Lower Extremity Arterial Thrombolysis

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Lower extremity arterial thrombolysis has proven to be a safe and effective means of treating acute limb ischemia due to in situ thrombosis or embolic occlusion. It is best utilized in patients with acute occlusions of less than 7 days duration and offers survival benefits compared with surgery primarily due to the lower risk of cardiopulmonary complications. Limb salvage rates are equivalent between thrombolysis and surgical thrombectomy but bleeding complications are more common with thrombolysis.

PREPROCEDURE

Proper patient selection is critical to successful thrombolysis. Absolute contraindications include a nonviable limb (i.e., absent motor and sensory function), ongoing severe bleeding, and intracranial lesion at high risk for hemorrhage. It is important to recognize that thrombolytic therapy most often requires at least 6 to 8 hours of continuous infusion prior to improvement in ischemia. Therefore, patients with rapidly progressing or profound ischemia are *not* good candidates for thrombolysis. Neither is any patient who cannot lay flat and cooperate during infusion therapy. As a rule of thumb, the more severe the underlying disease process causing acute occlusion, the more difficult it will be to achieve technically adequate thrombolysis. Conversely, a prosthetic graft, which may be more prone to thrombosis compared with a native venous bypass, is usually easier to treat.

The most important fact to recognize is that successful thrombolysis merely reestablishes the baseline condition, which was not optimal to begin with. Therefore, after successful thrombolysis, additional therapy (e.g., angioplasty of anastomosis, surgical revision, anticoagulation) must be done to ensure a durable result. If this later course is not pursued, repeat thrombosis is a

foregone conclusion. Patients should have pretherapy laboratories including complete blood count, prothrombin, partial thromboplastin, fibrinogen, fibrin degradation products, and international normalized ratio. Type and screen blood products prior to initiation of therapy.

PROCEDURE

Access

I typically perform a double-wall puncture using a micropuncture set on the femoral artery contralateral to the occlusion. (Many interventionalists recommend single-wall puncture but I have not seen one significant bleeding complication in my career at the access site attributable to a double-wall puncture using a 21-gauge needle.) I find a double-wall puncture technically easier to perform reliably, particularly for residents and fellows. If pulses are weak, an ultrasound-guided puncture can be performed, although I typically start by puncturing the artery at the middle third of the femoral head using fluoroscopic guidance.

Planning Angiography

After securing arterial access, I insert a 6F up and over sheath such as a Balkan sheath. A high-quality diagnostic pelvic and an extremity angiogram is performed via a 5F pigtail catheter (Fig. 1a). If necessary, a more selective angiogram is performed via an end-hole catheter positioned in the contralateral external iliac or common femoral artery (Fig. 1b, 1c).

If surgical bypass has been performed, it is crucial to have a facile understanding of the relevant anatomy. Typically, the most proximal portion of the thrombosed graft or vessel will be visualized as a small “nipple” that will enable catheterization.

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Figure 1 Thrombolysis of occluded prosthetic left femoral to posterior tibial artery bypass graft. (A) Pelvic arteriogram demonstrates right common iliac artery aneurysm and patent inflow to left femoral artery. (B) Arteriogram of the left thigh shows chronically occluded superficial femoral artery stents. The bypass graft is not visualized. (C) Arteriogram of left ankle shows delayed filling of the posterior tibial and dorsalis pedis arteries. (D) Fluoroscopic image shows infusion catheter being advanced into thrombosed bypass graft E–G. Angiogram obtained through the infusion catheter after period of thrombolysis shows antegrade flow in the bypass graft and continuous flow to the foot.

Thrombolytic Infusion

Presuming that the iliac arteries are widely patent, I advance the end of the sheath over the aortic bifurcation in the contralateral common iliac artery. The sheath performs several important functions. It prevents the infusion catheter from kinking at the aortic bifurcation. It is used to administer a low dose of heparin during infusion (~300 IU heparin per hour) and for all blood draws.

