that is usually performed

on an outpatient basis.<sup>73</sup> Although proponents acknowledge the limited reconstruction patency rates associated with endovascular treatment, especially for the high-risk lesions often encountered in CLTI, they argue that restenosis rarely jeopardizes subsequent surgery.<sup>73–75</sup> In contrast, others have found that prior ipsilateral intervention has a negative influence on subsequent bypass. An analysis of the BASIL data by treatment received found 1-year AFS was 40% for bypass that followed a failed endovascular intervention, compared with 70% for the bypass-only group.<sup>55</sup> The authors therefore do not endorse the concept of a “free shot” with an endovascular first approach. Nolan et al. also found a correlation of graft failure and prior endovascular intervention; in a study of CLTI patients who underwent lower extremity bypass in New England, those with a prior failed endovascular intervention had a higher incidence of major amputation (31% vs. 20%;  $P = 0.046$ ) and graft occlusion (28% vs. 18%;  $P = 0.009$ ) at 1 year.<sup>54</sup> Although a causative relationship has not been established, the concept of “burning bridges” with an aggressive endovascular-first approach clearly deserves further study.

### Conduit Availability

Another factor that may influence the decision of how to revascularize is the availability of adequate conduit for open bypass. Great saphenous vein of adequate caliber, even if it must be harvested from the contralateral leg, remains the conduit of choice for open bypass.<sup>76</sup> It has been shown to have superior durability compared with all other conduit choices: prosthetic grafts, short saphenous vein, spliced arm vein, and vein cuffs.<sup>77</sup> In the absence of good-caliber great saphenous vein for bypass, an endovascular revascularization becomes a more attractive option. Having said that, multiple authors have demonstrated excellent outcomes in large surgical bypass series using alternative autogenous vein options (cephalic vein, basilic vein, short saphenous vein).<sup>78–80</sup> Performance of vein mapping prior to arteriography is essential because of the strong influence it can have on the decision of how aggressively to pursue an endovascular revascularization strategy.

### The Role of Evidence from Clinical Trials

There is a striking paucity of level I data to guide decision making for endovascular treatment versus open surgery. In the United Kingdom the BASIL study represents the only randomized controlled multicenter trial comparing angioplasty (but without stenting) to open surgery for severe limb ischemia.<sup>34</sup> In this study of nearly 450 patients randomized to bypass or balloon angioplasty for the initial treatment of infrapopliteal disease, the findings support much of what is known about the two modalities and underscore several important caveats. Using AFS as the primary endpoint, the authors found that patients treated with a bypass-first strategy had comparable outcomes to patients treated with balloon angioplasty first at 6 months (amputation or death = 21% with bypass first vs. 26% with balloon angioplasty first;  $P = \text{not significant}$ ). Although the early mortality was similar in both treatment groups, surgery was associated with higher morbidity. Crossover treatment

after initial therapy (surgery to angioplasty or angioplasty to surgery) was common in both treatment groups, with more than half the angioplasty arm and approximately one-third of the surgical arm requiring further intervention. At the end of 5 years, 55% of patients were alive without amputation, 8% were alive with amputation, 8% were dead after amputation, and 29% were dead without amputation. After 2 years, both AFS (hazard ratio, 0.37;  $P = 0.008$ ) and overall survival (hazard ratio, 0.34;  $P = 0.004$ ) favored a bypass first strategy. (1)

The BASIL trial was widely interpreted as suggesting an advantage to bypass over angioplasty in those patients who live at least two years after revascularization. Also, the degree of treatment crossover in the BASIL trial was arguably its most remarkable finding. It stresses that angioplasty and open surgery are not “either/or” therapies but are complementary. It underscores the importance of training surgeons who manage lower extremity ischemia so that they possess both open and endovascular skill sets.<sup>81</sup>

The lack of high-quality evidence to guide therapy in patients with CLTI has prompted the initiation of two more large-scale trials that are currently well underway. The BASIL-2 trial (<https://www.birmingham.ac.uk/research/bctu/trials/portfolio-v/Basil-2/index.aspx>) is a multicenter, randomized clinical trial of “vein-bypass first” or “best endovascular therapy first” approach in patients with severe limb ischemia; it began recruitment across England, Scotland, and Northern Wales in June 2014.<sup>82</sup> The investigators report that they have recruited over 85% of the target study size. The primary outcome is AFS. A number of secondary outcomes will also be analyzed, including major adverse limb events, health-related QoL, crossover and re-intervention rates, and cost-effectiveness measures.

In the United States, a similar effort is underway to further define the best treatment strategy for patients with CLTI, the Best Endovascular versus Best Surgical Therapy in Patients with CLI Trial (BEST-CLI) (ClinicalTrials.gov: NCT02060630; <https://www.bestcli.com/study-design>).<sup>83</sup> This multicenter clinical trial reports having randomized over 1800 of 2100 planned study patients with CLTI, across the United States and Canada, to either best open or best endovascular therapy; the first patient was enrolled in September 2014. The primary endpoint is major adverse limb events. Planned secondary endpoints include freedom from clinical failure and from hemodynamic failure, health-related QoL, and cost–utility analysis.

Hopefully, these two landmark studies will better inform the complex decision-making process necessary to choose between endovascular treatment and open surgery for patients with CLTI.

## Threatened Limbs With or Without Peripheral Arterial Disease

In recognition of the fact that PAD patients are a subset of patients at risk for limb loss due to a variety of potential etiologies (diabetes mellitus, most commonly), the SVS commissioned the Lower Extremity Guidelines Working Group to create a more comprehensive classification system to serve as a more robust decision-making aid for this broader category

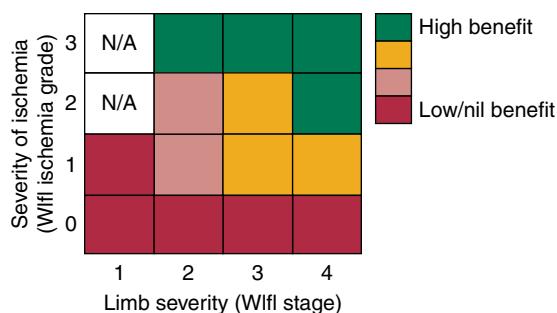
of patients. This new classification framework, entitled the SVS Threatened Limb Classification System incorporates three major factors that impact amputation risk and clinical management: Wound, Ischemia, and foot Infection (WIFI).<sup>84</sup> The intent of this new SVS WIFI classification system is to stage patients across a broad spectrum of lower extremity arterial occlusive disease of varying severity and distribution. In the SVS WIFI system, wounds are classified from grade 0 through grade 3, based on size, depth, severity, and anticipated difficulty achieving wound healing. Ischemia is classified from grade 0 through grade 4 according to ABI, ankle systolic pressure, toe systolic pressure, or transcutaneous oximetry. Infection is classified from grade 0 through grade 3 based on simple objective clinical observations. The combination of grades is used to categorize the limb into one of four clinical stages that correlate with major amputation risk at 1 year. Multiple studies have validated the SVS WIFI system as an accurate way in which to predict amputation risk and stratify patients to permit more meaningful analyses of outcomes for various forms of therapy in this challenging heterogeneous population.<sup>85–90</sup>

## Global Vascular Guidelines for the Management of Chronic Limb-Threatening Ischemia

The preceding text has made note of the prevalence of severe comorbid illness, reduced life expectancy and impaired functional status in CLTI patients, and the need to factor these into the decision-making process. Along these lines, in 2013, when several leading international societies convened the Global Vascular Guidelines Initiative, the first priority was to write a guideline for CLTI care that integrated all of the aforementioned considerations into one holistic approach to patient care, based on the best evidence and summary statements to date.<sup>32</sup> This extensive document is the most thorough and structured publication on this topic; it serves as the basis for this greatly abridged summary, which is not intended to replace it.

The patient-centered strategy they describe assesses three independent aspects of an individual patient: Patient risk estimation, Limb staging, and Anatomic pattern of disease characterization (PLAN). They note that these factors are listed ordinarily, meaning that patient risk estimation is the single most important factor in decision making. The authors suggest risk estimation for: (1) candidacy for limb salvage; (2) perioperative risk; and (3) life expectancy. Simons et al. developed a prediction model for this purpose using data on 38,470 infrapopliteal revascularizations for CLTI in the Vascular Quality Initiative registries. It predicts the likelihood of survival for the first 30 days, and over the first 2 years postoperatively, stratifying patients into low-, medium-, and high-risk groups for postoperative survival.<sup>91</sup> This work has subsequently been validated in a European cohort of non-revascularized CLTI patients as well.<sup>92</sup>

The limb staging piece includes application of the WIFI classification scheme described above. This system helps to classify patients in terms of the severity of limb threat, integrating the



**Figure 108.2** Society for Vascular Surgery Wound, Ischemia, and foot Infection classification. (With permission from Conte MS, Bradbury AW, et al. Global Vascular Guideline on the Management of Chronic Limb-threatening Ischemia. *J Vasc Surg.* 2019;69(6S);3S–125S.e40.)

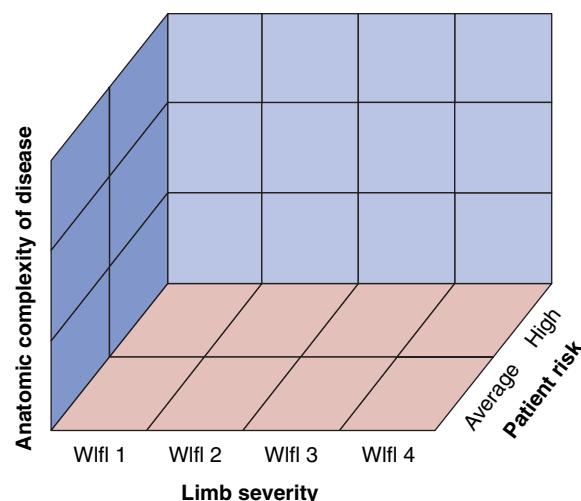
risks posed by wounds, degree of ischemia, and the presence/severity of foot infection (Fig. 108.2). The Global Vascular Guidelines do make one alteration to the original publication, noting that the benefit of revascularization is not applicable to WIfI stage 1 limbs.

Finally, the anatomic pattern of disease classification suggested in this new guideline is based on a novel scoring system: the Global Anatomic Staging System (GLASS). This system seeks to provide a more clinically driven classification of disease, rather than descriptions of lesions in individual anatomic segments. It incorporates the concept that in-line flow to the foot is required to heal CLTI. As a typically multi-level disease process, the authors describe the need to consider the target-artery path for revascularization. The GLASS system, while complex, elegantly integrates these concepts as well as the different factors at play for a successful anatomic outcome in open versus endovascular approaches.

Once a patient has been assessed on each of these three pillars of decision making, the PLAN algorithm can be employed to assess their options for evidence-based revascularization (Fig. 108.3). The resultant decision tree is featured in the chapter algorithm.

## RISK PREDICTION MODELS

The Global Vascular Guidelines for Management of Chronic Limb-Threatening Ischemia reference the need to risk stratify patients on an individual basis. In addition to the prediction models referenced within the guideline itself, there are several others that have been developed to aid in patient-specific risk stratification. The general concept with all of these tools is that they use statistical modeling based on patient-level data to identify predictors of a specific outcome, then apply a weighting system to them, such that a score may be given that corresponds to a likelihood of that outcome. For an individual patient, the score is based on the presence or absence of these factors. The sum then corresponds to a risk category, derived from the statistical modeling. The performance of the risk score can be assessed by tests of discrimination and calibration and should ideally be validated using data from another cohort of patient data. An ideal risk score uses easily obtainable and clearly defined factors that are available preoperatively. This



**Figure 108.3** Global Vascular Guidelines for Management of Chronic Limb-threatening Ischemia: Patient, Limb severity, ANatomic pattern of disease paradigm for evidence-based revascularization. (With permission from Conte MS, Bradbury AW, et al. Global Vascular Guideline on the Management of Chronic Limb-threatening Ischemia. *J Vasc Surg.* 2019;69(6S);3S–125S.e40.)

allows the surgeon to calculate the score and offer a bedside risk prediction. However, it is important to note that these risk scores are derived using a specific endpoint, at a specific point in time, and therefore should similarly be narrowly applied. When used properly, risk scores provide evidence-based risk stratification, individualized to each patient. Several scores have been described; they differ slightly in the outcome they predict, and the time point at which the outcome is predicted.<sup>93–96</sup> In addition, some have been externally validated in additional patient cohorts and have been tested using new endpoints. There is some commonality among the most widely recognized grading systems (Table 108.2), and some important differences described in more detail in later sections. However, it is important to note that prediction models complement clinical judgment rather than replace it, and more research is needed to optimize these models.

## Cost Considerations and Value-based Care

Decision making in the treatment of lower extremity PAD has focused on *how* to treat patients. In the future, as the financial condition of the healthcare system continues to deteriorate, decision making may shift to focus on *who* to treat. As healthcare costs continue to rise, decision making will increasingly be influenced by governmental and third-party payers. There is conflicting evidence regarding the most cost-effective methods of treating lower extremity PAD. Although there is evidence that revascularization is cost-effective compared with primary amputation,<sup>71,97–100</sup> the cost differential between strategies varies depending on the expense of rehabilitation after primary amputation in most series.<sup>98</sup> Indeed, primary amputation for patients forgoing rehabilitation (as might occur in a nursing-home patient) is cheaper than revascularization. Therefore, economic decision making depends on the patient's postoperative rehabilitation potential, which is often determined by preoperative functional status.<sup>63</sup>

**TABLE 108.2**

Comparison of the Finland National Vascular (Finnvasc), Project of Ex-Vivo Graft Engineering by Transfection III (PREVENT III), Bypass Versus Angioplasty in Severe Limb Ischemia (BASIL) Grading Systems, and the Vascular Quality Initiative (VQI)-Derived Risk Adjustment Model

	Finnvasc	PREVENT III	BASIL	VQI-Derived
<b>Score Application</b>	Critical limb ischemia	Critical limb ischemia	Severe limb ischemia	Critical limb ischemia
<b>Factor</b>				
Advanced age		++	+	+
Coronary artery disease	+	+	++	
Diabetes mellitus	+			+
Obesity			++	+
Chronic kidney disease/dialysis	+	++++	++	+++
Tissue loss	+	+++	+++	+
Smoking			+++	
Anatomic factors			+	+
Functional status				++
<b>Outcome Predicted</b>	Mortality and limb loss (30 days)	Amputation-free survival (1 year)	Survival (2 years)	Amputation-free survival (1 year)

In the case of claudication, there is little comparative effectiveness data that even uses the relevant endpoint that mirrors the indication for revascularization. Patient-reported outcomes will undoubtedly become required elements of care for these patients. Future economic decision making requires the identification of the most cost-effective single treatment for patients who present with PAD, both for claudication and CLTI.

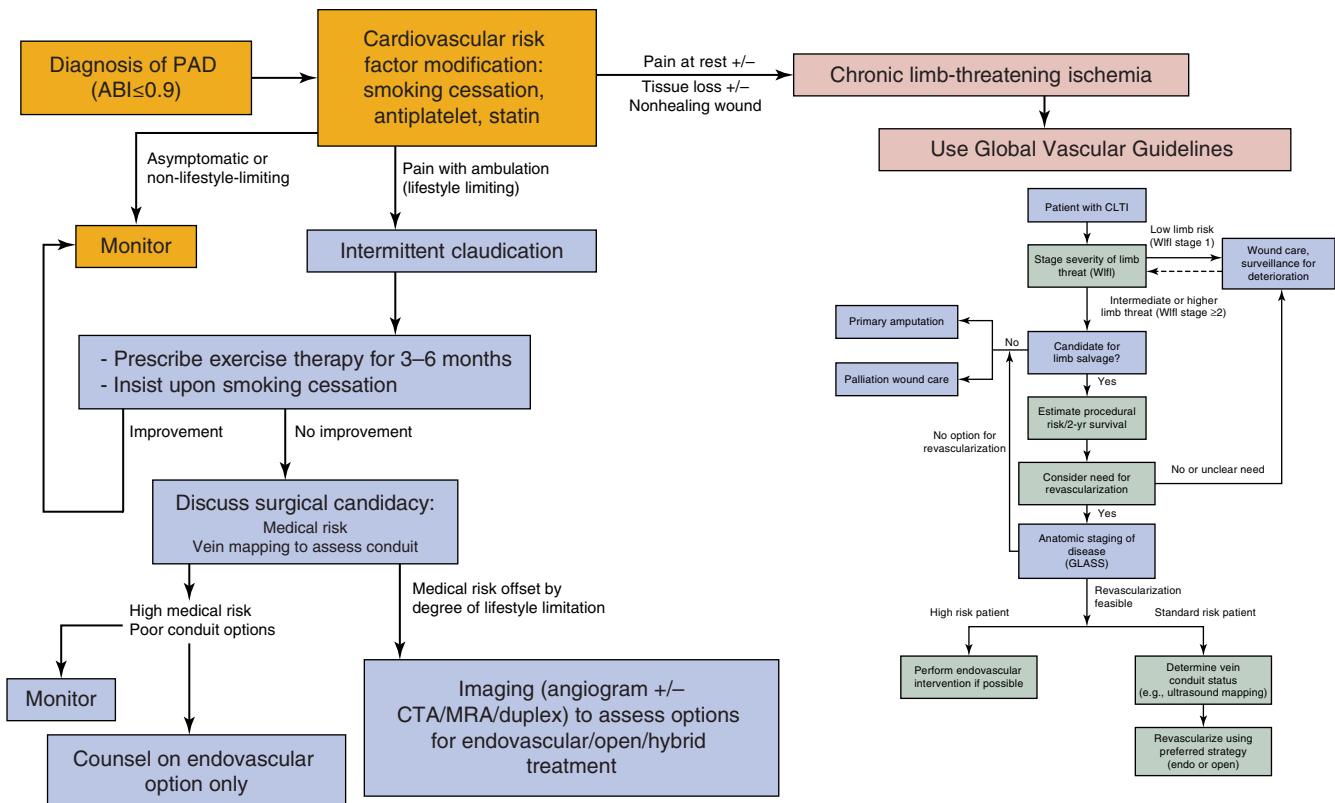
### Unmet Needs

Definitive high-level evidence on which to base treatment decisions, with an emphasis on clinical and cost-effectiveness, continues to be lacking. Treatment decisions in PAD are individualized, based on life expectancy, functional status, anatomy of the arterial occlusive disease, and surgical risk. For patients with aortoiliac disease, endovascular therapy has become first-line therapy for all but the most severe patterns of occlusion, and aortofemoral bypass surgery is a highly effective and durable treatment for the latter group. For infrainguinal disease, available data suggest that surgical bypass with vein is the preferred therapy for patients likely to survive 2 years or more, and for those with long segment occlusions or severe infrapopliteal disease who are acceptable surgical risk. Endovascular therapy may be preferred in patients with reduced life expectancy, those who lack usable vein for bypass or who are at elevated risk for operation, and those with less severe arterial occlusions. Patients with nonreconstructable disease, extensive necrosis involving weight-bearing areas, nonambulatory status, or other severe comorbidities may be considered for primary amputation or palliative measures. Given the myriad of contributing factors, each with its own extensive list of possible values, the potential combinations of disease states and patient situations are perhaps too numerous to ever study individually. A “clean” study, comparing two treatments in a population

that is balanced on all factors may not be achievable, even in the best of randomized controlled trials. Despite Herculean efforts on the part of the BASIL-2 and BEST-CLI investigators, it stands to be determined whether either of these studies will ultimately provide conclusive enough evidence that providers feel these questions of optimal treatment have been answered once and for all.

