Acute Arterial Thrombosis Prevention and Management During SFA and Popliteal Interventions

Acute limb ischemia carries a serious short-term risk, and knowing the ins and outs of treatment options is crucial for lowering the rates of morbidity, mortality, and amputation.

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Acute arterial thrombosis can cause myocardial infarction (MI), ischemic stroke, and acute limb ischemia (ALI). The annual incidences of such events are high; there were 935,000 MI and 795,000 stroke events in the United States in 2008.[1] However, the incidence and prevalence of acute peripheral arterial thrombosis is not well described, even in lieu of its devastating consequences, including morbidity, mortality, and limb loss.[1,2]

Acute peripheral arterial thrombosis may occur after endovascular intervention as a result of the erosion or rupture of atherosclerotic plaque[3,4] and/or distal embolization (DE). Both occurrences activate the coagulation and platelet systems, resulting in occlusion of the artery via thrombus formation. When left untreated, acute thrombotic ischemia will cause tissue infarction.[5] Within as early as 4 hours, nerves and muscle damage are evident before any histological or tissue changes occur.[5] Irreversible damage can be seen as early as 6 hours if ischemia is complete and there is no effective collateral circulation. The ensuing oxygen deficiency leads to anaerobic metabolism that produces and accumulates lactic acid, thromboxane, and potassium. The combination of high lactic acid levels, thromboxane, and potassium with myoglobin released from infarcted muscles causes renal failure, myocardial depression, and arrhythmias.[5,6] The effects of such events are most pronounced on reperfusion of severely ischemic limbs. Edema of ischemic tissues can cause compartment syndrome, and cellular edema can interfere with the microcirculation, rendering a no-flow state even after revascularization.

This article discusses the prevention and management of acute peripheral arterial thrombosis during endovascular intervention of the superficial femoral and popliteal arteries.

PREVENTION

Anticoagulation

Arterial thrombi produce tissue ischemia by impeding blood flow or by embolism into the distal vessels. Therefore, thrombotic events require activation of blood coagulation and platelets. Naturally, these two mechanisms are closely linked due to thrombin being a major clotting enzyme created by blood coagulation that activates platelet involvement in the coagulation process. Hence, the use of anticoagulants and platelet-suppressing pharmaceuticals is necessary to prevent and manage acute arterial thrombosis.[7] Typical anticoagulant drugs, or antithrombotic drugs, are antithrombin stimulators and direct thrombin inhibitors.[8] The two major drugs that will be discussed in this article are the antithrombin stimulator heparin and bivalent thrombin active-site inhibitor bivalirudin.[4]

Heparin interrupts the natural process of the coagulation cascade by inhibiting cofactors that promote proper thrombin formation.[4] A typical measurement of heparin treatment is activated clotting time (ACT). Although some studies claim that heparin doses of 100 U/kg to

achieve an ACT of 300 to 350 seconds should be the primary target, the majority of interventional cardiologists rely on ACT values between 200 and 250 seconds to maintain minimal bleeding.[9] Endovascular approaches within the superficial femoral and popliteal arteries aim for an ACT of at least 200 seconds.

Bivalirudin is a bivalent thrombin inhibitor that binds to the thrombin's catalytic site and fibrinogen-binding site.[10] This results in the inhibition of fibrinogen to be cleaved to fibrin and to the inhibitions of major thrombin factors.[11] The combined effects of the anticoagulant and antiplatelet activity are extremely useful in the setting of acute arterial thrombosis. The recommended dosage for bivalirudin during percutaneous peripheral interventions (PPI) is fixed and linear, rendering frequent monitoring not imperative.[12]

One of the largest PPI trials with bivalirudin is the Angiomax Peripheral Procedure Registry of Vascular Events (APPROVE) trial.[12] APPROVE is a multicenter study that summarizes the safety of replacing heparin with bivalirudin in patients undergoing PPI of the renal, iliac, or femoral arteries. Table 1 is a summary of femoral artery clinical outcomes within the trial.

Patients were treated with bivalirudin as the only procedural anticoagulant, with glycoprotein IIb/IIIa inhibitors used at the observers' discretion. Procedural success was determined at residual stenosis of ≤ 20%. Other successes included analysis of ACT values, ischemic and bleeding complications, as well as times to sheath removal, ambulation, and discharge. In this study, bivalirudin was administered as a 0.75-mg/kg bolus followed by a 1.75-mg/kg per hour intravenous infusion for the duration of the procedure.

