
C 4.3 Surgery

C 4.3.1 Indications
Immediate surgical revascularization is indicated in the profoundly ischemic limb, that is, class IIb and early class III (see Figure 17) (see C 2.3, Clinical Classification of Acute Limb Ischemia, p S142). Catheter embolectomy is also usually preferred for emboli to a nonatherosclerotic limb. Emboli in nonatherosclerotic limbs usually result in profound ischemia (IIb or III) and therefore are best treated surgically. In considering operative versus percutaneous revascularization, it must be recognized that the time from the decision to operate until reperfusion may be substantially longer than anticipated because of factors outside of the surgeons' control (eg, operating theater availability, anesthesis preparation, technical details of the operation).

Recommendation 60: Indications for surgery in acute limb ischemia
Immediately limb-threatening ischemia (class IIb and early class III) is preferentially treated surgically.

C 4.3.2 Surgical Technique
Emboli are preferentially removed surgically if they are lodged proximally in the limb or if there is reason to suspect that they have impacted on a nonatherosclerotic limb. When no further clot can be retrieved, an angiogram or angioscopy should be performed to visualize distal vessels. In up to one third of cases, there is residual thrombus, which, because of the continuing occlusion of the run-off vessels, can lead to failure. Some form of intraoperative monitoring of the adequacy of clot removal is required. The most common of these is "completion" angiography performed before arteriotomy closure. Fiberoptic endoscopy also has been advocated for this purpose but is probably inadequate for distal artery visualization.

Distal clot may be treated by intraoperative thrombolysis with instillation of high doses of thrombolytic agents for a brief period followed by irrigation or additional passages of the balloon catheter. Repeat angiography followed by clinical and Doppler examination of the patient should be performed on the operating table. This will determine whether the procedure has been adequate or whether additional attempts at distal clot removal or even bypass are needed. Percutaneous clot aspiration or thrombolysis, at a later point when the risk of hemorrhage is reduced, also has been recommended. It is important to continue efforts until there is reasonable assurance of a viable extremity. As a last resort, isolated limb perfusion technique has been advocated to reduce the systemic effects of thrombolysis.

Unlike embolism, in arterial thrombosis, an underlying local lesion must be sought after clot
extraction, in addition to residual thrombus. Often this may be suspected from the tactile sensations and need for deflation at points during the withdrawal of the inflated balloon catheter. Here completion angiography will help decide between proceeding with a bypass or PTA.

Fortunately, arterial thrombosis superimposed on an already narrowed artery will ordinarily cause a less severe degree of ischemia because of predeveloped collaterals. Under these circumstances, patients may not be operated on initially but will undergo catheter-directed lytic therapy.

**Recommendation 61: Perioperative angiography**

Unless there is good evidence that adequate circulation has been restored, eg, bounding pulses, reactive hyperemia, or excellent distal Doppler signals, intraoperative angiography should be performed to identify any residual occlusion or critical arterial lesions requiring further treatment. Imaging should be repeated so that complete clot clearance can be demonstrated.

### C 4.4 Results of Surgical and Endovascular Procedures for Acute Limb Ischemia

Catheter-directed thrombolysis (CDT) has become a commonly employed technique in the treatment of ALI. In the first randomized, controlled small study of surgery versus thrombolysis in patients with ALI (of duration between 24 hours and 14 days), the 1-month limb salvage rates were 87% and 90% for surgery and thrombolysis, respectively. Secondary procedures were, however, required in a considerable number of cases. Between 1994 and 1996, three large, prospective, randomized trials were reported that focused on the comparison of CDT and surgical revascularization (SR) for treatment of acute limb ischemia. Other studies have been reported but are not considered here because in some cases there was a lack of prospective randomization, selection bias, or case exclusions.

Limb salvage and mortality rates are recognized as the most important outcome, and the 1-year data are summarized in Table 36. Comparison of these studies is limited by certain differences in protocol and case mix (eg, acute vs subacute or chronic limb ischemia; thrombotic vs embolic occlusion; native vs bypass graft occlusion; proximal vs distal occlusions). End points in each of the studies also vary: the Rochester study used “event-free survival”; the STILE trial used “composite clinical outcome”; and the TOPAS study used “arterial recanalization and extent of lysis.” Only the Rochester trial showed any advantage for CDT by primary end points. The STILE trial favored surgery, and the TOPAS study showed no difference. Other advantages for CDT could only be shown by post hoc subgroup analysis. Moreover, none of the three published reports contain follow-up data regarding those patients treated concurrently at the participating institutions but not enrolled in the three studies; such data would help to determine the extent to which patients who might have been considered appropriate candidates for the respective therapies were not randomized.