Third-party payers in our current healthcare system will increasingly insist on the delivery of evidence-based care. Quality will be defined, increasingly monitored, and financially linked to compliance with Medicare All-Care measures. Care for lower extremity PAD will increasingly become protocol driven, placing a premium on value and durability. For all of the important reasons previously mentioned, future studies should continue to analyze the impact of comorbidities in patients with PAD. These studies need to be conducted in patients undergoing surgical bypass, endovascular repair, primary amputation, and conservative treatment because the effect of comorbidities can be very different based on the treatment type. A diverse set of standardized endpoints that attempt to capture the diverse experience relevant to patients with PAD needs to be defined. The time points at which these endpoints are studied also should be standardized. In this way, valid risk estimates can continue to inform the way we take care of patients and, in doing so, improve evidence-based patient care. Finally, the definitive treatment of lower extremity PAD has traditionally relied on procedural therapy, either open or endovascular revascularization. We are now at an exciting time point where mapping of the human genome, improved understanding of angiogenesis, and the growing ability to manipulate stem cell differentiation all hold great promise in providing meaningful medical solutions that may render many interventions unnecessary or render them more effective.

## CHAPTER ALGORITHM



(With permission from Conte MS, Bradbury AW, et al. Global Vascular Guideline on the Management of Chronic Limb-threatening Ischemia. *J Vasc Surg*. 2019;69(6S):3S–125S.e40.)

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Bradbury AW. BASIL Trial Participants. Bypass versus angioplasty in severe ischemia of the leg (BASIL): multicenter, randomized controlled trial. *Lancet*. 2005;366:1925–1934.

This rare randomized controlled multicenter trial concluded that surgery and angioplasty have similar amputation-free survival at 6 months (thus favoring angioplasty as the best first approach), but surgery has better amputation-free survival after 2 years. This study stressed the complementary nature of the two treatment approaches.

Conte MS, Bradbury AW, et al. Global Vascular Guideline on the Management of Chronic Limb-threatening Ischemia. *J Vasc Surg*. 2019;69(6S):3S–125S. e40.

This guideline, endorsed by the Society for Vascular Surgery, European Society for Vascular Surgery, and the World Federation of Vascular Societies, provides a comprehensive review of the definition, evaluation, and management of CLTI, with the stated goals of improving evidence-based care, and highlighting critical research needs. It describes the independent assessment of patients on three independent axes: Patient risk, Limb severity, ANatomic pattern of disease (PLAN). They also introduce novel approaches to anatomic classification using the Global Limb Anatomic Staging system (GLASS) and reinforced the role of the Wound, Ischemia, foot Infection (WIFI) classification system. They describe key algorithms for patient care.

Conte MS, Pomposelli FB, Clair DG, et al. on behalf of the Society for Vascular Surgery Lower Extremity Guidelines Writing Group. Society for Vascular Surgery practice guidelines for occlusive disease of the lower extremities: Management of asymptomatic disease and claudication. *J Vasc Surg*. 2015;61:2s–41s.

The Society for Vascular Surgery Lower Extremity Guidelines Writing Group reviewed the current evidence supporting clinical care in the management

of asymptomatic peripheral artery disease and intermittent claudication. Although first acknowledging the paucity of level 1 evidence, the group recommended revascularization for claudication “in selected patients with disabling symptoms, after a careful risk–benefit analysis.” They also determined that there was inadequate evidence to support screening for peripheral artery disease in asymptomatic patients.

McDermott MM. Exercise training for intermittent claudication. *J Vasc Surg*. 2017;66(5):1612–1620.

This manuscript summarizes the results of multiple randomized clinical trials of supervised treadmill exercise in PAD patients with claudication. As one of the leading experts in the field, Dr McDermott also provides insight into the mechanisms of how exercise therapy succeeds or fails, shedding light on opportunities for future study.

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.

The Society for Vascular Surgery Lower Extremity Guidelines Committee created a classification scheme for limb threat that reflects the contribution that diabetes mellitus plays in limb threat, as well as the expanded range of current techniques for revascularization in comparison to the previously established systems. This WIFI score was intended “to permit more meaningful analysis of outcomes for various forms of therapy in this challenging, but heterogeneous population.” WIFI assigns a score to grade the severity and extent of the wound, ischemia, and foot infection. The resultant score corresponds to four threatened limb clinical stages that estimate risk of amputation and potential benefit of revascularization.

A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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# Aortoiliac Disease: Direct Reconstruction

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Atherosclerotic disease of the abdominal aorta and iliac arteries is one of the most common therapeutic challenges encountered by vascular surgeons. The British anatomist and surgeon John Hunter first appreciated the implications of aortic bifurcation occlusive disease in the late 1700s. His dissection specimens remain on view at the Hunterian Museum in London and laid the groundwork for Lerche's later appreciation of the disease process that bears his name.<sup>1</sup> Wylie et al. in San Francisco extended dos Santos' technique of endarterectomy to the

aortoiliac (AI) level in 1951, but it would be another 10 years before synthetic grafts were regularly used for aortic bypass grafting.<sup>2,3</sup>

In recent years with the advent of less invasive therapeutic options, traditional aortobifemoral grafting is increasingly being performed for more complex patterns of disease or as a secondary or tertiary procedure in the setting of recurrent disease.<sup>4–6</sup> However, high levels of patient satisfaction and excellent long-term outcomes remain the hallmark

of aortobifemoral surgical revascularization. This chapter reviews the role of direct operative reconstruction in the current surgical management of aortoiliac occlusive disease (AIOD).

## PATHOLOGY AND CLINICAL PRESENTATION

### Pathology

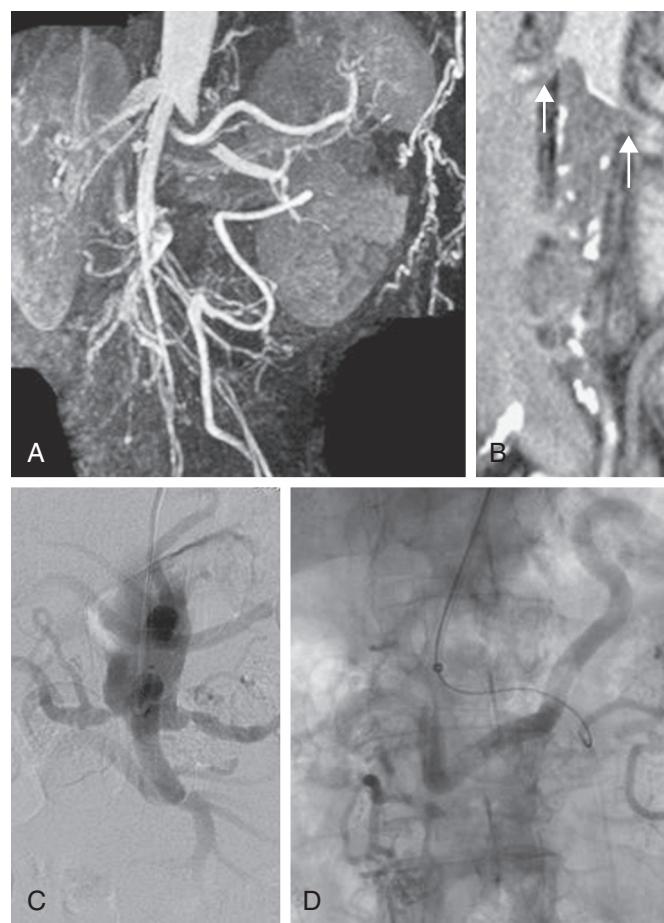
AIOD typically begins at the aortic terminus and common iliac artery origins and slowly progresses proximally and distally.<sup>7</sup> Progression is variable but may ultimately result in total aortic occlusion (Fig. 109.1). When collaterals are adequate, claudication symptoms are often tolerable and can be successfully managed nonoperatively for many years. Approximately one-third of patients operated on for symptomatic AIOD have significant orificial profunda femoris occlusive disease, and more than 40% have significant superficial femoral artery (SFA) disease. Disease can also extend superiorly to the level of the renal arteries (see Fig. 109.1). Although early reports indicated that up to one-third of patients with aortic occlusion went on to develop renal artery thrombosis during a period of 5 to 10 years,<sup>8</sup> later prospective studies failed to confirm this observation.<sup>9</sup> Renal or mesenteric arterial involvement sufficient to warrant concurrent repair is seen in only a minority of patients with AIOD.

### Collateral Circulation

Although focal AI atherosclerotic disease commonly gives rise to claudication of varying degrees, it is rarely associated with chronic limb-threatening ischemia (CLTI). This is largely the result of abundant collateralization around the point of obstruction, which reconstitutes the infrainguinal system with sufficient flow to ensure adequate resting tissue perfusion (Fig. 109.2). The primary compensatory networks develop from the lumbar and hypogastric feeding vessels and connect to circumflex iliac, hypogastric, femoral, and profunda recipients. Additional collaterals that arise in more severe cases include the internal mammary artery-to-inferior epigastric connection and the superior mesenteric artery-to-inferior mesenteric artery and hemorrhoidal artery pathway. The latter connection comprises the arc of Riolan and the meandering mesenteric artery (Fig. 109.3); it is important to recognize the presence of such a large and significant collateral because it should be preserved during surgical reconstruction.

### Epidemiology

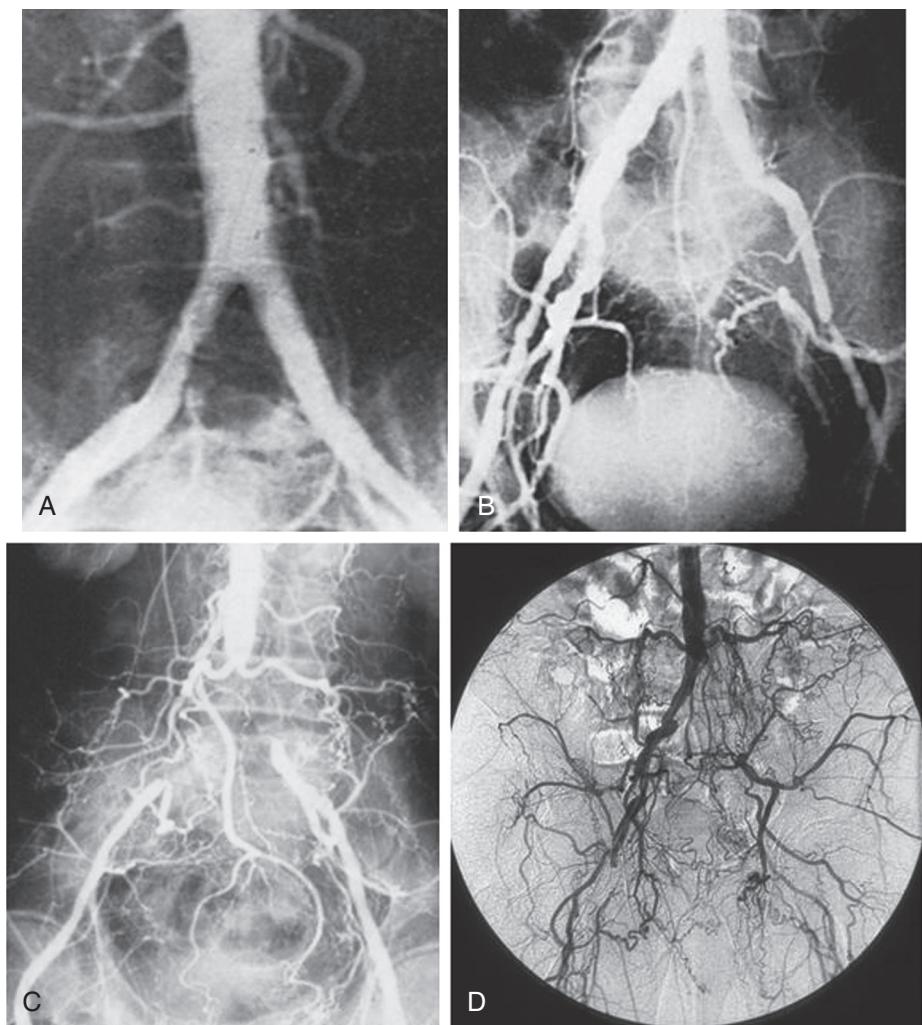
The majority of patients presenting today with AIOD have diffuse disease at multiple levels of the vascular tree; in most cases, AIOD is found in combination with femoropopliteal or infrageniculate occlusive disease. Patients with isolated AIOD are generally younger, have a higher relative prevalence of smoking and hypercholesterolemia,<sup>10</sup> are nearly as likely to be female as male, and typically have a normal life



**Figure 109.1** Two patients with total aortic occlusion extending to the level of the renal arteries. (A and B) Coronal computed tomography images in one patient demonstrate propagation of thrombus into the renal arteries (arrows). (C and D) The second patient also has associated renal artery occlusive disease. Meandering mesenteric arteries are demonstrated in both patients.

expectancy.<sup>11</sup> In contrast, patients with more extensive multilevel disease are commonly older, more frequently have diabetes and hypertension, and are more likely to be male and to have concomitant cerebrovascular, coronary, and visceral atherosclerosis.<sup>10</sup> Not surprisingly, patients with diffuse, multisegmental disease often present with ischemic rest pain or more severe perfusion impairment, leading to tissue loss or gangrene as opposed to isolated claudication.<sup>12</sup> Such patients manifest a significant reduction in life expectancy compared with their age-matched counterparts.<sup>11</sup>

A particularly virulent form of atherosclerotic disease is often found in young women who smoke.<sup>13,14</sup> Radiographic imaging in this subset of patients typically reveals atretic, narrowed vasculature with diffusely calcific atherosclerotic changes. Frequently, a focal stenosis is found posteriorly at or proximal to the aortic bifurcation (Fig. 109.4). This disease distribution and characteristic patient profile have been termed small aortic syndrome or hypoplastic aortic syndrome.<sup>15</sup> Such patients invariably have an extensive smoking history but may lack other typical risk factors for atherosclerosis. The diminutive size of the aorta and iliac vessels has important treatment implications in such patients; the durability of



**Figure 109.2** (A–D) Aortoiliac occlusive disease of increasing severity, with a progressively well-developed pattern of iliolumbar to hypogastric and femoral circumflex collateralization. Male patients with a disease distribution illustrated in B–D may be impotent secondary to compromised hypogastric perfusion.

endovascular intervention or local endarterectomy is generally poor, particularly in the presence of continued cigarette use.

### Presenting Symptoms

Chronic obliterative atherosclerosis of the distal aorta and iliac arteries commonly is manifested as symptomatic arterial insufficiency of the lower extremities, producing a range of symptoms from mild claudication to the spectrum of CLTI. Patients with hemodynamic impairment limited to the AI system may have intermittent claudication of the calf muscles alone or involvement of the thigh, hip, or buttock; patients with CLTI usually have multilevel disease of the AI and infrainguinal arteries. Those presenting with claudication secondary to AIOD are, on average, nearly a decade younger than those with claudication stemming from infrainguinal occlusive disease.<sup>13</sup> Up to 30% of affected men may have difficulty achieving and maintaining an erection owing to inadequate perfusion of the internal pudendal arteries.<sup>16</sup> In men, the well-characterized constellation of symptoms and signs known as **Leriche syndrome**, associated with terminal aortic occlusion, includes claudication (thigh, hip, or buttock), atrophy of the leg muscles, impotence, and

reduced femoral pulses.<sup>17</sup> The equivalent impact of impaired pelvic perfusion in women remains poorly understood but has attracted investigative attention.<sup>18</sup>

## DIAGNOSIS

### History and Physical Examination

The diagnosis of AIOD can usually be made after a careful history and physical examination. In a patient with multiple vascular risk factors, claudication, and absent femoral pulses, the diagnosis of AIOD is straightforward. In other patients, symptoms of claudication can sometimes be difficult to distinguish from those of hip arthritis or nerve root irritation due to lumbar disk disease or spinal stenosis.<sup>19</sup>

The variability of presenting signs and symptoms in patients with AIOD may cause diagnostic confusion. Although proximal claudication is most common, patients with AIOD in isolation or those with combined infrainguinal disease may present exclusively with calf claudication. Although the involved muscle groups may be atrophic from disuse in claudicants, the lower extremities frequently appear well perfused at rest. Femoral and even pedal pulses may be palpable at rest, reflecting the



**Figure 109.3** Large meandering mesenteric artery associated with total superior mesenteric and celiac artery occlusion. Aortobifemoral bypass with an end-to-side proximal anastomosis would best preserve both mesenteric and pelvic perfusion.

presence of robust collateral networks; pulses may diminish or become absent only after exercise. Similarly, a palpable thrill or audible bruit at the lower abdominal or groin level may only become detectable after exertion. Conversely, femoral bruits or diminished femoral pulses arising from CFA or profunda femoris stenoses can mistakenly be attributed to AI inflow disease.