If the thrombosed vessel or graft is able to be catheterized, a soft tipped guidewire is advanced distally through the clot. This *guidewire traversal test* gives prognostic information regarding potential success of thrombolysis. Hard thrombus (i.e., chronic and organized) tends to be resistant to thrombolysis and portends a poor prognosis for endovascular therapy. I lace a small dose of thrombolytic agent (e.g., 2–4 mg of tissue plasminogen activator) directly along the entire course of the clot as I pull the catheter back. Subsequently, the wire is again advanced distally and the end-hole catheter is exchanged for an infusion catheter. I do not have a strong preference for a particular type of infusion catheter. In my experience, most work very well. The infusion catheter is positioned into the clot with the most proximal sidehole in the patent portion of the vessel (Fig. 1D).

We currently use tissue plasminogen activator (TPA; alteplase, Genentech, South San Francisco, CA) exclusively for limb thrombolysis although this is an institutional bias and I am not convinced there is clear superiority of one agent versus another. During the day, we infuse at 0.5 mg per hour (e.g., 5 mg of TPA is mixed in a 500-mL bag of normal saline and infused at a rate of 50 mL per hour) and repeat angiogram is performed through the infusion catheter every 4 to 6 hours (Fig. 1E–G). At night, the infusion is continued until the morning. As noted above, heparin is administered at a rate of ~300 IU per hour and patients are monitored in the intensive care unit.

Laboratories

We monitor routine laboratories plus complete blood count, prothrombin, partial thromboplastin, fibrinogen, and fibrin degradation products. Patient is typed and screened for blood prior to infusion.

Common Pitfalls

INABILITY TO VISUALIZE ORIGIN OF TARGET GRAFT

Usually, you can see the stump of the target graft. If not, there are two general strategies. The first is to probe *anteriorly* with a curved catheter such as a C1 recognizing that anastomoses often originate from the **anterior** wall of the femoral artery. If this fails to

uncover the graft, I typically position the catheter in the expected region of the anastomosis and simply initiate thrombolysis hoping that the stump of the graft will be “uncovered” during infusion therapy (Fig. 2).

EARLY FAILING (<1 YEAR) BYPASS GRAFTS

When bypass grafts occlude in the early postoperative period, it typically indicates a technical problem that requires surgical revision or a poor quality vein graft. Neither is particularly amenable to percutaneous thrombolysis.

SITE BLEEDING

Localized bleeding can usually be handled by simply compressing the site for 10 minutes—for refractory cases, the infusion is decreased by 50% with increased compression. For continued bleeding, infusion is again decreased by 50% and heparin discontinued with continued compression. Finally, cryoprecipitate is given with continued pressure and infusion is discontinued at the discretion of the physician.

DECREASED FIBRINOGEN

There is no clear protocol for decreased fibrinogen levels. Some interventionalists do not monitor levels. I tend to evaluate patients on a case-by-case basis and occasionally use levels to influence my decision to alter course of therapy if levels fall dramatically (i.e., <100 mg/dL).

INCREASING LEG PAIN

Increasing pain is common during thrombolysis, which some have termed the “storm before the calm” and often indicates progressive thrombolysis. Nonetheless, the limb should be examined for motor and sensory loss and the possibility of reperfusion injury (i.e., compartment syndrome) should always be considered. For pain control, morphine 5 mg intravenous is administered every 1 to 2 hours as needed.

ENDPOINTS

There are four possible endpoints to thrombolytic infusion:

1. Reestablishing flow in the graft or vessel with complete clot dissolution (Fig. 3) or reestablishing baseline condition.
2. Thrombolytic stagnation: no change in angiogram with continued thrombus over two or three incremental angiograms
3. Complication: remote bleeding, compartment syndrome, irreversible ischemia
4. Maximal dose: generally considered to be 40 mg with catheter-directed infusion therapy

Figure 2 Catheter-directed thrombolysis in patient with unclear anatomy. (A) Initial angiogram of the left thigh shows occlusion of superficial femoral artery. After probing the area of common femoral artery, the graft could not be catheterized. (B) Fluoroscopic image of end-hole catheter positioned in common femoral artery for initiation of thrombolysis. (C) Angiogram through catheter after 8 hours shows patent proximal graft. (D) Fluoroscopic image of infusion catheter advanced into graft.