In the Rochester study, patients with class II limb-threatening ischemia of less than 7 days duration were randomly assigned to either CDT with urokinase or SR. This included patients with both thrombotic and embolic occlusions of native arteries and bypass grafts. Any anatomic lesions were subsequently treated with balloon angioplasty or surgery, but predominantly the

| Table 36: Comparison of catheter-directed thrombolysis (CDT) and surgical revascularization (SR) in treatment of limb ischemia |
|---|---|---|---|---|---|---|
| **Results at** | **Patients** | **Limb salvage (%)** | **Mortality (%)** | **Patients** | **Limb salvage (%)** | **Mortality (%)** |
| Rochester | 12 mo | 57 | 82 | 16 | 57 | 82 | 42 |
| STILE | 6 mo | 246 | 88.2 | 6.5 | 141 | 89.4 | 8.5 |
| TOPAS | 12 mo | 144 | 82.7 | 13.3 | 54 | 81.1 | 15.7 |
latter. Although the cumulative limb salvage rates were identical in both groups (82%), the 12-month mortality rates were markedly higher in the surgical group (42% vs 16%, p = 0.01). This was primarily as a result of the increased frequency of in-hospital cardiopulmonary complications in the surgery group (49% vs 16%, p = 0.001). This study indicated a clear survival advantage of thrombolytic therapy in the characteristically high-risk patients treated acutely during an episode of truly limb-threatening ischemia.

The STILE trial enrolled patients with thrombotic native artery or bypass graft occlusions of less than 6 months’ duration. Unfortunately, close to three quarters of these patients had ischemia of over 14 days’ duration, and, importantly, the number with class II limb-threatening ischemia was negligible. According to prestudy statistical analysis, the trial was originally designed to include a total of 1,000 patients. However, the interim analysis showed a highly significant difference at 1 month in the rate of ongoing/recurrent ischemia (54.0% vs 25.7%, p < 0.001) and the composite clinical outcome (61.7% vs 36.1%, p < 0.001) in the thrombolytic group compared with the surgical group. The trial was therefore terminated prematurely. A critical feature of this and the other trials was the higher-than-anticipated incidence of failure to successfully traverse the occlusion with a guidewire (28% of patients), obviating lytic therapy. These patients were then considered treatment failures on an intention-to-treat basis. Whether these strictly monitored trial data are closer to the truth than clinical reports have suggested has been debated.

The disappointing overall results have led to the STILE data often being presented without the higher rates of ongoing or recurrent ischemia and major complications for thrombolysis and with postrandomization stratification into “before” and “after” 14 days of ischemia. The cut-off of 14 days is arbitrary (and probably unrealistic) in discussing the outcome of “acute” limb ischemia. The results of thrombolysis are not statistically different between the two periods (although the results of surgery performed sooner than 14 days being much worse than when it is performed after more than 14 days improves the comparison in favor of thrombolysis for the early period). Nevertheless, the early period presents a more reasonable view of thrombolysis in the acute setting.

In the trials discussed here, very few patients enrolled had acute limb ischemia category II or greater as defined in Recommendation 45 and Recommendation 47. The frequent citing of these references in discussions on ALI has led to a review of the results as follows (accepting that they may apply to only a small subset of patients with ALI): patients with less than 14 days’ duration of ischemia had fewer deaths or amputations combined at 6 months in the CDT group compared with the SR group (15.3% vs 37.5%, p = 0.01). Even with this finding, the combined clinical outcome favored surgery. This trend was reversed in the group of patients presenting with “chronic” symptoms (>14 days’ duration), although the difference was not statistically significant (17.8% vs 9.9%, p = 0.08). Subgroup analysis disclosed that, among patients with native artery occlusions (at 30 days), those treated with CDT had a greater incidence of ongoing/recurrent ischemia (54.7% vs 23.5%, p < 0.001) and a worse limb salvage rate (4.1% vs 2.0% major amputation, p = 0.364) compared with the surgical group. Weaver et al carried out a further subgroup analysis of STILE patients with native artery occlusions. In patients with less than 14 days’ duration of ischemia, at 1 year by intent-to-treat, the mortality rate was less in the CDT group (6.3% vs. 18.8%, NS), but the amputation rate was higher compared with surgery (6.3% vs 0%, NS). The persisting/recurrent ischemia and major complications were higher for thrombolysis. Thus, in the STILE trials, there seems to be a trade-off between mortality and amputation and persistent/recurrent ischemia, and major morbidity (Table 37).