### Noninvasive Hemodynamic Assessment

Noninvasive arterial segmental systolic blood pressure measurements and pulse volume recordings can help confirm a clinical diagnosis of PAD and define the level and degree of obstruction (see Ch. 19, Clinical Evaluation of the Arterial System).<sup>20</sup> A resting difference of 20 mm Hg systolic or greater between the brachial and the proximal thigh pressures reflects a significant stenosis in the aorta or iliac arteries, but it may be confounded by proximal SFA occlusion. It is also important to recognize that upper thigh pressure is normally higher than brachial pressure, and that collaterals may offset a pressure gradient at rest but not during exertion. Thus, the absence of a resting pressure gradient meeting this threshold does not necessarily rule out the presence of symptomatic stenoses. A further reduction in pressure between the thigh and ankle level suggests concomitant femoropopliteal or tibial outflow disease. In patients with disabling symptoms with normal or near-normal resting ankle-brachial indices, repeating measurements after provocative graded exercise treadmill testing can be particularly useful if there is still clinical suspicion of AIOD. A careful history and physical examination combined with noninvasive hemodynamic studies usually provide sufficient data



**Figure 109.4** Short-segment stenoses localized to the distal aorta are particularly common in young female smokers and are amenable to endarterectomy.

to establish the diagnosis. Further imaging is warranted only after risk/benefit assessment and the clinical decision to intervene has been reached.

Diagnostic imaging modalities that also facilitate revascularization planning include duplex ultrasound and axial imaging in the form of computerized tomographic angiography (CTA), magnetic resonance angiography (MRA), and arteriography; this topic is discussed in Chapter 108 (Lower Extremity Arterial Disease: Decision Making and Medical Treatment).

## INDICATIONS FOR SURGICAL INTERVENTION

### Impact of Endovascular Treatment

A significant paradigm shift has occurred in the treatment of PAD.<sup>19,21</sup> Angioplasty and stenting have become first-line therapy for most patients with AI, renal, subclavian, and coronary occlusive disease.<sup>22</sup> Whereas percutaneous treatment of the aorta and iliac arteries was previously limited to short-segment, TransAtlantic Inter-Society Consensus (TASC) type A or B iliac lesions, it is now routinely applied to even long-segment (TASC type D) occlusions extending the length of the iliac arteries. In no other vascular territory has the shift from open surgery to interventional treatment been more apparent than in the AI segment. Using the Nationwide Inpatient Sample, one report documented an 850% increase in the use of percutaneous transluminal angioplasty and stenting for AIOD from 1996 to 2000, along with a simultaneous decrease of 16% in the rate of aortobifemoral grafting.<sup>22</sup> Further reflecting this

transformation in management strategy, in anatomically favorable circumstances, concomitant renal or mesenteric artery stenosis might be treated percutaneously as a staged initial procedure, even when subsequent open surgical AI reconstruction is planned.<sup>23</sup> Decision making for surgical versus endovascular treatment is discussed in detail in Chapter 108 (Lower Extremity Arterial Disease: Decision Making and Medical Treatment).

In the current era, in which direct reconstruction for AIOD has been relegated to a second- or even third-line therapy, open bypass is increasingly undertaken in patients in whom endovascular treatment has failed or in those with such extensive disease that an endovascular approach is deemed inadvisable. This paradigm shift has been reflected in reports documenting the increasing complexity of aortobifemoral grafting, with a higher incidence of suprarenal clamping, adjunctive visceral revascularization, simultaneous operative inflow and outflow disease, and repeated grafting.<sup>4,5,24</sup> Patients with a combination of more proximal aneurysmal disease and common or external iliac occlusive disease continue to be good candidates for open reconstruction, although this group will continue to diminish with ongoing technologic advancements. Even patients with extensive calcification at the aortic bifurcation thought to be at risk for rupture with balloon angioplasty or those with disease extending to the CFA are no longer considered unsuitable for an endovascular approach. The incidence of rupture has proved low in the former group, and the introduction of low-profile covered stents and techniques of primary stenting is likely to further increase the safety of endovascular treatment in this setting. The latter patient subgroup can be managed with a hybrid approach, whereby the CFA plaque is treated with a traditional endarterectomy and patch repair and the iliac component is concurrently addressed with endovascular techniques.<sup>25,26</sup>

Patients with early recurrence of AIOD after angioplasty or stenting represent a growing group for whom open surgical repair may be indicated. Patients with significant renal failure in whom endovascular therapy entails a prohibitive risk of triggering dialysis dependence may also be considered better suited for operative repair. Complications of endovascular treatment, including dissection and vessel rupture, are infrequent indications for surgical reconstruction.

## Claudication

The traditional indications for surgical reconstruction for symptomatic AIOD are disabling claudication, ischemic rest pain, and tissue loss. Claudication is a relative indication for intervention, given the natural history of the disease. Multiple reports, among them the Framingham Heart Study, indicate that patients with claudication have increased rates of cardiovascular mortality but an overall low risk of associated limb loss.<sup>7,27</sup> The majority of claudicants demonstrate a stable pattern of disease throughout their lifetimes or have an improvement in symptoms as a result of risk factor modification, whereas 20% to 30% require operation within 5 years as a result of disease progression. The annual rates of mortality and limb loss in patients with claudication have historically been reported as 5% and 1%, respectively.<sup>28</sup> Some

have suggested that claudicants with AIOD are more likely to progress to CLTI.<sup>29</sup> In any case, the degree of disability that a particular level of claudication represents remains a subjective assessment by both the patient and the surgeon. As the associated risks of AI balloon angioplasty and stenting have fallen and the relative success rates have risen in recent years, the threshold for offering endovascular treatment to claudicants at all points along the clinical spectrum has significantly decreased. Indeed, patients once considered appropriate only for risk factor modification, exercise therapy, and medical treatment are now increasingly being offered percutaneous revascularization as a primary treatment option.<sup>30</sup> Balloon technology is also increasingly being applied to hypogastric arterial disease, primarily for buttock or hip claudication, to a degree not previously seen and not paralleled by an increase in surgical revascularization.<sup>31</sup>

The indications for surgical reconstruction for claudication have not shifted appreciably during this same period. Given its relatively benign natural history, maximal medical therapy continues to be appropriate for many patients with claudication. In contrast to patients with CLTI, it has been argued that an overly aggressive approach might place patients without limb-threatening conditions at unnecessary risk for adverse outcomes. The majority of claudicants remain stable for years, allowing time for collateral pathways to develop; this often results in sufficient improvement, making intervention unnecessary.<sup>32</sup> On the other hand, in patients of low surgical risk with disabling symptoms from disease limited to the aortobifemoral segment, surgical bypass is an appropriate option. With current levels of perioperative morbidity and mortality, bypass can be undertaken safely and with the expectation of excellent long-term patency.

## Chronic Limb-Threatening Ischemia

Although broad in spectrum, CLTI is associated with a more significant risk of amputation without revascularization. As such, the presence of ischemic rest pain, frank ulceration, or digital gangrene are well-accepted indications for surgical correction of AIOD. Patients with pregangrenous skin changes or frank gangrene typically have hemodynamically significant infrainguinal as well as AIOD.<sup>12</sup> Thus, whereas patients treated for claudication or rest pain usually require only a single-stage inflow operation, simultaneous or staged inflow and outflow revascularization should be considered in patients with tissue loss where the goal remains the re-establishment of inline, pulsatile flow to the distal extremity to ensure healing (see Multilevel Occlusive Disease, below).<sup>33</sup>

Patients with an aortic or iliac source of distal emboli, typically from an ulcerated atheromatous plaque or so-called "shaggy aorta," represent another group in which operative reconstruction is usually indicated.<sup>34</sup> Such patients may lack symptoms of claudication, and the culprit lesion(s) may not be hemodynamically significant. In these cases, the goal of intervention is to prevent recurrent distal embolization.

Studies have documented the generally excellent outcomes of aortobifemoral grafting in elderly patients, suggesting that in older patients who are otherwise good surgical risks, surgical

therapy should not be withheld.<sup>35</sup> Conversely, lower long-term patency rates with aortic bypass in younger patients (particularly those less than 50 years of age) or those with small aortic diameters suggest caution for considering early surgical intervention in such patients.<sup>5,35</sup>

## SURGICAL TREATMENT

Historically the surgical options for AIOD included AI endarterectomy, aortobiliac bypass, ABFB, and extra-anatomic bypass (iliofemoral, femorofemoral, or axillofemoral; see Ch. 110, Aortoiliac Disease: Open Extra-Anatomic Bypass). Given superior long-term patency, aortobifemoral grafting is currently considered the open revascularization procedure of choice unless the patient is a poor surgical candidate.

### Aortoiliac Endarterectomy

The first successful endarterectomy of an atherosclerotic CFA lesion by dos Santos was serendipitous, in that he had not originally intended to remove any intima or media. His success, after multiple failed attempts, was attributed to the novel use of heparin.<sup>2</sup> Wylie et al.<sup>3</sup> soon extended this technique to the AI level, and during the 1950s and 1960s, endarterectomy was the standard therapy for severe AIOD. Enthusiasm for the procedure dimmed, however, with the introduction of prosthetic graft material 10 years later, and AI endarterectomy was largely replaced by bypass grafting.

### Patient Selection

Since endarterectomy eliminates the need for a prosthetic graft, it is an appealing alternative in the setting of infection and removes the possibility of myriad late graft-related complications. Advocates have likewise pointed to the advantages of endarterectomy in younger patients or those with small vessels who are less than ideal candidates for endovascular therapy or aortobifemoral grafting.<sup>36</sup> Patients with erectile dysfunction attributable to proximal hypogastric occlusive disease are also well suited to this approach. Such patients can be expected to have a greater degree of improved pelvic perfusion after thorough endarterectomy of their AI and hypogastric segments compared with those undergoing ABFB grafting, and high rates of restored sexual function have been reported.<sup>36,37</sup>

Endarterectomy is most feasible and durable when it is applied to focal stenotic lesions in large-caliber, high-flow vessels. Indeed, the technique has proved particularly efficacious in patients with localized disease limited to the distal aorta or proximal common iliac arteries (Figs. 109.4 and 109.5), and excellent long-term patency rates, on a par with aortic bypass grafting, have been reported.<sup>36,38–40</sup> In distinction, results in cases of long-segment disease involving the entire infrarenal aorta and extending into the external iliac arteries have been disappointing.<sup>41</sup> The rise of endovascular therapy is further eroding the already small proportion of patients considered suitable for endarterectomy. As a result, the number of vascular surgeons who are comfortable and facile with this technique is limited.



**Figure 109.5** Anteroposterior (A) and left anterior oblique (B) angiographic images of bulky calcific atherosclerotic disease limited to distal aorta and proximal common iliac arteries, amenable to aortoiliac endarterectomy. Note the hypertrophic inferior mesenteric artery and iliolumbar collateral vessels. (C) Completion angiogram after distal aortic and bilateral common iliac artery endarterectomy and Dacron patch angioplasty. (D) Continued durability of result 3 years postoperatively.

## Technique

Endarterectomy is a **direct disobliterative, debulking technique** that takes advantage of the pathologic localization of atherosclerosis to the intima and media. Typically, a **cleavage plane** is easily developed **between the plaque and the outer layers of the vessel wall**, with the exact plane dependent on the size, location, and muscle content of the involved artery. Haimovici<sup>42</sup> has characterized the **three cleavage planes** encountered in the operative setting as **subintimal, transmedial, and subadventitial**. In his view, the last two planes are preferable because the **subintimal plane predisposes to subsequent thrombosis**. The **residual outer layer** is generally of sufficient mechanical strength to hold surgical sutures and to resist disruption or progressive **enlargement** when subjected to arterial pressure. **Rarely** the **residual adventitia** may be so attenuated that reconstruction of the wall with a **patch** or, in extreme cases, an **interposition graft** proves necessary. In practice, this most often occurs when the **plaque is extensively calcified**.

The various techniques all involve **blunt separation of the plaque, termination by spontaneous tapering or sharp division, and careful attention to the endpoints** (Figs. 109.5 and 109.6). Tacking sutures should be used when necessary, particularly to secure the **distal endpoint**, which must be firmly adherent to resist dissection or flap elevation leading to thrombosis. The simplest technical approach is the so-called **open method**, which employs a **longitudinal arteriotomy** that allows direct visualization of both endpoints as well as the entire endarterectomized surface; this technique is most commonly used for disease limited to the aorta and common iliac arteries. If primary closure is

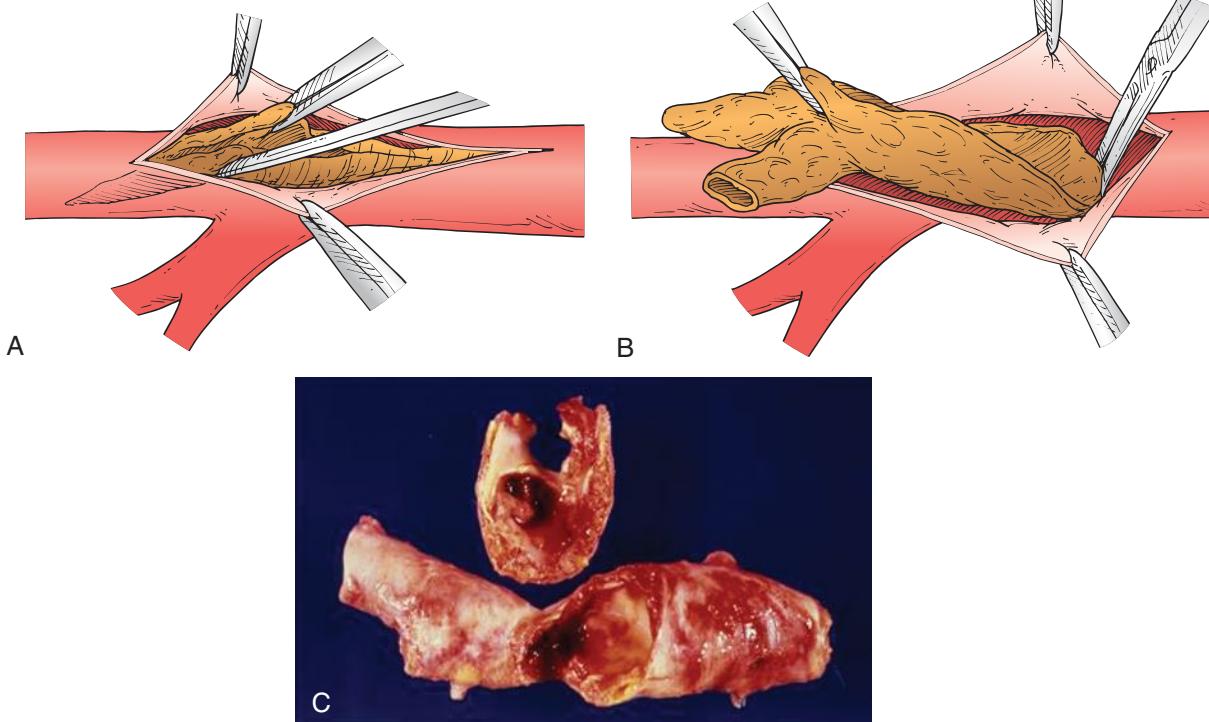
problematic due to small vessel caliber, **patch angioplasty** with vein, synthetic, or bovine pericardial material should be undertaken. Extraction, eversion, and semiclosed methods are variations that can be helpful in specific anatomic situations.

## Aortobifemoral Bypass

Adequate intravenous access, intra-arterial pressure monitoring, Foley catheter placement, and preoperative antibiotics to minimize the risk of infection are routine aspects of aortic replacement surgery. Although the use of **intraoperative blood salvage** is advantageous in patients with relative anemia, its **cost-effectiveness** has not been firmly established in routine cases.<sup>43</sup> Attention should be paid to maintaining normothermia throughout the procedure to reduce the significant organ dysfunction and operative mortality associated with intraoperative hypothermia.<sup>44</sup> This is typically achieved with the use of forced-air body warming devices. ABFB grafting is performed under general endotracheal anesthesia. An **epidural catheter** is usually placed for postoperative pain control, although other analgesic adjuncts have been used successfully for other abdominal procedures and are under investigation ([ClinicalTrials.gov](#) identifier: NCT03657979).

## Exposure

The initial vascular exposure and proximal and distal vessel control are attained before the institution of systemic anticoagulation in an effort to minimize blood loss. The **femoral vessels** are typically exposed first through bilateral longitudinal or



**Figure 109.6** (A) The technique of endarterectomy involves the initial separation of plaque in the appropriate cleavage plane, with mobilization facilitated by a fine spatula. (B) Ideally, the endarterectomy is terminated by feathering to a tapered endpoint. (C) Photograph of an operative specimen removed by endarterectomy.

oblique incisions to reduce the time during which the abdomen is open, the viscera exposed, and insensible losses thereof. The extent of exposure is dictated by disease severity and the level of reconstruction planned at the CFA and its bifurcation. In general, the distal extent of the dissection involves circumferential control of the proximal SFA and profunda femoris arteries; the inferior epigastric and circumflex iliac branches at the anatomic transition from the external iliac to the CFA mark the proximal extent of the dissection. In addition to collaterals which may have developed in the setting of occlusive disease, a circumflex femoral arterial branch frequently arises from the posterior aspect of the distal CFA and must be controlled to avoid troublesome back-bleeding. The inferior aspects of the retroperitoneal tunnels through which the graft limbs will course to reach the femoral region are begun with blunt digital dissection posterior to the inguinal ligament, which can be partially divided posteriorly to prevent graft limb compression. The tunnels should track directly along the anterior aspect of the external iliac artery, with care taken to elevate all soft tissues to ensure that the ureters remain anterior. A crossing vein normally present beneath the inguinal ligament must be ligated or carefully avoided to prevent bleeding during the tunneling process.