Both aspirin and clopidogrel were administered to 96.8% and 95% of patients, respectively. Glycoprotein IIb/IIIa inhibitors were used in 4.4% of the patients in the study. Overall procedural success was calculated to be 95% in all patients and 94% in the femoral patient population.[12] ACT measurements were consistent among patient groups with mean ACT values 5 minutes after bolus injection at 343.53 seconds for the femoral population. This high ACT average was clear evidence of bivalirudin demonstrating consistent anticoagulation. During the study, there were no deaths and one MI (0.5%) through 30 days. There were four instances of unplanned revascularization or surgical interventions (2.2%), and amputation occurred in two patients (1.1%) by 30 days. Bleeding events were also found to be low. Protocol-defined major and minor hemorrhage occurred in 1.6% and 10.3% of patients, respectively, and the rates of TIMI major and minor hemorrhage were 0.6% and 2.2%, respectively.

TABLE 1. FEMORAL ARTERY CLINICAL OUTCOMES IN THE APPROVE TRIAL

Outcomes: Femoral (N = 184)	n	%
Procedural success	172	94
Death	0	0
MI	1	0.5
Unplanned revascularization/ surgical intervention	4	2.2
Amputation	2	1.1
Major bleeding, protocol defined*	3	1.6
Minor bleeding, protocol defined*	19	10.3
TIMI major hemorrhage*	1	0.6
TIMI minor hemorrhage*	4	2.2

**Hemorrhage by discharge.*

Choosing proper antithrombotic drugs is imperative to the success of PPI. Clinical trials show the superiority of heparin and bivalirudin as primary drugs in anticoagulation therapy to prevent acute arterial thrombosis.

Embolic Protection

Thrombus burden, type of lesion, and device characteristics are potential predictors of DE during peripheral lower extremity interventions. Any type of treatment device can result in DE. The incidence of embolic debris after angioplasty and stenting has been reported to be 0% to 25%, 2.8% to 7% with thrombolytic therapy, and 25% to 65% with rheolytic thrombectomy.[13] As more aggressive treatment techniques, such as atherectomy and stenting, are adopted to treat long, chronic lesions, there may be a higher propensity for clinically significant DE.

Shammas et al[14] describe the higher incidence of DE in a randomized trial comparing lower extremity arterial interventions with primary balloon angioplasty versus SilverHawk atherectomy (Covidien) and adjunctive balloon angioplasty. In patients treated with atherectomy, the SpiderFX embolic protection filter (Covidien) was used in 17 patients, 11 of whom (64.7%) had macroembolization with debris > 2 mm at its longest axis captured in the filter. None of these patients had embolization distal to the filter. In addition, one patient without a filter who had been treated with atherectomy had a clinically significant DE that required further mechanical and pharmacologic therapy. In the primary percutaneous transluminal angioplasty arm, embolic filter placement was used in 10 patients, none of whom had significant macroembolization captured in the filter.

Compared with percutaneous transluminal angioplasty, atherectomy was associated with significant DE (P = .001). This study is consistent with earlier studies in which atherectomy was a strong predictor of significant DE.[9-12] However, the use of embolic filter protection appears to be effective in capturing large debris and is therefore likely to reduce clinically significant DE distal to the filter.

Shrikande et al[15] also attempted to define the proper lesion and patient characteristics that were more prone to DE. They tried to identify lesion types that might be more prone to embolization and stratify different techniques for their embologenic potential. A total of 34 embolization events occurred for a rate of 1.6%. The Jetstream (Boston Scientific Corporation) (4 of 18; 22%) and Diamondback 360 (4 of 18; 22%) had significantly higher rates of embolization than PTA alone (5 of 570; 0.9%), PTA and stent (5 of 740; 0.7%), SilverHawk atherectomy (14 of 736; 1.9%), and laser atherectomy (2 of 55; 3.6%; P = .001). The rates of embolization of SilverHawk (P = .068) and laser atherectomy (P = .076) were not significantly different compared with PTA alone or PTA and a stent.

There was a significantly higher rate of embolization for in-stent restenosis (6 of 188; 3.2%) and chronic total occlusions (15 of 615; 2.4%) than with stenotic lesions (13 of 1,334; 0.9%; P = .01). A significantly higher rate of embolization was found in TASC C and D lesions (26 of 1,208; 2.2%) compared with TASC A and B lesions (8 of 929; 0.9%; P = .018). There was no significant difference in the embolization rates between TASC C and D lesions (P =.849). Rates of DE were not affected by preoperative runoff status (P = .152). Furthermore, there was no difference in DE rates between lesions undergoing single or multiple interventions (P = .108). The higher rate of DE in in-stent restenosis could reflect the nature of the material within the stent, which may be softer and more friable than standard atherosclerotic plaque. Although this was a retrospective review, it does highlight differences in embolization rates based on lesion type.

Several distal embolic protection devices have been introduced to allow the capture and retrieval of friable, lipid-rich plaque, as well as calcific plaque constituents. These include filters attached to a wire, such as Angioguard XP (Cordis Corporation), Accunet (Abbott Vascular), FilterWire EZ (Boston Scientific Corporation), SpiderFX, Gore Embolic Filter (Gore & Associates), and FiberNet (Medtronic, Inc.), as well as and filters that are not attached to a wire (Emboshield Nav6, Abbott Vascular).