The TOPAS trial investigated patients with limb ischemia of less than 14 days’ duration caused by embolic and thrombotic native artery and bypass graft occlusions. The phase I report emphasized the comparison of three different dosages (2,000 IU/min, 4,000 IU/min, 6,000 IU/min) of recombinant urokinase. Primary end points were recanalization and extent of clot lysis on the arteriogram 4 hours after the infusion. There was no significant difference among
Table 37: Summary of major findings of the retrospective analysis of the STILE trial data.

<table>
<thead>
<tr>
<th>Data group</th>
<th>Time</th>
<th>End point</th>
<th>Surgery (%)</th>
<th>CDT (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>1 mo</td>
<td>Composite clinical outcome</td>
<td>36.1</td>
<td>61.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(morbidity, recurrent ischemia, complications)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>1 mo</td>
<td>Ongoing/recurrent ischemia</td>
<td>25.7</td>
<td>54.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subgroup analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All vessels ≤14 days</td>
<td>6 mo</td>
<td>Death, amputation</td>
<td>37.5</td>
<td>15.3</td>
<td>0.01</td>
</tr>
<tr>
<td>All vessels &gt;14 days</td>
<td>6 mo</td>
<td>Death, amputation</td>
<td>9.9</td>
<td>17.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Native artery ≤14 days</td>
<td>12 mo</td>
<td>Mortality</td>
<td>18.8</td>
<td>6.3</td>
<td>NS</td>
</tr>
<tr>
<td>Native artery &gt;14 days</td>
<td>12 mo</td>
<td>Major amputation</td>
<td>0</td>
<td>6.3</td>
<td>NS</td>
</tr>
<tr>
<td>Native artery (all duration)</td>
<td>1 mo</td>
<td>Ongoing/recurrent ischemia</td>
<td>23.5</td>
<td>54.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Native artery (all duration)</td>
<td>1 mo</td>
<td>Major amputation</td>
<td>2.0</td>
<td>4.1</td>
<td>0.364</td>
</tr>
</tbody>
</table>

*Intent-to-treat analysis. 28% technical failure (failure to traverse occlusion) with CDT.

The three urokinase dosages in achieving recanalization. The dose of 4,000 IU/min urokinase was shown to be the safest, with the lowest incidence of hemorrhagic events.

Comparison of CDT for the different urokinase dosages showed no significant difference in amputation-free survival rates and no advantage over surgery. The actual procedure performed was less extensive than predicted in 49.7% of CDT patients as compared with 13.8% of SR patients. However, in the procedure severity scale used, thrombectomy or PTA were considered lesser procedures than digital or transmetatarsal amputation. Thrombectomy with revision/repair of an existing bypass graft was considered a lesser procedure than placement of a new bypass. A subsequent analysis of the TOPAS trial determined which patient factors predicted successful therapy in terms of amputation-free survival. Of 28 variables, eight were found to be predictive using a Cox proportional hazards multifactor analysis. None of these eight favored one form of treatment over another. The length of occlusion, however, predicted whether a patient would fare better with thrombolysis or surgery, with occlusions shorter than 30 cm doing better with surgery and those longer than 30 cm doing better with CDT.17

The only statistically significant overall survival benefit of CDT was found in the Rochester trial and was related primarily to patients with cardiac disease.6 These findings were interpreted to suggest that CDT may be safer for such patients and can achieve equivalent limb salvage. The magnitude of the surgical procedure was reduced in approximately 50% of patients in whom CDT constituted initial therapy even though treatment of underlying lesions was predominantly surgical. The type of agent used—urokinase, recombinant urokinase, or recombinant tissue plasminogen activator—was not shown in the various trials to play a role in determining the results of CDT. Bleeding complications in patients treated with CDT occurred in 5% to 20% of patients, but in most this was categorized as minor. No predictors of major bleeding could be identified by patient characteristics, although a fibrinogen level less than 150 mg/dL increased the likelihood of major bleeding.