Infrarenal aortic exposure is often performed through a transperitoneal approach by a longitudinal midline laparotomy, although some prefer a transverse incision. This incision typically extends from below the xiphoid process to just inferior to the umbilicus; as such, it is shorter than the incision normally employed for abdominal aortic aneurysm repair. The transverse colon is retracted cephalad, and the small bowel is shifted to the patient's right side. The ligament of Treitz is then taken down, and the duodenum is mobilized to the right, allowing access to the infrarenal aorta. The retroperitoneal tissue overlying the aorta is dissected superiorly to the level of the left renal vein, and the larger lymphatic vessels encountered within the retroperitoneal lymphatic network are ligated. If renal artery reconstruction is not planned, the dissection can often be limited to the region between the renal arteries and the inferior mesenteric artery. Extensive dissection anterior to the aortic bifurcation and proximal left iliac artery should be avoided because the autonomic nerve plexus regulating erection and ejaculation in men sweeps over the aorta in this region. If exposure in the area of the plexus proves necessary, dissecting along the right lateral aspect of the infrarenal aorta and reflecting rather than transecting the tissue overlying the terminal aorta and proximal iliac arteries can minimize the risk of iatrogenic neurogenic sexual dysfunction.

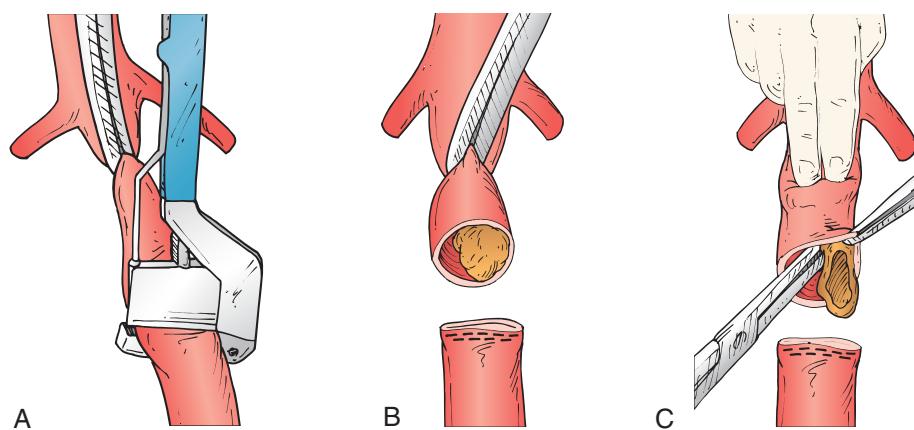
Should thrombus or significant aortic calcification extend to the level of the renal arteries, it may be necessary to continue the proximal aortic dissection to the suprarenal level to allow safe proximal clamp placement. Alternatively, proximal control may be obtained by intraluminal balloon deployment or supraceliac clamping via the gastrohepatic ligament. In all cases, it is important to extend the reconstruction close to the level of the renal arteries to minimize the risk of failure secondary to disease progression in the remnant infrarenal aortic neck. If end-to-side repair is planned, exposure and control of all relevant

lumbar or accessory renal arteries before the aortotomy is performed helps avoid back-bleeding, which can be challenging to control with cross-clamps in place and the aorta compressed. The superior aspects of the graft limb tunnels are completed with further digital manipulation from above and below, again with care taken to maintain a course anterior to the iliac vessels but posterior to the ureters. The left limb tunnel passes beneath the sigmoid mesentery and slightly more laterally to avoid disruption of the autonomic nerve plexus. Moist umbilical tapes or Penrose drains may be passed with a smooth aortic clamp to mark the tunnels. After vessel exposure and tunnel creation, but before vascular occlusion, a standard intravenous bolus of heparin sodium anticoagulation is given. Additional doses may be necessary, depending on the length of the operation and the requirement for additional periods of flow occlusion, and may be guided by the measurement of the activated clotting time. For peripheral vascular operations, the initial dose typically ranges between 70 and 100 units/kg, and an activated clotting time in the 250- to 350-second range is adequate.

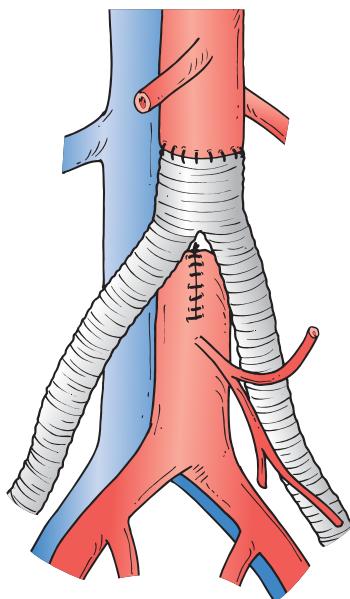
### Clamp Placement

With non-contrast-enhanced CTA guidance, when available, to delineate sites of heavy calcification, the aorta is carefully palpated to identify the optimal sites for application of the cross-clamps. In the event of asymmetrical plaque, the technique of clamping soft plaque against hard plaque minimizes the risk of emboli. It also lessens the risk of a traumatic clamp injury, which can be a formidable technical problem in a heavily calcified aorta. Anterior to posterior clamping may be necessary in the presence of a soft anterior but calcified posterior aortic wall. Appropriate atraumatic vascular clamps are selected, and after sufficient time is allowed for the heparin to circulate, the aorta is clamped first proximally or distally at the site of least disease to avoid dislodgement and potential distal embolization of plaque. The distal clamp is usually placed above or below the inferior mesenteric artery. The proximal clamp is placed just below the renal arteries if the disease pattern does not obligate suprarenal clamping, with as little dissection of the renal artery origins as possible.

If an end-to-end anastomosis is planned, the aorta is transected several centimeters below the proximal clamp, and the distal aorta is oversewn in two layers with running monofilament suture or stapled with a surgical stapler (Fig. 109.7A). A short segment of the distal aortic cuff is often excised to improve exposure of the aortic neck and aid precise proximal reconstruction. This maneuver also allows the graft to lie more flatly against the vertebral column rather than in an anterior orientation, and facilitates retroperitoneal coverage (Fig. 109.8). If necessary, it is important to carry out a complete thromboendarterectomy of the infrarenal neck (see Fig. 109.7B). Removal of all thrombotic debris and calcified plaque facilitates both suture placement and creation of a widely patent proximal anastomosis. Brief repositioning of the proximal clamp to the suprarenal position or the application of digital pressure sufficient to temporarily occlude the suprarenal aorta may be helpful to ensure the thorough removal of all intraluminal debris (see Fig. 109.7C). Mobilization and cephalad or



**Figure 109.7** (A) The end-to-end proximal anastomosis for aortofemoral reconstruction can be initiated with the infrarenal aorta cross-clamp placed in an anteroposterior direction, as close to the origin of the renal arteries as possible. The aorta is then stapled or occluded with a second clamp just proximal to the origin of the inferior mesenteric artery. (B) After excision of a short segment of aortic cuff, a complete thromboendarterectomy of the remaining proximal cuff is carried out. (C) Brief digital or clamp control of the juxtarenal aorta may prove necessary to complete the thromboendarterectomy.



**Figure 109.8** The end-to-end proximal anastomotic configuration for aortofemoral reconstruction allows the graft to lie flat against the vertebral column and results in less turbulent flow.

caudad retraction of the left renal vein can facilitate adequate exposure of the juxtarenal aorta. Division of the left renal vein is usually unnecessary but acceptable if additional exposure is required, provided the adrenal, lumbar, and gonadal collateral branches are preserved. If suprarenal clamping is undertaken, preemptive clamping of the renal arteries is advisable to prevent the potentially adverse effects of inadvertent emboli.

A minority of patients present with an aortic occlusion extending to the level of the renal arteries. These patients are best managed by controlling the renal arteries and then thrombectomizing the infrarenal cuff, without placement of an infrarenal proximal aortic clamp, which could displace thrombotic material proximally. The aortic plug encountered at this location is often soft, propagated, secondary thrombus that can be

easily removed. After aortic pressure is used to flush out the remaining plug, suprarenal control is briefly used. Remnant debris is cleared from the infrarenal cuff, the aorta is flushed again, the renal arteries are back-bled, and then an infrarenal clamp is placed.

### Graft Selection

A bifurcated graft appropriately sized to match the aorta and femoral vessels is selected. Although some surgeons prefer polytetrafluoroethylene grafts, knitted polyester (Dacron) grafts are more commonly used. Current low-porosity knitted versions have excellent handling and hemostatic properties and a proven track record of durability (see Ch. 66, Prosthetic Grafts). They also develop a more stable pseudointima than earlier woven grafts, although their tendency to dilate over time has been documented.<sup>45</sup> Greater appreciation of the importance of sizing the graft to the runoff vessels followed an early experience with limb thrombosis believed to be secondary to sluggish flow from oversizing.<sup>46,47</sup> Bifurcated grafts measuring 18 by 9 mm or 16 by 8 mm are typically chosen for male patients; grafts measuring 14 by 7 mm or even 12 by 6 mm are usually suitable for female patients.

### Anastomoses

One technical consideration related to ABFB grafting that has prompted considerable debate involves the type of proximal anastomosis. The published literature has established that both end-to-end and end-to-side techniques are acceptable and effective. Despite strong preferences expressed by various surgeons, neither approach has demonstrated overall superiority, but each may be preferred in certain circumstances.

#### End-to-end

Those favoring an end-to-end configuration claim that it facilitates a more comprehensive thromboendarterectomy of the proximal stump and allows a better in-line flow pattern, with less turbulence and more favorable hemodynamic characteristics

(see Fig. 109.8).<sup>48</sup> Lower rates of proximal suture line pseudoaneurysm and better long-term patency rates reported in some series lend support to this view.<sup>49</sup> Stapling or oversewing of the distal aorta with the end-to-end technique also has the benefit of reducing the risk of clamp-induced emboli to the lower extremities after release of the distal clamp compared with the end-to-side option. Further, those in favor of this approach assert that because the graft lies flatter in the retroperitoneum, this enhances the ability to close the retroperitoneum over the graft, resulting in a lower rate of late graft infection and aortoenteric fistulae; there is, however, little direct evidence to support this claim. The creation of an end-to-side anastomosis can be technically challenging in a heavily diseased aorta, particularly if it is partially occluded by a side-biting clamp (favored by some surgeons). In the setting of concomitant aneurysmal disease or complete aortic occlusion extending up to the level of the renal arteries, an end-to-end approach is recommended.

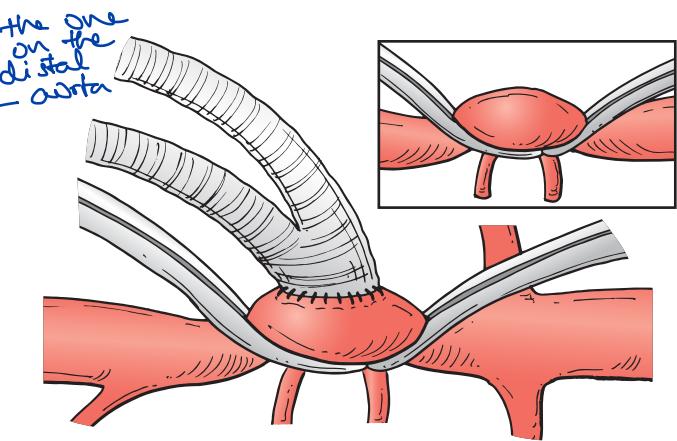
### End-to-side

There are certain circumstances in which an end-to-side proximal anastomosis is advantageous. The most common indication is in patients with occluded or severely diseased external iliac arteries but patent common and internal iliac arteries, in whom the interruption of forward aortic flow may result in the loss of critical pelvic perfusion. Without the retrograde flow through the external iliac arteries normally present in an end-to-end configuration, pelvic ischemia, ranging from mild hip claudication to severe buttock rest pain or ulceration, may result.<sup>50,51</sup> Additional ischemic complications, such as erectile dysfunction in men and rarely seen paraplegia secondary to cauda equina syndrome,<sup>52</sup> can potentially be avoided with an end-to-side approach. Preservation of either a large inferior mesenteric artery, sometimes necessary to avert colonic or mesenteric ischemia, or an important accessory renal artery arising from the distal aorta or an iliac artery can more easily be accomplished with an end-to-side technique. Alternatively, these vessels can be reimplanted onto the side of an end-to-end graft.

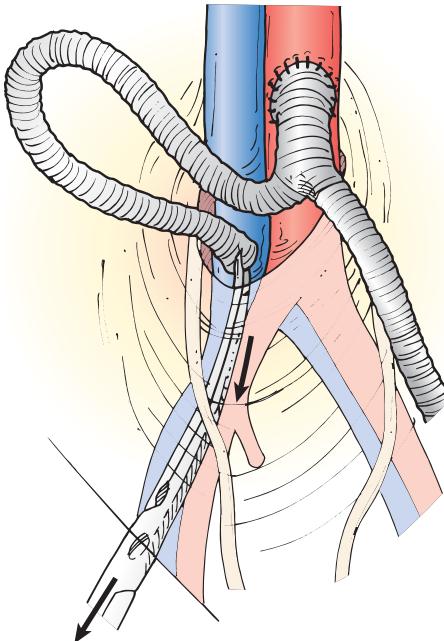
### Technique

For end-to-end proximal anastomoses, the main body of the graft is shortened to minimize graft redundancy and to allow the graft limbs to straddle rather than to override the transected aortic stump (see Fig. 109.8). The anastomosis is performed with running 3-0 polypropylene suture. If an end-to-side anastomosis is to be performed, a beveled anastomosis is fashioned after an approximately 3-cm longitudinal aortotomy is created as close to the renal arteries as practical (Fig. 109.9). Care is taken to remove all loose debris and mural thrombus from the excluded portion of the aorta, and a particular effort is made to ensure adequate backflushing of clot and debris before re-establishment of forward flow in the native aorta and graft. Side-biting clamps are best avoided in performing an end-to-side anastomosis because they compress the aortic sidewalls, rendering both adequate thromboendarterectomy and accurate suture placement more difficult (see Fig. 109.9).

After completion of the abdominal portion of the procedure, the graft limbs are clamped with soft-jaw insert clamps



**Figure 109.9** An end-to-side proximal anastomosis for aortofemoral grafting is required to preserve antegrade pelvic perfusion in situations in which retrograde flow would be compromised by heavily diseased or occluded external iliac arteries.



**Figure 109.10** Aortobifemoral graft limbs are carefully tunneled beneath the ureters to avoid kinking.

and flushed with heparinized saline. They are then passed through the retroperitoneal tunnels, with care taken to prevent twisting and to eliminate excess redundancy (Fig. 109.10), and attention is turned to the distal anastomoses. Proximal femoral control is typically obtained with either a soft-jaw clamp or a Satinsky clamp placed from a lateral direction, and distal control is usually achieved with vessel loops or atraumatic bulldog or profunda clamps. For those patients with normal femoral and distal runoff, a longitudinal arteriotomy limited to the distal CFA is sufficient. More commonly, extension of the arteriotomy across the profunda femoris artery origin and profundaplasty will prove necessary (see Adjunctive Profundaplasty, below). The distal anastomoses are completed in a beveled end-to-side fashion with 5-0 polypropylene, again carrying out retrograde and antegrade flushing maneuvers

before the anastomoses are completed and flow is restored. It is important to alert the anesthetic team before clamp release, given the expected blood pressure drop with limb reperfusion.

### Closure

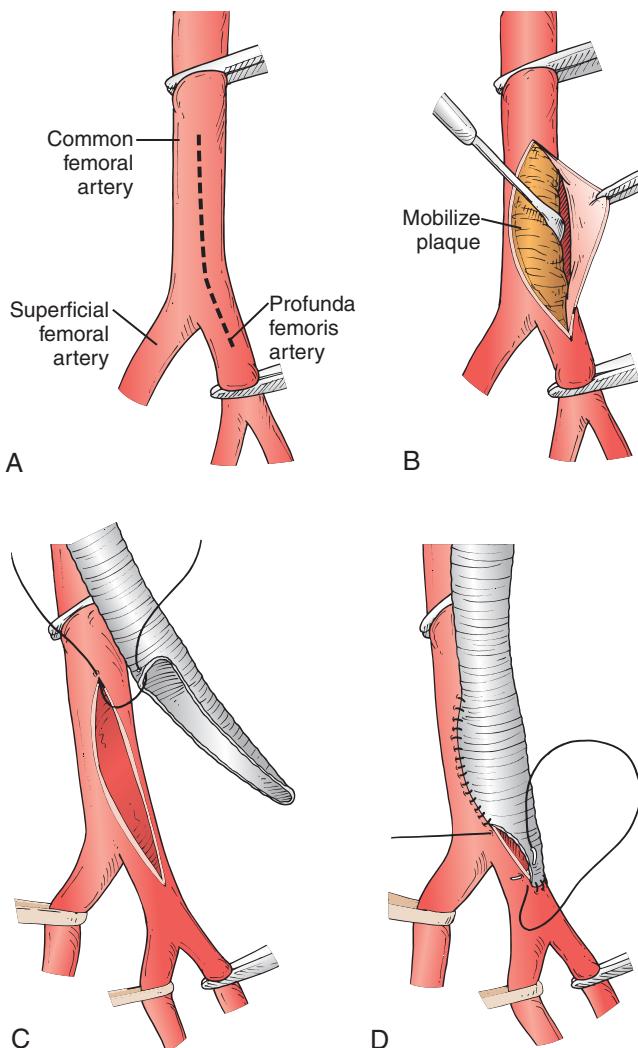
Before wound closure, the surgeon must confirm adequate distal perfusion and absence of distal embolization. The quality of the pulses and Doppler signals just beyond the distal anastomosis and at the pedal level is assessed, as are the color, temperature, and general appearance of the feet. If the revascularization is deemed satisfactory and no further distal reconstruction is to be undertaken, the effects of heparin can be reversed by administering protamine sulfate (1 mg/100 units of circulating heparin) at the surgeon's discretion to help attain hemostasis. Once hemostasis is sufficient, the abdomen is irrigated and the retroperitoneum is closed over the proximal anastomosis and graft behind the duodenum to the extent possible. If adequate retroperitoneal coverage is not possible, particularly with an end-to-side proximal anastomosis, a sleeve of omentum should be fashioned to cover any exposed segment of the anastomosis and to separate the graft from the adjacent bowel. It is important to tack down this omental apron to prevent small bowel herniation. The groin wounds are copiously irrigated and the deeper tissue is closed in several layers with absorbable polyglactin sutures.