Figure 3 Catheter-directed thrombolysis of femoral-to femoral artery bypass graft. (A) Initial digital subtraction angiogram shows catheter advanced from right femoral approach through the graft into the native left external iliac artery. There is a high-grade stenosis of the common femoral artery at the graft anastomosis which was presumed to cause thrombosis. (B) Angiogram obtained through infusion catheter after trial of thrombolysis showing flow within the graft. (C) Digital subtraction angiogram of both thighs showing antegrade flow in both superficial femoral arteries.

DISCUSSION

Several methods exist for administering a fibrinolytic agent. As noted above, for proximal occlusions (at or above the knee) I prefer a direct intrathrombotic approach with continuous infusion of a fixed amount of thrombolytic agent (TPA 0.5 mg/h) after intra-thrombus bolusing. For very distal occlusions, I more commonly use an end-hole catheter positioned above the occlusion, particularly if the size of the catheter approaches the size of the occluded artery. Thrombolysis has proven to be at least equivalent to surgery in many patients with acute limb-threatening ischemia and is considered the standard of care for acute peripheral arterial occlusions. In my experience, the most important prognostic indicators for success are vessel outflow and ability to easily advance a guidewire through the occluded segment. If the outflow is robust to the foot, flow can usually be reestablished relatively quickly. As noted earlier, some intervention after clot

dissolution is nearly always mandatory to ensure a durable result (Fig. 4).

Recently, we have begun to use computed tomography angiography (CTA) more liberally to evaluate patients with lower extremity pain and suspected acute limb-threatening ischemia. I have found this to be helpful, especially in patients who have had previous surgery at outside institutions to help triage those who may benefit from catheter-directed thrombolysis and to plan the intervention. CTA can also help to differentiate in situ thrombosis from peripheral embolization in some patients.

Many interventionalists combine mechanical and pharmacologic thrombolysis. The general strategy is to “debulk” clot with mechanical devices then “clean up” the residual clot using pharmacologic thrombolysis. I employ this strategy most commonly for deep venous thrombolysis where infusions are commonly protracted and clot burdens are larger. The cost effectiveness of this

Figure 4 Thrombolysis and angioplasty of prosthetic left femoral to popliteal bypass graft. (A) Initial pelvic arteriogram showing moderate global atherosclerotic disease of iliac arteries. (B) Angiogram of the left thigh fails to demonstrate bypass graft. (C) Digital subtraction image shows infusion catheter advanced into thrombosed bypass graft. Note stagnant contrast within the bypass. (D) Angiogram obtained through the infusion catheter shows flow reestablished within the bypass.

strategy is unclear and is currently undergoing further investigation.

The most feared complication of thrombolysis is intracranial hemorrhage. In our institutional experience, this has occurred twice. Both instances occurred shortly after urokinase became unavailable when we were relatively inexperienced with TPA. We used

doses threefold higher (1.5 mg per hour) than our current regimen and both patients were nearly systemically heparinized. Currently, we use doses of no more than 0.5 mg per hour with subtherapeutic heparinization. A second complication that must be quickly recognized when it arises is reperfusion injury (i.e., compartment syndrome). This was the topic

Figure 4 (Continued) (E) Angiogram of bypass shows high-grade distal anastomotic stenosis. (F) Fluoroscopic image shows balloon angioplasty of anastomotic stenosis. (G) Angiogram after angioplasty shows good flow through the angioplasty site without residual stenosis.

for a previous Morbidity and Mortality case in *Date Journal*.

SUGGESTED READINGS

Kessler R, Funaki B. Compartment syndrome following external iliac artery stenting and lower extremity thrombolysis. *Semin Intervent Radiol* 2009;26:159–163

van den Berg JC. Thrombolysis for acute arterial occlusion. *J Vasc Surg* 2010;52:512–515

Patel N, Sacks D, Patel RI, et al; Society of Interventional Radiology Technology Assessment Committee. SIR reporting standards for the treatment of acute limb ischemia with use of transluminal removal of arterial thrombus. *J Vasc Interv Radiol* 2003;14(9 Pt 2):S453–S465