A meta-analysis reviewing two of these trials has shown an advantage in limb salvage and mortality for catheter-directed thrombolysis.18 Reviewing the data from the few randomized, prospective studies in ALI, CDT may be viewed as offering advantages when compared with surgical revascularization in terms of reduced mortality rates and complexity of the surgical procedure required in exchange for a higher rate of failure to avoid persistent or recurrent ischemia, major complications, and ultimate risk of amputation. In addition, it appears that reperfusion with CDT is achieved at a lower pressure and may reduce the risk of reperfusion injury.18 Thus, if the limb is not immediately or irreversibly threatened, CDT offers a lower-risk opportunity for arterial revascularization.19 Using this approach, the underlying lesions can be further defined by angiography, and the appropriate percutaneous or surgical revascularization proce-
dure can be performed. Therefore, it seems reasonable to recommend CDT as initial therapy in these particular settings, to be potentially followed by surgical revascularization as needed (see Recommendation 57, p S151).

Critical Issue 22: Comparison of therapeutic options for acute limb ischemia
There is a need for prospective, randomized trials to rigorously compare catheter-directed thrombolysis (CDT), percutaneous mechanical thrombectomy (PMT), percutaneous aspiration thromboembolectomy (PAT), intraoperative thrombolysis, and surgical revascularization (SR) for the treatment of thrombotic versus embolic occlusions of native arteries versus bypass grafts, and that are specifically designed to include determination of cost-effectiveness and long-term outcome, including functional status.

Critical Issue 23: Further factors when considering choice of treatment for acute limb ischemia
There is a need, when considering choice of treatment for acute limb ischemia, for further studies to obtain additional information concerning:

• the length of time that the lower extremity will tolerate profound ischemia without permanent damage
• The effect of the duration of the occlusion on the success of recanalization

References
C 4.5 Immediate Postprocedural Issues

C 4.5.1 Reperfusion Injury

Reperfusion injury is one of the most common complications leading to prolonged morbidity. The sudden return of oxygenated blood to acutely ischemic muscle causes the generation and release of oxygen free radicals and subsequent cellular injury. Failure to anticipate or recognize this complication can lead to the rapid development of compartment syndrome and myonecrosis. Treatment consists of fasciotomy. Prevention of reperfusion injury is the focus of much experimental research, but effective drug regimens have not been established for clinical practice.

Other long-term complications include the persistence of sensory or motor impairment. Loss of sensation in the toes and foot increases the likelihood of development of neurotrophic ulceration. Such ulcers are more common in the setting of impaired motor function. A polyneuropathy is the most common form of residual nerve impairment, although selective damage to individual nerves has been reported. The manifestations of nerve damage include wasting of the small muscles of the foot associated with painful dysesthesias, leading to an alteration in gait. Treatment consists of attempts at pharmacological control of pain, bracing of the foot, and physical therapy until neuromotor function improves. This may require many months of intensive therapy.

C 4.5.2 Fasciotomy

Although fasciotomy in every case would produce unacceptable and unnecessary morbidity, in practice it is often left too late. Compartment pressure measures have been employed to some advantage, but there is disagreement on pressure criteria for proceeding with fasciotomy. After revascularization, fasciotomy also should be performed if there are signs of increased ischemia without evidence of reocclusion. A long skin incision and opening of all compartments, including the deep posterior compartment, are needed unless initial inspection shows no muscle death or swelling.

Recommendation 62: Fasciotomy in acute limb ischemia

Fasciotomy should be performed at the primary procedure if the acute severe ischemia has been prolonged or if signs of increased compartment pressure develop. This applies irrespective of how the clot was removed.

Critical Issue 24: Predicting the requirement for fasciotomy

There is a need for an easy and accurate test to predict which patients require a fasciotomy.

C 4.6 Treatment of the Underlying Lesion

Simply removing the occluding lesion, whether it is a thrombus or an embolus, is unlikely to be successful as the sole treatment. If the occlusion was caused by an embolus, the source has to be identified and treated. If the acute occlusion was caused by thrombosis superimposed on preexisting atherosclerosis, then this underlying lesion also has to be treated to avoid a recurrence of the acute occlusion. This may be accomplished by either an endovascular or an open surgical technique, depending on the balance between durable success and procedural risk. The results of PTA in the literature are dependent on morphology of the lesion and patient selection and the criteria used to define technical and clinical success and patency. These are well discussed in sections B 4.3, Endovascular Procedures for Intermittent Claudication (p S97), D 4.6, Aortoiliac Disease—Endovascular Treatment (p S214), D 4.9, Infrainguinal Lesions—