### Adjunctive Profundaplasty

The important role of profundaplasty in preserving the long-term patency of anatomic or extra-anatomic grafts in patients with AIOD has been widely established.<sup>11,41,53–56</sup> In patients with normal proximal SFAs and profunda femoris arteries, the distal anastomosis of an aortobifemoral graft can be performed to the CFA. However, most patients with AI disease severe enough to warrant aortofemoral bypass in the endovascular era have both profunda and SFA disease that limits outflow and increases the likelihood of graft thrombosis. In patients with severe AI, SFA, and profunda disease causing CLTI, a concomitant profundaplasty may be sufficient to sustain the patency of the inflow graft and to salvage the limb, particularly if there is good profunda collateral circulation to a patent popliteal artery. Some authors have even recommended that the aortofemoral bypass graft limb should be extended to the profunda in every case of SFA occlusion, even in the absence of orificial profunda disease, arguing that a "functional" obstruction on the order of 50% stenosis is present in these patients.<sup>57</sup> Although this position has not been universally adopted, it is now common practice to extend the hood of the distal anastomosis over the origin of the profunda femoris artery to enhance the graft outflow, particularly if the SFA is occluded or severely diseased. In the presence of significant CFA or profunda femoris origin plaque, an endarterectomy or profundaplasty is almost always indicated (Fig. 109.11).

### Technique

The profunda is usually exposed by distal extension of the dissection used to access the CFA, although a lateral approach through a fresh tissue plane with medial retraction of the



**Figure 109.11 (A–D)** In the setting of superficial femoral artery and orificial profunda femoris artery disease, extending the common femoral arteriotomy to the origin of the profunda and performing a profundaplasty before completion of the distal anastomosis of the aortobifemoral bypass can improve outflow and maximize graft patency.

sartorius can be used to avoid a scarred or infected groin. Every effort should be made to spare all collateral branches arising from the CFA and profunda femoris artery because they may prove vital to preservation of lower extremity perfusion in the event of later graft thrombosis.

Once exposed, the CFA and profunda femoris should be palpated to gauge the degree of atherosclerotic plaque present, particularly given the well-known tendency of angiography to underestimate the extent of disease. Profunda arterial plaque not uncommonly ends at the first or second major branch point. The profunda orifice can be visually inspected after the CFA is incised, and its lumen can be further assessed by noting the quality of back-bleeding and by gentle interrogation with a series of sizing metal probes. The dissection is continued along the anterior aspect of the artery as necessary; the extent is guided by the location of a suitable endpoint as identified by palpation, inspection, and reference to the preoperative angiogram. The lateral femoral circumflex vein coursing deep to the

SFA and crossing anteriorly over the proximal profunda must be ligated in most cases. Isolated orificial plaque can sometimes be entirely removed by an eversion technique through the CFA. If it becomes necessary to extend the arteriotomy to the profunda, care should be taken to avoid incising the crotch of the superficial and deep femoral arteries. The endarterectomy is performed as described earlier. In the event that an extensive endarterectomy proves necessary, it may be preferable to close the endarterectomy site with a vein or bovine pericardial patch, onto which the distal anastomosis can then be attached, rather than to create a long profunda patch with the graft limb.<sup>53</sup> If an outflow bypass is to be performed, this can be taken off either the distal patch or the graft limb if a prosthetic conduit is utilized, or the native profunda artery just distal to the aortobifemoral graft if a autogenous conduit is selected.

## Other Operative Considerations

### External Iliac Anastomosis

Early in the operative experience for AI occlusive disease, the tendency was to place the distal anastomosis of aortic bypass grafts at the iliac level. With time came a growing appreciation of the benefits of extending the distal anastomosis to the femoral level; creation of the distal anastomosis is technically easier at the groin level, and long-term patency rates for aortobifemoral grafts are notably improved compared with AI grafts.<sup>58</sup>

In addition, with meticulous surgical technique and improvements in graft materials, the feared increase in graft infection caused by moving the distal dissection to the femoral level has not proved to be a significant problem in the majority of patients.<sup>59</sup> There are certain circumstances, however, in which performing an aortobiiliac bypass remains advantageous. Patients with hostile groin creases from prior surgery or radiation therapy, for example, are likely to be better served by this option, as are obese, diabetic patients with an intertriginous rash at the inguinal crease and patent external iliac arteries.

### Multilevel Occlusive Disease

The optimal management of patients with multilevel occlusive disease is often difficult to determine. The question frequently arises whether or under what circumstances concomitant versus staged outflow procedures should be performed in association with an inflow operation. The impact of synchronous SFA disease on the results of AI revascularization remains undefined in the current literature; some reports have indicated similar patency rates between patients with and without SFA occlusion,<sup>24</sup> whereas others have reported lower long-term patency rates in this setting.<sup>60,61</sup> If an atretic or prohibitively diseased profunda is present in addition to a severely diseased SFA, infringuinal bypass grafting is likely to be necessary to ensure sufficient outflow for graft patency and perfusion of the foot. An investigation that specifically addressed the impact of diabetes concluded that diabetic patients with multilevel occlusive disease were no more likely to require subsequent infringuinal revascularization after an inflow reconstruction than were nondiabetics.<sup>62</sup> Further, although up to 80% of patients with claudication and both

inflow and outflow disease manifest symptomatic improvement after aortofemoral bypass grafting alone,<sup>12,63</sup> some studies indicate that as many as two-thirds have some degree of persistent claudication.<sup>64</sup>

No single criterion mandates a combined procedure; however, the severity of distal ischemia is probably the most important factor to be considered. If significant tissue loss is present, concurrent inflow and outflow procedures are probably warranted if limb salvage is to be achieved.

### Associated Renal or Mesenteric Artery Occlusive Disease

#### Renal

Whether to address coexisting renal or mesenteric disease at the time of aortic reconstruction is a challenging decision that warrants careful consideration of multiple individual factors, the obligatory increase in operative time and complexity, and the greater operative mortality and morbidity. In the setting of multidrug-refractory hypertension or ischemic nephropathy believed to have a potentially reversible functional component on the basis of a thorough diagnostic assessment, simultaneous repair of significant renal occlusive disease may be indicated.

Combined repair is also appropriate when accessory renal arteries arise from the diseased aortic segment. Simultaneous revascularization is more controversial when the functional significance of the renal artery stenosis is uncertain or is thought to be clinically silent.

Advocates of an aggressive treatment approach cite the clinical deterioration seen with the progression of untreated renal artery occlusive disease and the increasing safety of combined aortic and renal reconstruction. Those who favor a more conservative position believe that the increased surgical risk does not offset the potential clinical gain. Perioperative mortality rates for patients undergoing simultaneous aortic and renal repair have consistently been in the 5% to 6% range,<sup>65-67</sup> in comparison to rates of 1.7% and 0.7% for those undergoing renal or aortic reconstruction alone, respectively.<sup>65</sup> A favorable response to hypertension has been reported in 60% to 70% of patients undergoing combined revascularization, and improvement in renal excretory function has been reported in up to 33% of patients.<sup>65,66</sup> The most common reconstruction approach is aortorenal bypass from the aortic graft, with the use of either saphenous vein or prosthetic graft. In select cases, *in situ* thromboendarterectomy, endarterectomy with reimplantation onto the aortic graft, or extra-anatomic splenorenal or hepatorenal grafting may prove preferable (see Ch. 128, Renovascular Disease: Operative Treatment). With regard to visceral artery occlusive disease, strict attention to preservation of the inferior mesenteric artery usually suffices (including end-to-side proximal anastomosis allowing continued antegrade flow to the inferior mesenteric artery via the native aorta) to prevent postoperative mesenteric ischemia, and simultaneous revascularization of the celiac or superior mesenteric arteries is rarely required. Staged open or percutaneous revascularization of the renal or mesenteric arteries is another option in specific circumstances, although the role of simultaneous renal reconstruction versus angioplasty before or after surgery remains unclear.<sup>68,69</sup>

### Coexistent Abdominal Aortic Aneurysms

While open repair of infrarenal abdominal aortic aneurysms is most typically completed with an aortic tube or aortobiiliac graft, coexistent AIOD may necessitate aortofemoral bypass grafting. Although aortofemoral bypass grafting is more complex than aortic tube or aortobiiliac reconstruction in patients with both aneurysmal disease and iliac outflow occlusive disease, our own institutional experience has led us to believe that concern for associated increased short- or longer-term mortality in such patients is not justified and should not be the basis for denying surgery. A review of more than 1000 consecutive open abdominal aortic aneurysm repairs performed over a recent 24-year period at the Brigham and Women's Hospital revealed a significantly higher postoperative morbidity rate in patients undergoing aortofemoral reconstruction for concomitant aneurysmal disease and AIOD, due to higher rates of postoperative renal insufficiency and groin wound complications.<sup>6</sup> Similarly, reintervention rates were higher in those undergoing aortofemoral bypass. While 30-day mortality was similar, 5-year survival was lower in those with concomitant AIOD (63% vs. 72% in the standard AAA repair group).<sup>6</sup> However, demographic characteristics, comorbidity profile, and aneurysm characteristics were different in the two groups; after adjustment with multivariate regression age, comorbidities, and aneurysm features were found to be independent predictors of reintervention and long-term mortality, but repair type was not.<sup>6</sup> Thus aneurysm disease patients with AIOD exhibit greater clinical complexity, but their outcomes justify ABFB when patients in this subset are appropriately selected.<sup>6</sup>

### Retroperitoneal Approach

Although the retroperitoneal approach to the infrarenal aorta is a well-accepted alternative to the more standard transperitoneal technique in the setting of aneurysmal disease, it is also favored by some surgeons in select patients with occlusive disease.<sup>70,71</sup> This option may be advantageous in patients with a history of multiple prior abdominal operations, abdominal wall stoma, concurrent renal or mesenteric arterial disease requiring suprarenal exposure, or severe cardiopulmonary disease. Stated benefits of reduced pulmonary morbidity and lower rates of postoperative ileus have not been consistently supported by the literature.<sup>72</sup> Clear disadvantages of the retroperitoneal approach include the attendant difficulty in accessing the right renal and iliac arteries and the right groin, particularly in obese patients.

### Minimally Invasive Approaches

Reflecting widespread trends toward more minimally invasive approaches in other areas of surgery, the technique of performing aortofemoral bypass grafting through a shorter midline incision has been reported.<sup>73</sup> The described minilaparotomy is less than 10 cm long, and the procedure is undertaken without displacement of the small bowel. Enthusiasm for the technique is currently limited.

There has also been recent, ongoing interest in applying laparoscopic and robotic techniques to the treatment of AIOD. This approach has been supported by a small body of literature mainly composed of individual case series (Table 109.1).<sup>74-79</sup> Some enthusiasts have championed a more limited application

**TABLE 109.1** Reports of Total Laparoscopic Aortofemoral Bypass for Aortoiliac Occlusive Disease

Series	Year	No. of Patients	Conversion to Open Repair (%)	RESULTS	
				Mortality (%)	Morbidity (%)
Said et al. <sup>113</sup>	1999	7	0	1 (14)	0
Alimi et al. <sup>114</sup>	2000	15	1 (7)	1 (7)	2 (13)
Barbera et al. <sup>115</sup>	2001	30	5 (17)	0	4 (13)
Dion et al. <sup>116</sup>	2004	49	4 (8)	1 (2)	3 (6)
Olinde et al. <sup>117</sup>	2005	22	2 (9)	1 (5)	4 (18)
Rouwers et al. <sup>118</sup>	2005	30	6 (20)	0	11 (37)
Remy et al. <sup>76</sup>	2005	21	1 (5)	0	5 (24)
Cau et al. <sup>119</sup>	2006	72	2 (3)	0	3 (4)
Dooner et al. <sup>120</sup>	2006	13	3 (23)	0	1 (8)
Di Centa et al. <sup>121</sup>	2008	150	5 (3)	4 (3)	21 (4)
Fournau et al. <sup>122</sup>	2010	139	19 (14)	3 (2)	23 (17)
Jongkind et al. <sup>123,a</sup>	2011	24	4 (14)	1 (4)	4 (14)
Novotny et al. <sup>81,b</sup>	2011	40	2 (5)	0	1 (2.5)
Tiek et al. <sup>124</sup>	2012	14	0	0	0
Ghammad et al. <sup>125</sup>	2015	173	21 (12.1)	4 (2.3)	12 (6.9)

<sup>a</sup>Robot assisted.

<sup>b</sup>Bypasses: 21 aortofemoral, 19 aortobifemoral.

with hand-assisted techniques and smaller incisions,<sup>80</sup> whereas others have advocated for the use of complete laparoscopic or robot-assisted revascularization.<sup>81–83</sup>

The presumptive benefits of reduced hospital length of stay, less perioperative pain, fewer postoperative complications, potentially lower overall cost, and improved quality of life are balanced against longer operative times and the absence of long-term data to support the durability of this alternative strategy.<sup>84</sup> The lack of exposure to the technique during routine general and vascular surgical training, the associated inherent technical challenges and prohibitive learning curve, and the declining indications for this approach with the advent of even less invasive endovascular alternatives have contributed to its limited popularity. Whereas morbidity and mortality rates for laparoscopic aortic bypass approach those for open aortic reconstruction (see Table 109.1), lower rates of gastrointestinal and pulmonary complications have been noted. Proponents of laparoscopic surgery also highlight the minimal incidence of incisional hernias and adhesion-related bowel obstruction. Open conversion rates in the reported series to date have generally been low but reached the 20% range in two reported series.<sup>85,86</sup> Although long-term patency rates for laparoscopic bypass have yet to be defined, intermediate-term results compare favorably with those reported for open ABFB.<sup>77,87,88</sup>

## RESULTS

The short- and long-term results of both endarterectomy and ABFB have generally been excellent, particularly in more recently published series. When endarterectomy is performed for disease limited to the distal aorta and proximal iliac segments, 5-year patency rates of 95% and 10-year rates between 85% and 90% are consistently achieved.<sup>39–42</sup> In contrast to the nearly 7% perioperative mortality rates reported in the early experience of endarterectomy, more recent reports reflect improvements in patient selection and perioperative management, with rates as low as 1%.<sup>38–41</sup>

Several large meta-analyses evaluating the comprehensive experience with ABFB grafting from its inception in the mid-1950s through the 2000s have indicated similar overall 30-day mortality rates of between 4.0% and 4.4%.<sup>89–91</sup> Several more recent single-institution series that better reflect the current era report an operative mortality of near 1%,<sup>24,35,62,92–94</sup> on par with that of elective abdominal aortic aneurysm repair. Increasing age, chronic pulmonary disease, and a low-volume hospital setting predict higher perioperative mortality (Table 109.2).

The accumulated experience to date has shown that 5-year primary patency rates between 85% and 90% and 10-year rates between 75% and 85% can be expected with aortobifemoral

**TABLE 109.2** Outcomes of Aortobifemoral Bypass: Operative Mortality and Long-Term Patency Rates

Series	Year	No. of Patients	Operative Mortality (%)	5-Year PP (%)	5-Year SP (%)	10-Year Patency (%)	15-Year Patency (%)
de Vries and Hunink <sup>89,a</sup>	1997	1429	4.4	88–91		82–87	75–82
de Vries and Hunink <sup>89,b</sup>	1997	1429	4.4	80–86		72–79	63–72
McDaniel et al. <sup>90,c</sup>	1997	2689	4	82–92		74–78	69
Ballard et al. <sup>60</sup>	1998	54	1.9	93 <sup>d</sup>			
Onohara et al. <sup>92</sup>	2000	38	0	89	97	94	
Faries et al. <sup>62</sup>	2001	370	0	93			
Mingoli et al. <sup>126</sup>	2001	130	4.6	81	87		
Dimick et al. <sup>95</sup>	2003	3073	3.3				
Reed et al. <sup>35</sup>	2003	281	1	85	93		
Back et al. <sup>4</sup>	2003	107	3.7				
Hertzer et al. <sup>24</sup>	2007	224	1.2	88		81	71
Chiesa et al. <sup>93</sup>	2009	822 <sup>e</sup>	0.1	97	98	90	
Burke et al. <sup>94</sup>	2010	118	0.8	89			
Chiu et al. <sup>91,f</sup>	2010	5738	4.1	86			
Sharma et al. <sup>5</sup>	2018	359	0.8	82	90		

<sup>a</sup>Meta-analysis of 23 studies between 1975 and 1996, limb-based.

<sup>b</sup>Meta-analysis of 23 studies between 1975 and 1996, patient-based.

<sup>c</sup>Meta-analysis of 18 reports between 1985 and 1992.

<sup>d</sup>Primary patency rate at 42 months.

<sup>e</sup>Aortobiiliac bypass in 3.8%.

<sup>f</sup>Meta-analysis of 29 studies between 1970 and 2007.

PP, primary patency; SP, secondary patency.

>60yrs = 95%  
<60yrs = 66%  
AFBC · 5yr patency = 85–90%.  
10yr " " . 75–85%.

Endarterectomy for disease limited to  
distal aorta + prox iliac : 5yr patency  
95%.  
10yr patency  
85–90%.

grafting (see Table 109.2).<sup>24,35,60,62,89-95</sup> Age has proved to be a significant predictor of outcome<sup>96</sup>; in one report, primary patency rates at 5 years were greater than 95% for patients older than 60 years but only 66% for those younger than 50 years (Fig. 109.12).<sup>35</sup> Although it is not clear why younger patients have inferior long-term patency rates, one could speculate that they have a more aggressive form of atherosclerosis or are at a different point in disease evolution than their older counterparts.

The reported influence of gender on graft patency has been more inconsistent, with some studies indicating less favorable outcomes in women and others demonstrating equivalent long-term patency rates in men and women.<sup>24,35,40,89</sup> Similarly, conflicting results have been documented with regard to the impact of preexisting SFA occlusion, with some but not all reports suggesting improved late patency when a simultaneous outflow procedure is performed at the time of aortobifemoral grafting.<sup>24,60,61</sup> In contrast, the benefits of combining profundaplasty with the inflow procedure have been unambiguously demonstrated.<sup>11,41,53-56</sup> Of note, no major differences in aortobifemoral graft durability have been noted between the transperitoneal and retroperitoneal approaches, between end-to-end and end-to-side anastomotic techniques, or between the indications of claudication and CLTI.<sup>24,35,71,72,89</sup> The single series directly comparing percutaneous treatment of AIOD with aortobifemoral grafting demonstrated similar 3-year secondary patency and limb salvage rates.<sup>97</sup>

In general, patients with occlusive disease limited to the AI region can expect to have excellent relief of symptoms after aortobifemoral grafting; those with multilevel disease generally have a lesser degree of symptom reduction. In one study, more than 80% of patients reported satisfaction with their result 5 years after undergoing ABFB.<sup>98</sup> Similarly, although 10-year survival rates are as low as 50% in patients with diffuse disease, those with more localized AI disease have a life expectancy not appreciably different from that of their normal age- and sex-matched counterparts.<sup>11,99,100</sup>

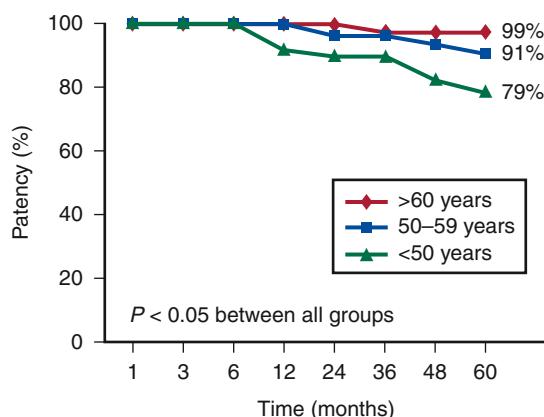
It has been questioned whether the excellent outcomes of aortic bypass surgery, the result of decades of technical refinement, and accumulated experience with the procedure remain

valid in the modern endovascular era.<sup>101</sup> In the most comprehensive report to date, a meta-analysis spanning the last 40 years, a decrease in patency rates for both ABFB and iliofemoral bypass grafts was noted over time when results were compared by decade of publication.<sup>91</sup> Postulated reasons for this finding have included greater operative complexity (i.e., more reoperative indications and an increased need for suprarenal clamping, adjunctive visceral segment revascularization, or concomitant outflow procedures) and a substantial decline in the experience of more recently trained surgeons in open aortic reconstruction.<sup>101</sup> Supportive evidence for this view can be found in one report indicating increased mortality and lower long-term patency rates when ABFB is performed in the setting of chronic infrarenal aortic occlusion.<sup>102</sup> In a review of our institutional experience with ABFB over a 30 year period, we discovered substantial shifts in the demographic and clinical features of the contemporary cohort of patients who underwent repair following the shift in the predominant therapeutic approach in this vascular territory to endovascular intervention.<sup>5</sup> There were a higher percentage of CLTI patients, increasing numbers of concomitant femoral endarterectomy and profundaplasty were required, and nearly 20% of patients in this contemporary cohort had undergone and failed AI endovascular revascularization. While short-term mortality remained below 1%, 5-year primary, primary-assisted, and secondary patency were reduced to 82%, 86%, and 90%, respectively.<sup>5</sup> Multivariate adjustment revealed the change in patency and major adverse limb event (MALE) outcomes to be primarily related to decreasing age, prior aortoiliac procedures, and decreasing graft diameters in the contemporary cohort. Limb salvage remained 98% at 5-years.<sup>5</sup> Thus ABFB remains an important surgical option even in the era of proliferation of endovascular techniques to treat AIOD.

## Early Complications

Reported overall morbidity rates range from 17% to 32% after aortic surgery for occlusive disease (Table 109.3). Cardiac complications are the most common cause of mortality<sup>5,6,24,63</sup> and result from the hemodynamic stress associated with major vascular surgery and the obligatory fluid shifts during the early postoperative period. Pulmonary complications are also common and are most likely to occur in the elderly or those with chronic obstructive pulmonary disease, a significant smoking history, or poor preoperative nutritional status.<sup>103</sup>

Acute renal failure after aortic reconstruction for occlusive disease is relatively uncommon in patients with normal preoperative renal function, even when suprarenal clamping proves necessary. Adequate hydration and the avoidance of repetitive aortic cross-clamping and perioperative hypotension are valuable prophylactic maneuvers; less clear is the benefit of the adjunctive use of mannitol and furosemide (Lasix) to trigger diuresis before aortic cross-clamping. Ureteral injury during dissection, graft tunneling, or retroperitoneal closure can usually be avoided with careful, diligent surgical technique. Spinal cord ischemia is a rare (occurring in only 0.3% of reconstructions for AIOD in one series) but particularly



**Figure 109.12** Overall 5-year cumulative secondary patency rates in a recent cohort of patients undergoing aortobifemoral bypass grafting, indicating an inverse relationship between age and graft patency.<sup>20</sup>

**TABLE 109.3** Complications of Aortobifemoral Bypass

Complication	Percentage
<b>Early (Perioperative)</b>	
Hemorrhage	1–2
Renal failure	<5
Acute limb ischemia	1–3
Bowel ischemia	2
Groin complications (lymphocele, lymphocutaneous fistula, wound infection, hematoma)	3–15
Sexual dysfunction	≤25
Ureteral injury	<1
Spinal cord ischemia	0.25
Pneumonia	<7
Myocardial infarction	1–5
Death	0–4
<b>Late</b>	
Graft thrombosis	5–30
Graft infection	0.5–3
Aortoenteric fistula	<3
Anastomotic pseudoaneurysm	1–5

devastating complication of infrarenal aortic surgery. The central component of prophylaxis is careful preservation of hypogastric perfusion; however, the use of gentle technique to minimize the risk of atheroemboli and the avoidance of perioperative and postoperative hypotension have also proved to be important preventive measures.

### Hemorrhage

Bleeding complications associated with AI endarterectomy, particularly for extensive disease, were partly responsible for the waning popularity of this technique. With modern suture and patch materials and the less extensive disease typically repaired in the current era, bleeding associated with endarterectomy has become less of a problem. For patients undergoing aortobifemoral grafting, postoperative hemorrhage is a relatively rare event, occurring in 1% to 2% of cases.<sup>104</sup> This rarity is due in part to a greater awareness of bleeding disorders, better intraoperative anticoagulation and blood product management, and improved hemostatic properties of the grafts used (see Chapter 39, Disorders of Coagulation: Hemorrhage).

Bleeding points in the anastomotic suture line after a test release of the aortic or femoral clamps are usually effectively managed with repair sutures reinforced with felt pledges. It is important to replace the clamp before placing any necessary repair stitches because attempted placement under tension risks extending the defect and worsening the bleeding. In cases in which the walls of the infrarenal aortic cuff are particularly thin after thromboendarterectomy, a previously positioned

sleeve of graft advanced over the aortic suture line can act as a prophylactic bolster. Intraoperative venous injuries can occur during dissection between the aorta and vena cava or from a tear in a lumbar vein; such injuries can often be controlled with judicious tamponade. A number of sealants, glues, and thrombin-based hemostatic adjuncts are now available to help control troublesome diffuse oozing and persistent needle hole bleeding. Delayed bleeding may occur if the postoperative blood pressure is appreciably higher than the pressure at the time of closure.

### Intestinal Ischemia

Intestinal ischemia after aortic reconstruction has been reported in 2% of cases.<sup>105</sup> The involved segment is usually the rectosigmoid, and the cause is multifactorial. Although sacrifice of either the primary or the main collateral source of perfusion to the colon during reconstruction is the most common causative event, perioperative hypotension leading to insufficient perfusion and atheroemboli are other possible contributors. If compromised bowel perfusion is recognized intraoperatively after the creation of an end-to-end anastomosis, inferior mesenteric artery reimplantation is indicated. Although some surgeons advocate routine reimplantation of all patent inferior mesenteric arteries as the safest means to avoid colonic malperfusion,<sup>106</sup> this practice has not been universally adopted. Given the frequency of delayed presentation, maintaining a high index of suspicion and having a low threshold for performing sigmoidoscopy during the early postoperative period are critical in the effort to avoid potentially catastrophic colonic perforation.

### Late Complications

Late complications after aortobifemoral grafting include graft limb thrombosis, aortoenteric fistula, graft infection, and anastomotic pseudoaneurysm (see Table 109.3).

#### Graft Thrombosis

Graft thrombosis is the most frequently encountered late complication (see Ch. 48, Graft Thrombosis). It occurs in as many as 30% of cases in some series in which the grafts were observed for 10 years or longer.<sup>107</sup> Occlusion of the entire graft is relatively rare and usually stems from placing the proximal anastomosis inappropriately low in relation to the renal arteries, with subsequent progression of proximal atherosclerosis. A more commonly encountered scenario is unilateral limb thrombosis, which most often reflects progressive intimal hyperplasia at the distal anastomosis or progression of outflow disease. Flow can frequently be restored with aggressive efforts using special thrombectomy catheters designed to remove the chronically adherent fibrinoid thrombus typically encountered. If inflow is successfully restored, revision of the distal anastomotic site with a profundaplasty or extension of the graft may prove necessary. If more extensive progression of outflow disease is identified, or if extraction of a distally propagating thrombus is unsuccessful, the addition of an

outflow graft may be needed to ensure patency of the revascularized limb. A femorofemoral or axillofemoral graft usually suffices as a secondary source of inflow when an aortobifemoral limb is not successfully reopened.

### False Aneurysm

Anastomotic false aneurysms are far less common in modern practice compared with the early experience of aortic grafting, but they continue to be seen as a late complication in 1% to 5% of cases (see Ch. 50, Anastomotic Aneurysms).<sup>104,108</sup> They arise secondary to a weakening in the suture line as a result of structural fatigue or fabric degeneration. Undue tension, poor suturing technique, and focal weakening of the recipient arterial wall after endarterectomy have been implicated as causative factors. Infection undoubtedly plays a role in many cases, despite the frequent absence of any obvious clinical signs; *Staphylococcus* species are the predominant organisms identified in culture. Femoral anastomotic false aneurysms are most common and typically are manifested as a slowly enlarging, asymptomatic groin bulge. Proximal anastomotic false aneurysms are often discovered incidentally during radiographic evaluation for other reasons or come to attention when they rupture. Given the potential complications of thrombosis, embolization, or rupture, repair is generally recommended for femoral false aneurysms larger than 2 cm or aortic false aneurysms greater than 50% of the graft diameter. Treatment has classically consisted of debridement of the degenerated tissue and placement of a short interposition graft, although stent grafts are being increasingly utilized to treat aortic anastomotic pseudoaneurysms percutaneously.<sup>109,110</sup>

### Graft Infection

Prosthetic graft infection is a particularly feared complication of aortic reconstruction, given its high associated morbidity and mortality (see Ch. 49, Graft Infection).<sup>111</sup> The diagnosis is typically reached by a combination of clinical suspicion and computed tomography (CT) or isotope-labeled leukocyte scanning, with the groin being the most common site of presentation. On occasion, exploration is needed to confirm or to refute the diagnosis. Preventive efforts include strict adherence to sterile technique, particularly in the setting of infected, distal ulcerations, and the timely administration of preoperative antibiotics. Graft contamination at the time of implantation is difficult to prove but is believed to be common. Once infection is diagnosed, graft excision is usually indicated.

### Aortoenteric Fistula

Aortoenteric fistula is another relatively rare but potentially devastating late complication associated with aortobifemoral grafting (see Ch. 51, Local Complications: Aortoenteric Fistula).<sup>112</sup> The most common pathophysiologic process is erosion of the proximal aortic suture line through the third or fourth portion of the duodenum, although fistulae between the iliac anastomoses into the small bowel or colon

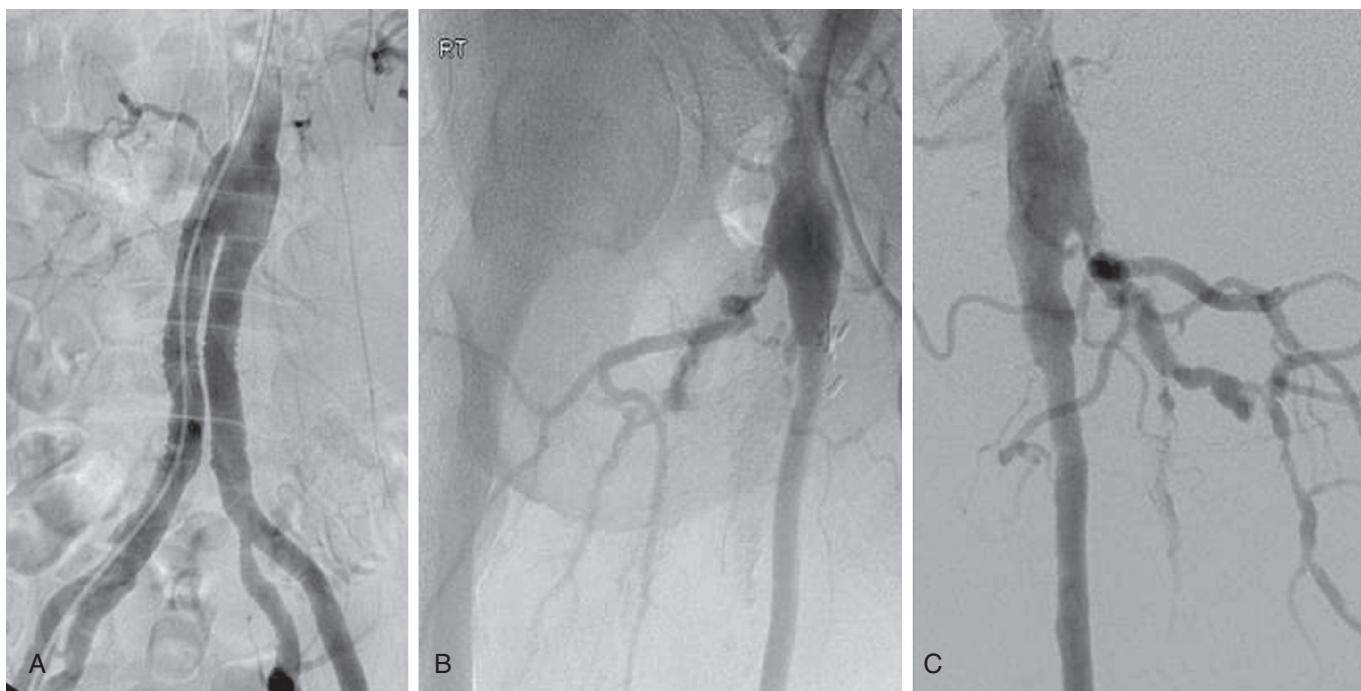
are also well described. The diagnosis can be challenging and typically involves some combination of CT scanning, endoscopy, and angiography. The classically described triad of gastrointestinal bleeding, sepsis, and abdominal pain is present in only a minority of patients. Far more commonly, a small, self-limited "herald bleed" presages a large gastrointestinal bleed, which can be massive in nearly a third of cases. In many respects, treatment is similar to that for graft infection; extra-anatomic bypass and graft removal are usually required, in addition to repair of the involved gastrointestinal tract. Dedicated efforts to ensure adequate tissue coverage between the graft and the overlying bowel before abdominal wall closure are important in preventing this highly lethal complication.

## ISOLATED PROFUNDAPLASTY

The last 3 decades have been marked by an increased awareness of the critical role of the deep femoral artery in achieving successful lower extremity revascularization. Profunda circulation is frequently spared, even in the setting of severe obliterative disease of both the AI and femoropopliteal arterial segments. When present, profunda occlusive disease is often limited to the orifice or proximal segment (Fig. 109.13). This has important implications for the unique role of the profunda in maintaining collateral perfusion because even in the presence of proximal profunda disease, the more distal segments beyond the obstruction can continue to support key anastomotic networks. In extreme cases, these pathways can serve as the sole limb-sustaining bridge between pelvic or abdominal wall inflow vessels proximally and geniculate connections distally. In some diabetic patients, however, profunda disease is more diffuse, and distal collaterals are minimal.

The value of the profunda in supplying sufficient distal perfusion in the setting of SFA occlusion has been known since the early 1960s. Although isolated profundaplasty is less common in the current era of more aggressive percutaneous and open surgical reconstruction for lower extremity occlusive disease, it can be an effective alternative to either balloon angioplasty or surgical bypass of the SFA. It is particularly useful when ① infected infrainguinal grafts require removal or in the setting of ② failed bypass grafts when suitable autogenous conduit is absent and "redo" surgery is less appealing. It may also allow healing of ③ a below-knee amputation in situations in which distal bypass is no longer an option.

The optimal conditions for an isolated profundaplasty are widely patent inflow and good distal profunda runoff beyond a diseased proximal profunda; longer diseased segments are more amenable to profunda bypass. The operative technique is as described earlier for adjunctive profundaplasty. Associated mortality and morbidity are low, with morbidity most commonly related to a lymphatic leak or other groin-related issues. Three-year limb salvage rates in the range of 75% have been reported in patients with critical ischemia, and 5-year patency rates of 88% have been achieved when isolated profundaplasty was performed for claudication.



**Figure 109.13** A patient with widely patent aortobifemoral and bilateral femoroperoneal bypass grafts (A) developed limiting bilateral thigh claudication secondary to profunda femoris occlusive disease (B, C). Symptoms resolved after bilateral staged isolated profundaplasties.

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# Aortoiliac Disease: Open Extra-Anatomic Bypass

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JOSEPH SCHNEIDER

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Direct replacement or bypass procedures for aortoiliac or infrainguinal arterial disease were developed in the 1950s. The procedures discussed in this chapter were generally developed shortly after that as alternatives to more direct procedures. These alternative so-called “extra-anatomic” bypass procedures offered the potential benefit of a less formidable operation than aortofemoral bypass in patients with advanced comorbidities, a less hazardous approach in patients with “hostile abdomen” (previous surgery, visceral stomas, and active infection including infection of previously placed vascular grafts among these), and as a remote site for bypass grafts in the face of arterial infection to reduce the risk in infection of the newly placed grafts. Two of the procedures, axillofemoral and femorofemoral bypass, are clearly less injurious to the patient than would be direct aortofemoral bypass. However, the so-called obturator bypass is probably more injurious than a direct femoropopliteal bypass, although obturator bypass remains the standard approach to re-vascularize the lower leg in the face of groin sepsis or other problems that make a more conventional procedure in the groin undesirable. The technical demands of these extra-anatomic procedures are distinct from and the hemodynamic and patency results may not be the same as those of the direct procedures. This chapter addresses the indications, preoperative evaluation, conduct of the procedure, follow-up and performance expectations for these procedures.

Although the procedures described are mature and have not changed appreciably in decades, the roles of these procedures continue to evolve. Younger patients tend to have more discrete proximal arterial disease and are more likely to be treatable with the rapidly expanding set of endovascular tools. In contrast, older patients with many comorbidities tend to have more diffuse arterial disease and endovascular techniques may not be optimum in such cases.<sup>1</sup> However, endovascular techniques are improving and the fraction of patients for whom endovascular

solutions are applicable continues to increase.<sup>2–4</sup> On the other hand more conventional surgical techniques such as aortofemoral bypass, once thought too invasive for older patients with multiple comorbidities, may now be extended to these patients since anesthetic and perioperative critical care have also continued to improve, thus reducing the risks of these procedures. Nonetheless, the inexorable aging of western populations will likely cause us to be faced with progressively older and frailer patients for whom these extra-anatomic procedures may be appropriate. The outcome of critical limb ischemia is quite poor if the patient is not treated with some technique to enhance blood flow to the limb<sup>1,5,6</sup> and if the patient has any level of independence and function some procedure will ultimately be required to maintain the limb. Thus, although the procedures may be mature, the profiles of the patients for whom these procedures are appropriate have evolved and will likely continue to evolve with time.

As with any procedure, all efforts should be made to optimize the patient’s status and to treat coexistent problems before proceeding to surgery. In particular, any infection should be treated and controlled with drainage and antibiotics to the extent possible. Preoperative “optimization” of any medical problems including diabetes mellitus, coronary artery disease, congestive heart failure, and nutritional deficits is also desirable. Treatment of any of these problems will improve the patient’s general condition and reduce the risk of infection of the graft. However, because the extra-anatomic bypass procedures to be discussed in this chapter are often required in urgent or emergent situations, such patient “optimization” may not be possible.

Preoperative planning requires adequate anatomic information. Quality imaging is necessary to assess the outflow and inflow (including the axillary inflow for axillofemoral bypass in some cases). This has traditionally required conventional

transarterial catheter-based angiography. Early on, CT angiography suffered from interference from calcium in atheromata, and artifacts from implanted metal devices, but the emergence of dual-energy CT has markedly improved the quality of CT angiography in these patients.<sup>7,8</sup> MRI has also advanced significantly now with the ability to produce high-quality angiograms without contrast as well,<sup>9</sup> although the expense, the proprietary nature of these techniques and dependence on high flux systems seems to have limited the deployment of and publication of scientific articles describing the clinical use of these newer MR techniques. Planning using exclusively ultrasound-based techniques would be unusual and only appropriate for a small number of cases.

Any of these procedures may be contraindicated in patients at extreme medical risk with short expected survival. Obturator bypass is a significantly invasive procedure, clearly physiologically taxing, and may be a larger injury than some patients can be expected to tolerate. One should seriously question performing one of these procedures in the face of active, inadequately treated infection. When no other alternative exists, then one should consider an autologous conduit, such as great saphenous vein or femoral vein, a human allograft vein, or perhaps an antibiotic-soaked protein-impregnated graft.<sup>10</sup>

## FEMOROFEMORAL BYPASS

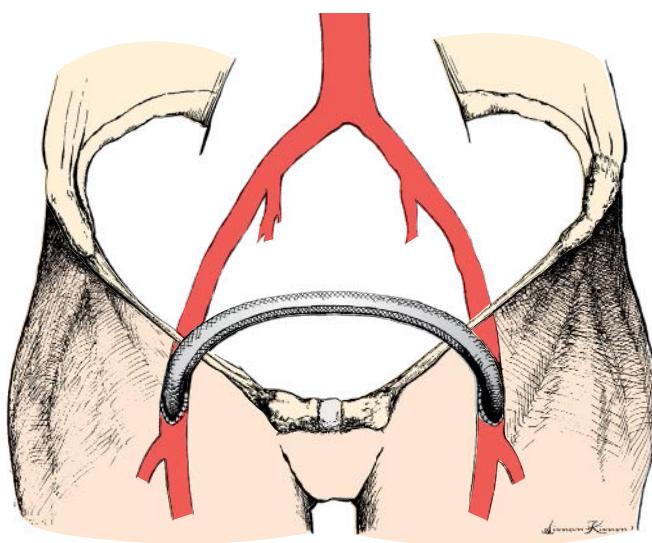
Femorofemoral bypass was first described as a stand-alone procedure in 1952,<sup>11</sup> but the first substantial series of patients with follow-up information was published in 1960.<sup>12</sup> The procedure involves diversion of some blood from one iliac system to the contralateral leg and depends on the concept that one healthy iliac artery has the capacity to supply adequate flow to both the ipsilateral donor leg and the contralateral recipient leg.<sup>13</sup> Femorofemoral bypass has been a frequently applied procedure in patients with dominant unilateral iliac artery disease and more recently in patients whose suboptimal “donor” iliac artery can be improved with endovascular techniques.<sup>14–16</sup> Even more recently, endovascular techniques have continued to improve and many patients who would have been treated with femorofemoral bypass may now be completely treated with endovascular techniques. Femorofemoral bypass has found a new application as an accompaniment to aortouniliac endovascular aortic aneurysm repair and seems to perform better in that application than when used for chronic arterial occlusive disease.<sup>17,18</sup> One should also consider the more direct common iliac to femoral bypass, which appears to have the same performance as the benchmark aortofemoral bypass procedure.<sup>19,20</sup>

If there is any question about the adequacy of the inflow because of disease in the iliac arterial system one should consider a pharmacologic physiologic stress test of the inflow,<sup>21,22</sup> treat the diseased inflow with endovascular techniques as discussed above, or abandon the plan for femorofemoral bypass in favor of an alternative procedure. With respect to outflow, either a minimally diseased normal caliber deep femoral or minimally diseased superficial femoral artery is sufficient outflow in most cases to support graft patency (as discussed further below) and

adequately improve perfusion of the leg. It is rarely necessary to add a simultaneous infrainguinal bypass procedure on the recipient side to enhance distal perfusion, at least to treat resting ischemia of the recipient limb.

Femorofemoral bypass is performed with the patient in the supine position and can be performed with general, regional, or even with local anesthesia in selected patients. Prophylactic antibiotics are appropriate in elective cases and targeted antibiotics are appropriate for patients with active infection who require urgent treatment. The operation may be performed with a limited area of sterile preparation to include only the lower abdomen, groins, and upper anterior thighs, but in most cases we would perform the operation with preparation and draping to expose essentially the entire anterior abdomen to allow access to the iliac arteries or even the aorta should this become necessary. The preparation and draping of the patient may also include circumferential exposure of both legs to allow intraoperative assessment of perfusion to the level of the ankles upon completion of the operation. In most cases, longitudinal groin incisions provide the most flexibility for exploring and inspecting the donor and recipient femoral arterial systems. A graft is tunneled from one groin to the other in an inverted U configuration, usually in the subcutaneous area (anterior to the abdominal wall fascia), but on rare occasion in the retrofascial space. This tunnel can be created with a specialized tunneler or simply with aggressive finger dissection and a large clamp. Care must be taken to prevent entering the peritoneal cavity and in the case of previous abdominal surgery, great care must be taken when tunneling through scarred areas to prevent visceral injury. The first ever femorofemoral bypass was performed with an endarterectomized occluded superficial femoral artery autograft. In current practice, despite the vast majority of femorofemoral bypasses being performed with prosthetic materials, there is a small fraction of procedures performed with venous or arterial autografts, or even allografts when the infection is extensive or in patients with intestinal or urinary stoma. Although multiple prosthetic graft types have been touted as superior to their alternatives, there is no compelling evidence that polyester fabric, supported polyester, ePTFE, supported ePTFE, heparin bonding or other graft lining or any other graft type performs better than others in terms of hemodynamics or patency in the femorofemoral application.<sup>23,24</sup> Notwithstanding, a recent publication demonstrated a trend toward improved patency using femoral vein compared to prosthetic conduit in a uniquely large femorofemoral bypass experience using vein conduit.<sup>25</sup> The author's conduit preference is a 6-mm or 7-mm supported ePTFE graft, depending on patient size and native arterial diameter.

Care should be taken to prevent kinking of the graft in the anteroposterior direction, especially in patients with protuberant abdomens. Technical nuances such as shortening of the anastomosis, placing the anastomosis more distally (possibly to include the deep femoral or superficial femoral arteries), or both will allow a less acute angle at the heel of the anastomosis and decrease the possibility of graft kinking.<sup>26</sup> Another key point is to create the subcutaneous tunnel in a more uniform larger radius arc, generally by making the most superior part of



**Figure 110.1** Standard “inverted C,” perhaps better termed “inverted U,” configuration of a femorofemoral bypass graft.

the graft well superior to the pubis (Fig. 110.1) to reduce the risk of kinking in the coronal plane.

Intravenous heparin, or in the case of patient heparin sensitivity another suitable short-acting anticoagulant is administered prior to placement of vascular clamps. Arteriotomy and anastomotic sites are selected based on review of the preoperative arteriogram and local examination of the artery at the time of exploration of the femoral arteries. These may include the common, deep, or superficial femoral artery or some combination thereof. A conventional end graft-to-side artery anastomosis as described in earlier chapters in this text is nearly always appropriate on both sides. The anastomosis may be facilitated by extending the arteriotomy and the toe of the graft onto the deep or superficial femoral artery or even placing the entire anastomosis to the deep or superficial femoral artery. The right and left anastomoses may be performed simultaneously, thus saving significant time if two surgeons are available. If the anatomy dictates, extension of the anastomosis out onto the deep femoral artery, may actually reduce the tendency of the graft to kink adjacent to the anastomosis as well. Once the anastomoses have been completed and the clamps removed, a sterile continuous wave Doppler probe should be used to confirm that flow is enhanced in the recipient side outflow artery or arteries and that there is no apparent deterioration in flow in the donor side outflow arteries. Once again, as long as there is a normal diameter, minimally diseased or adequately improved donor iliac artery, the graft should not “steal” from the donor leg at rest.

Some authors have observed that femorofemoral graft patency is better if the superficial femoral artery is patent on the recipient side, but the author and others have observed no difference.<sup>14,27</sup> We make sure that there is adequate outflow to at least the deep or superficial femoral artery, using adjunctive techniques such as using the graft anastomotic hood to perform “patch angioplasty”, and insuring that a 3.5-mm diameter dilator will pass easily beyond the toe of the anastomosis into at least one of the recipient femoral arteries. We have found that this is generally associated with adequate patency.

Patients are treated long-term with antiplatelet agents and hospital stay is determined primarily by comorbidities. Some patients may be ready for discharge on postoperative day one or two. Although the literature is sparse with respect to the value of surveillance noninvasive testing,<sup>28</sup> we have adhered to a program of surveillance with ankle-brachial indices, continuous wave Doppler waveforms at the ankle, and graft duplex scans. Our protocol calls for a graft duplex every three months for the first year, twice in the second year, and yearly thereafter if graft performance is stable, similar to our protocol for infringuinal bypass grafts.<sup>29</sup>

Operative mortality for femorofemoral bypass should be much less than 5% and should be lower for femorofemoral than for aortofemoral bypass given otherwise similar patients.<sup>30</sup> A femorofemoral graft does not as perform as well as a direct aortofemoral bypass based on patency or hemodynamic improvement.<sup>14</sup> In particular, femorofemoral bypass may not be a hemodynamically complete treatment for claudication. However, as measured by freedom from major adverse limb events, femorofemoral bypass is nearly if not as effective as aortofemoral bypass<sup>31</sup> and may be a better choice than direct aortofemoral bypass based on patient factors. Predicted primary patency at 5 years for patients whose indication is atherosclerotic occlusive disease is approximately 70% based on assessment of recent pertinent publications and is probably better in patients having femorofemoral bypass as part of aortouniliac endovascular repair of aortic aneurysm.<sup>23,32</sup> Finally, femorofemoral bypass has become a key salvage technique for limb thrombosis after endovascular repair of aortic aneurysm.<sup>33</sup> Causes of femorofemoral bypass graft failure include technical errors, progression of inflow or outflow disease, and perianastomotic stenosis due to intimal hyperplasia. There are few complications specific to femorofemoral bypass, but they would include visceral injury, particularly if the graft is tunneled in a retrofascial position or if there is a hernia. In difficult circumstances with a high-risk patient, a femorofemoral bypass is a relatively low risk way to reperfuse a leg with dominant unilateral iliac artery disease and is likely to be an essential skill for the vascular surgeon for the foreseeable future.

## AXILLOFEMORAL BYPASS

The first reported axillofemoral bypass procedures were performed to treat patients at unacceptable risk for conventional aortofemoral bypass and for extraanatomic bypass at the time of removal of an infected graft.<sup>34</sup> These are examples of two of the three primary indications for axillofemoral bypass: (1) patients with symptomatic aortic and/or bi-iliac arterial occlusive disease thought to be at excessively high physiologic risk for direct aortic repair; (2) patients with infected native aorta or aortic graft or the closely related problem of aortoenteric fistula; and (3) patients with “hostile abdomen,” generally with multiple previous surgeries, active intra-abdominal infection, or the presence of intestinal or urinary stoma. Although there was a period of popularity of axillofemoral bypass as a primary procedure for aortoiliac occlusive disease, for example as promoted by Johnson et al.<sup>35</sup> and later by the group at the Oregon

Health Sciences University,<sup>36</sup> it is fair to say that this approach was not widely adopted. There was also a period of interest, for example at the Albany Medical College, in axillofemoral bypass combined with ligation of the infrarenal aorta as primary treatment for abdominal aortic aneurysm,<sup>37</sup> but this approach was generally abandoned when it was observed that a number of such patients later died of ruptured abdominal aortic aneurysm.<sup>38</sup> Conventional thinking in the peak period of the operation was that axillofemoral bypass should nearly always be performed in a bifemoral configuration to improve outflow of the graft.<sup>39</sup> However, some of the same people who advocated this later reported that axillounifemoral bypass performed just as well as axillobifemoral bypass configurations.<sup>40</sup> Thus the choice of axillouni- vs. axillobifemoral bypass should be based on whether one or both legs would benefit from improved flow.

Many patients with aortic and/or bi-iliac arterial occlusive disease are now treated completely or partially with the ever-expanding endovascular armamentarium. Furthermore, it is likely that some of these patients who might have been selected for axillofemoral bypass in the past are now seen as manageable low risk for direct aortofemoral bypass. Thus, axillofemoral bypass has likely declined in volume from a likely peak in the 1970s and 1980s. Nevertheless, this procedure remains an essential tool for the vascular surgeon. Similar to the assumption with femorofemoral bypass, axillofemoral bypass assumes that one axillosubclavian artery has adequate blood volume flow capacity to supply the donor side arm and one or both legs, at least at rest.

One unique preprocedure question is which axillary artery is to be used for the donor? The graft is generally tunneled in the midaxillary line and lateral abdomen from the donor iliac artery to the ipsilateral femoral recipient artery. Certainly coexistent thoracic or abdominal problems may dictate the side of the procedure. For example, the impending need for thoracotomy or abdominal surgery for other problems may dictate use of the contralateral axillary artery. The presence of intestinal or urinary stomas may dictate placement of the axillofemoral graft contralateral to those stomas. Some surgeons ask the patient on which side they sleep and will place the graft contralateral to that, although the need for this questioning is equivocal. If none of the above seems to point to one or the other side, most surgeons would place the graft on the side of the more symptomatic leg if axillounifemoral configuration is to be used. We would recommend against placement of an axillofemoral bypass based on the side of an existing arteriovenous hemoaccess fistula, since this might provoke or worsen existing steal symptoms in that arm. We insist on a triphasic brachial artery Doppler waveform and a blood pressure no more than 10 mm Hg lower in the proposed donor arm than in the contralateral arm. If these criteria are not met then we will proceed to upper extremity angiography and if necessary inflow artery treatment prior to surgery.<sup>41</sup>

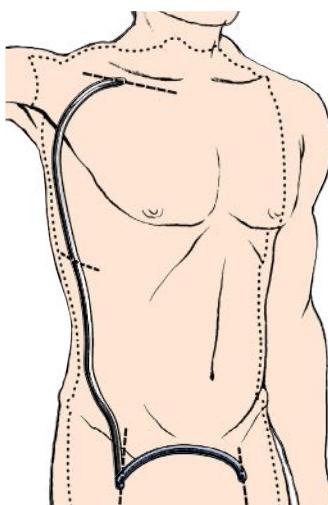
The procedure is performed in the supine position. Although it may be possible to perform segments of the operation with local or regional anesthesia, creating the axillofemoral tunnel would be difficult and for practical purposes the operation is always performed with general anesthesia. We place a gel pad or a towel-wrapped 1 liter bag of fluid between the operating table and the posterolateral back on the side of the axillofemoral graft to elevate the flank and lower chest to allow slightly more

posterior prepping and draping for better visualization during tunneling. Some surgeons position the ipsilateral arm at the patient's side, but we have always positioned the ipsilateral arm at 90° abduction both to allow visualization of the ipsilateral lateral chest and abdomen during tunneling and to elevate the clavicle slightly to enhance exposure of the donor axillary artery. The sterile preparation should be wide and should include at a minimum the anterior and ipsilateral neck base and suprACLAVICULAR fossa over to the anterior shoulder area, the axilla, anterior and ipsilateral chest and abdomen and the groin and superior anterior thigh. In particular, we have always thought it prudent to prep widely to allow a thoracotomy in the case of an injury or other problem with the axilosubclavian donor artery, although we have never had to proceed to thoracotomy. In the case of axillobifemoral bypass the preparation and draping must include the contralateral lower abdomen, groin, and anterior upper thigh. Prophylactic or, in the case of active infection, targeted antibiotics are administered.

Groin exposure is consistent with that for femorofemoral bypass as discussed above. The donor axillary artery is exposed with a transverse incision a few centimeters inferior to the clavicle and by splitting of the pectoralis major muscle fibers. The axillary artery should be exposed and controlled from the clavicle medially to the pectoralis minor muscle. This is typically about 3–4 cm in length. This artery is more fragile than the more familiar common femoral artery and great care must be taken not to injure the artery during dissection and clamp placement.

A subcutaneous tunnel is created from the ipsilateral groin incision to the axillary artery exposure incision. This tunnel must be kept in the midaxillary line to minimize changes in path length during flexion and extension of the torso and to avoid graft compression at the costal margin, which is often more prominent anterior to the midaxillary line. In the early experience with axillofemoral bypass a separate flank incision was required about half the distance from the axillary artery exposure incision to the ipsilateral groin incision since there were no adequate tunnelers to traverse the entire distance. However, there are now several tunnelers that will traverse the entire distance and the intermediate incision in the flank can be abandoned. Care must be taken to remain subcutaneous and superficial to the abdominal wall deep fascia and to avoid entering the thoracic cavity during tunneling. Although some have advocated tunneling anterior to the pectoralis minor muscle or even division of the pectoralis minor, we have always tunneled posterior to the pectoralis minor.

Axillofemoral bypass is virtually always performed with a prosthetic graft and as with femorofemoral bypass there is no clear advantage of one graft type over another. Although both polyester and ePTFE grafts can be purchased with pre-constructed connections between the axillofemoral and femorofemoral components, given the current relative infrequency of axillofemoral bypass, we perform the procedure with two segments of straight graft anastomosing one graft to the other (Fig. 110.2). We tend to use an 8-mm supported ePTFE graft for the axillofemoral component and if the bypass is to be axillobifemoral, we typically use a 6-mm supported ePTFE graft for the femorofemoral component. On rare occasions when performing an axillounifemoral bypass in a small patient, a



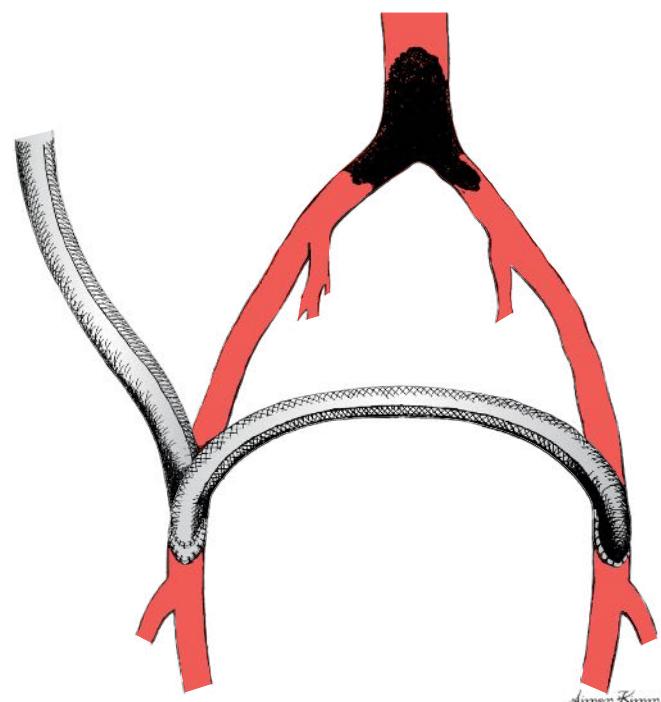
**Figure 110.2** Typical area of exposure for an axillobifemoral bypass graft. The right axillary artery is the donor artery in this case. The intermediate incision in the right lower chest or upper flank is generally unnecessary if an appropriate tuneler is used.

6 mm diameter graft may be used in part to try to enhance velocity, which may improve patency.<sup>42,43</sup>

Heparin or other suitable short-acting anticoagulant is administered before clamps are placed on the arteries. As with femorofemoral bypass, conventional end graft-to-side artery anastomoses are usually appropriate. An axillobifemoral bypass with two separate graft segments requires four anastomoses including one that connects the axillofemoral and femorofemoral components and pairs of these anastomoses may be performed simultaneously. Thus, axillofemoral bypass, particularly axillobifemoral bypass, is greatly facilitated if two surgeons are present.

It is critical to create the axillary artery to graft anastomosis in such a way that there is no tension on this anastomosis when the arm is abducted. We employ two technical concepts to try to avoid this problem. First, the anastomosis should be placed as medial as possible on the axillary artery since this part of the artery will move less than the more lateral part of the artery when the arm is abducted. This also tends to bring the graft into a more nearly parallel relationship to the artery, also reducing the tendency to produce traction on the anastomosis when the arm is abducted. The principle of leaving the pectoralis minor muscle intact and tunneling the graft posterior to this muscle tends to force the surgeon to keep the anastomosis medial. A second principle is to allow some redundancy of the graft and even to allow some bowing of the graft into the axilla posterior to the pectoralis minor muscle, again hoping to reduce the risk of traction on the anastomosis with ipsilateral arm movements.<sup>44</sup>

In the “heyday” of axillobifemoral bypass a commonly recommended technical point was to place the connection between the femorofemoral and axillofemoral components as close to the femoral artery anastomosis as possible to try to maximize flow throughout the entire length of the axillofemoral graft. This concept is plausible and we adhere to it, but there is no observational evidence that this provides a real advantage. Nevertheless it is usually simple to either complete a conventional femorofemoral bypass and then sew the axillofemoral graft to a graftotomy in the ipsilateral anastomotic hood of the



**Figure 110.3** Typical configuration of an axillobifemoral bypass graft. In this case the right axillary artery is the “donor” and the axillofemoral component has been anastomosed to the native right common femoral artery, after which the right end of the femorofemoral component has been anastomosed to an ovoid graftotomy in the anterior wall of the anastomotic hood of the axillofemoral component.

femorofemoral graft or alternatively to complete the anastomosis between the inferior end of the axillofemoral graft and the ipsilateral groin target artery and then sew the ipsilateral side of the femorofemoral graft to a graftotomy in the femoral anastomotic hood of the axillofemoral component (as is depicted in Figure 110.3). In either case, unlike a pliable native artery where a simple arteriotomy creates an adequate opening, a prosthetic graft tends to be rigid and not to gap adequately after a simple longitudinal graftotomy. Therefore, anastomosing a graft to the side of a prosthetic graft requires excision of an oval of the graft material at the point where anastomosis is to be created. No matter whether the graft is performed in axillounifemoral or axillobifemoral configuration, the same principles described above for femorofemoral bypass to assure adequate outflow (for example using the graft hood as a patch and assuring that a 3.5 mm diameter metal dilator will pass easily into at least one outflow artery) are equally applicable to axillofemoral bypass.

A sterile handheld Doppler probe is used to confirm that flow is augmented in the outflow artery or arteries with the graft open as compared to with the graft clamped. The surgeon must also assure that there is normal flow in the distal arm on the donor side, for example by confirming the presence of a palpable pulse in the radial artery or by confirming satisfactory pulse oximetry in a donor side digit with the graft open (with blood flowing to the lower extremities).

Just as is the case with femorofemoral bypass, an axillofemoral graft does not perform as well as a direct aortofemoral bypass based on patency or hemodynamic improvement.<sup>45</sup> In fact, our previous work suggests that the predicted ankle-brachial index

after axillofemoral bypass with normal (undiseased) infrainguinal outflow is less than 0.7, compared to slightly more than 1.0 after direct aortofemoral bypass.<sup>45</sup> However, axillofemoral bypass performs acceptably and may be a better choice than direct aortofemoral bypass based on patient factors.

The literature of axillofemoral bypass has one of the broadest range of reported long-term patencies for any open vascular surgical procedure, probably related to the broad range of patient characteristics in that literature.<sup>23</sup> However, a fair estimate for predicted primary patency at 5 years among patients whose indication is atherosclerotic occlusive disease should be about 60%–70%. In a patient with advanced age and comorbidities, bilateral iliac artery disease that cannot be improved adequately on at least one side with endovascular techniques to allow a femorofemoral bypass, a patient with an infected native aorta or aortic graft, or a “hostile” abdomen, an axillofemoral bypass provides a less invasive approach to reperfusing one or both legs. In practice, patients selected for axillofemoral bypass tend to have both shorter survival and an increased risk of major adverse limb events.<sup>23,31</sup>

With respect to surveillance of axillofemoral bypass, the literature is even less revealing than for femorofemoral bypass. Just as with femorofemoral bypass, since the predicted patency for axillofemoral bypass is clearly less than for aortofemoral bypass, we are consequently much more aggressive with noninvasive surveillance and obtain ankle pressures, ankle-level Doppler waveforms, and graft duplex scans every three months for the first year, twice in the second year, and yearly after that.<sup>29</sup> Complications specific to axillofemoral bypass include disruption of the axillary artery to graft anastomosis<sup>46</sup> and thromboembolic complications in the native arteries after thrombosis of the axillofemoral graft.<sup>47</sup>

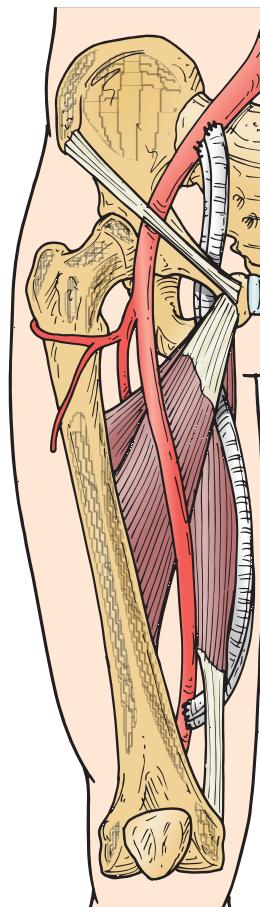
## OBTURATOR BYPASS

Shaw and Baue first described three cases of obturator bypass as a method to maintain perfusion of the leg after dealing with arterial infection in the groin.<sup>48</sup> The technique requires tunneling a graft from the iliac arterial system through the obturator fossa in the pelvis to the infrainguinal arterial system, a path proposed at least two years before Shaw and Baue's first description.<sup>49</sup>

The primary indication for this procedure is arterial infection in the femoral artery area. Our most recent experience with this operation has been predominantly in patients with mycotic aneurysms as a complication of arterial puncture for angiography or endoarterial procedures. However, other causes include mycotic aneurysms related to recreational drug use, infection early or late after direct surgical exposure of the femoral artery for embolectomy, endarterectomy, or other direct arterial surgery, or “hostile groin,” for example after previous procedures or therapeutic radiation.

The operation is performed with the patient in the supine position with the entire ipsilateral leg prepped circumferentially and draped so that the entire leg is available and can be moved in the sterile field. The groin and abdomen are also prepped and draped to allow access to the iliac arteries or the aorta if necessary. Inflow is typically from the ipsilateral common or less often the external iliac artery, although inflow could be taken from the aorta or the contralateral iliac arterial system.

The approach is most often through an oblique ipsilateral low abdominal incision and retroperitoneal exposure of the iliac arteries, although transperitoneal approach and control of the inflow artery is also possible. Outflow is usually the above-knee popliteal or superficial femoral artery, exposed as would be the case for femoropopliteal bypass (discussed in other chapters in this text), although on occasion will be the deep femoral system or an infragenicular popliteal or other more distal artery. The graft is tunneled through the obturator foramen posterior to the adductor longus (Fig. 110.4). The obturator foramen is approached medial to the external iliac vein posterior to the superior side of the pubic ramus and the obturator internus muscle is bluntly dissected away from the obturator membrane. The obturator membrane is very strong, cannot be perforated bluntly and requires incision with scissors, scalpel, electrocautery, or other suitable technique. It is difficult to see this well enough to perforate under direct vision, certainly if a small incision is used, and care must be taken not to damage adjacent structures such as the urinary bladder when creating the tunnel and the defect in the obturator membrane. The incision should be in the anteromedial part of the obturator membrane to avoid the obturator nerve and artery. The graft is usually placed in the potential space between the adductor magnus posteriorly and the adductor longus and brevis anteriorly, although it may be brought into the area of the superficial femoral artery



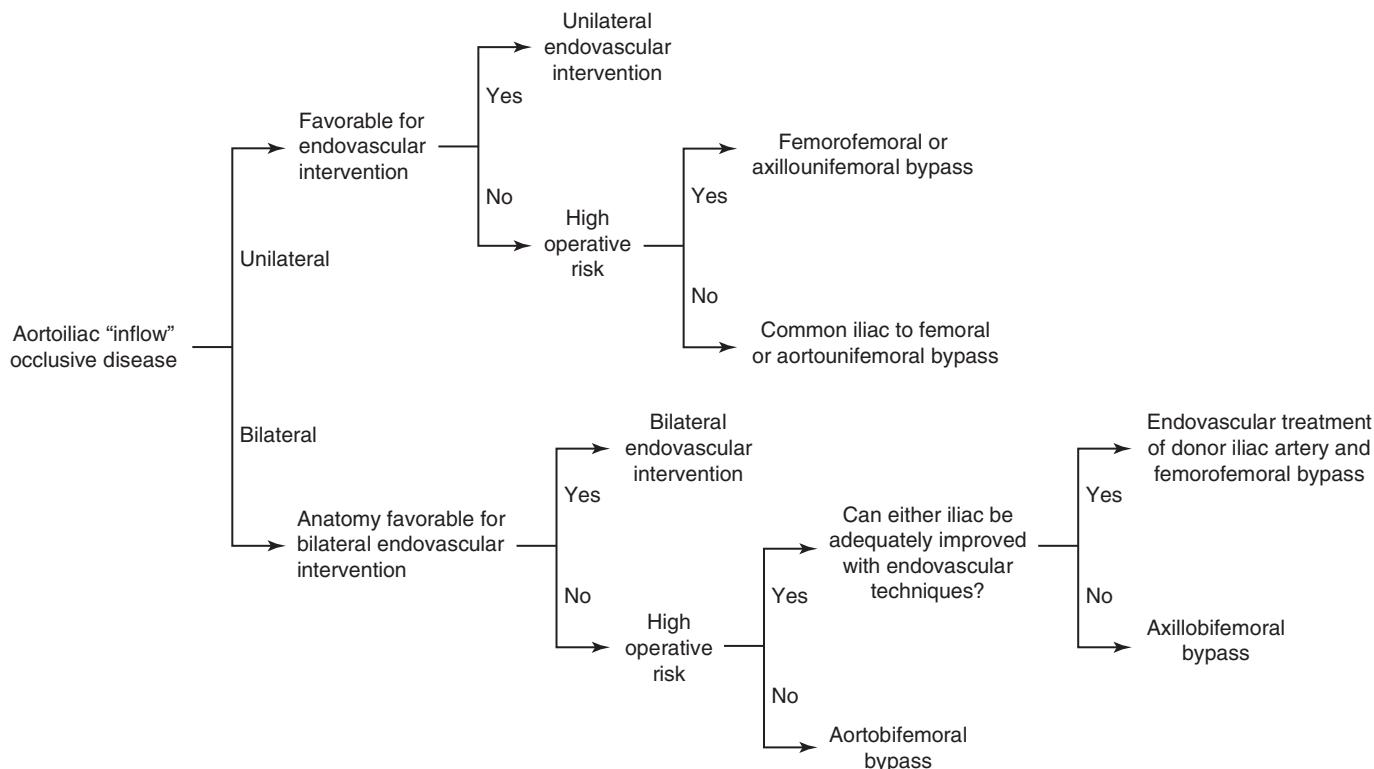
**Figure 110.4** Typical course of the obturator bypass graft, in this case originating from the most proximal portion of the right external iliac artery, passing through the obturator foramen, and terminating at the popliteal artery.

by bringing the tunnel between the adductor longus and brevis muscles. Anastomoses to the inflow and target arteries are performed in conventional fashion with heparin or other suitable anticoagulation during the time that the arteries are clamped. Conventional end graft-to-side native artery anastomoses as described elsewhere in this text are nearly always appropriate for both donor and recipient arteries.

Shaw and Baué's first three cases were all performed with polyester textile grafts. However, it is clear from the original publication that there was persistent infection in at least two of these operations, one patient ultimately dying from complications of infection, and we would recommend autologous grafts whenever possible. In my personal experience I have never used anything other than an autologous vein graft, but a prosthetic graft may be required in some cases.

Just as is the case with the other two procedures described in this chapter, obturator bypass probably does not perform as well as the index procedure of femoropopliteal bypass as measured by patency. Five-year estimated primary patency is probably in the range of 50%–60%.<sup>50–52</sup> However, once again this procedure is far superior to the alternatives and provides satisfactory early outcomes in the situations for which obturator bypass is appropriate.<sup>23,53,54</sup> We use the same postoperative protocol for obturator bypass graft surveillance (ankle–brachial indices, ankle level continuous wave Doppler waveforms, and graft duplex scan every three months in year one, every 6 months in year 2, and yearly thereafter) as we do for conventional infrainguinal bypass grafts.<sup>29</sup> Complications specific to obturator bypass include urinary bladder injury or other visceral injury at the time of surgery.

## CHAPTER ALGORITHM



## SUMMARY

Each of the procedures described in this chapter will provide acceptable perfusion of the target limb and acceptable patency in the long term. Limb loss is rare for all of these procedures with a patent bypass graft. Obturator bypass can be expected to perform well hemodynamically and with respect to patency nearly as well as a conventional infrainguinal bypass. However, it is clear that femorofemoral and axillofemoral bypass do not achieve quite the same excellent hemodynamic and patency results seen after direct aortofemoral bypass. Nevertheless, each of these procedures provides a way to solve a difficult problem in patients not suitable for the more conventional procedures due to comorbidities, infection, or other patient factors. The indications and patient selection for femorofemoral and axillofemoral bypass have evolved and on balance these procedures are likely less often used than would have been the case 20 or 30 years ago. Nevertheless, familiarity and experience with these procedures is essential to the practicing vascular surgeon since these may be the best way to solve some very difficult problems. Obturator bypass may be increasingly common due to the continued increase in the number of transfemoral endovascular procedures and parenteral recreational drug use, each of them accompanied by a risk of femoral arterial infection. Although not often the first choice for most patients requiring infrainguinal bypass, in the face of groin infection, previous surgery or radiation in the groin, or other unusual situations that dictate avoidance of arterial reconstruction in the groin, the obturator bypass is an essential procedure to maintain perfusion of the leg.

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*Best-designed and conducted study (and to our knowledge the only level 1 evidence) comparing the two commonly used prosthetic graft materials in axillofemoral and femorofemoral bypass.*

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A complete reference list can be found online at [www.expertconsult.com](http://www.expertconsult.com).

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