Overall, each embolic system holds its own intrinsic limitations, and protection provided by these devices is not nearly "complete."[13,16] Sources of incomplete embolic protection include device crossing profile (with larger profiles leading to potential embolization), incomplete filter apposition (mainly in bending segments of the vessel), filter pore size being too small or large, insufficient protection of secondary branches, device-inflicted vessel wall trauma, and impediment of platelet/white cell embolization from the target area.[13,16]

MANAGEMENT

It is estimated that the incidence of ALI in the general population is 14 per 100,000.[17] The two major causes of ALI are embolism or thrombosis.[17] An embolism may activate the coagulation and platelet system, ultimately resulting in thrombus formation. ALI management is imperative to reduce both mortality and morbidity. Five management approaches are discussed herein.

Basic Syringe Aspiration

These devices are universally available and easy to assemble and use. The majority of these systems contain a monorail catheter with a central lumen that communicates with one or multiple holes found at the tip.[18] The catheter is connected proximally to a syringe for manual aspiration. Manual thrombectomy devices commonly used in clinical settings are Pronto (Vascular Solutions), Export (Medtronic, Inc.), Driver CE (Medtronic, Inc.), QuickCat (Spectranetics Corporation), and Hunter (IHT Cordynamic). Each of these devices are founded on the same basic principles; however, they differ by means of catheter material, aspiration lumen size, and configuration, with differences in deliverability and thrombus extraction.[18]

Advanced Mechanical Aspiration

The Aspire mechanical thrombectomy system (Control Medical) allows users to increase, maintain, or pulse the thrombectomy force. There are two system components, the aspirator and large lumen catheters. The aspirator has a one-way valve to allow fluid to flow only into the barrel. There is another one-way valve on the plunger to purge air, aspirant, or other fluid in the barrel. The handle allows clinicians to operate the aspirator with one hand while they control the catheter with the other hand. There are two large-lumen catheters as part of the system, the MAX 5 has a 5-F or 0.066-inch outer diameter and a 0.055-inch inner diameter, and the MAX 6 has a 0.076-inch outer diameter with a 0.065-inch inner diameter. The aspirator and catheter are a closed fluid system, allowing 250 mL to be aspirated without multiple catheter disconnections.[19]

Electromechanical Aspiration

The Indigo system (Penumbra, Inc.) contains the electrical Penumbra MAX pump, aspiration catheter, and separator.[20] The continuous vacuum pump allows for hands-free aspiration and clot extraction. There are two catheters, which are 6- and 4-F in diameter. They are 132 and 150 cm in catheter length and are tracked over a 0.014-/0.038-inch wire.[20] These catheters have the largest extraction lumen designed for vessels below the knee.[20] The proprietary separator allows for clot dislodgement in the catheter while thrombus is being extracted into the collection canister on the pump.

Rheolytic Thrombectomy

The AngioJet system (Boston Scientific Corporation) contains a catheter attached to a drive unit. The drive unit has a piston pump that creates a high-pressure pulsed flow rate of 10,000 psi at 40 mL/min through a hypotube.[21] The hypotube releases saline at a loop in the catheter tip. This system is designed to remove thrombus using the Venturi-Bernoulli effect with several high-velocity, high-pressure saline jets that are present through the orifices in the distal tip of the catheter. These cause a localized low-pressure zone, creating a vacuum-like effect with the entrainment and dissociation of thrombus.[22]

Catheter Thrombolysis

The Cragg-McNamara valved infusion catheter (Covidien) is a single-lumen catheter created to be introduced into the vasculature over a guidewire.[23] As soon as the catheter is in position, thrombolytic agents can be delivered through a standard luer lock adapter at the proximal end. The infusion area is marked by the distal and proximal radiopaque indicator to promote fluoroscopic visualization. The valved tip of the catheter allows infusion without requiring a tip-occluding guidewire. Typically, these patients should not be treated for more than 72 hours.

CONCLUSION

Patients presenting with ALI have a severe short-term outlook both in terms of loss of the leg and mortality, with 30-day amputation rates between 10% and 30% and a mortality rate of approximately 15%.[17] The fact that overall mortality rates after intervention for ALI have not improved dramatically over the last 2 decades unquestionably reflects on the severity of the underlying diseases in these high-risk patients.[17]

Percutaneous thrombectomy and mechanical thrombolytic devices have evolved, with significant improvements in the efficiency of clot removal while limiting DE. It is anticipated that these results will continue to improve in combination with the introduction of locally active thrombolytic agents that can be administered in high doses with limited adverse systemic effects and utilization of embolic protection devices. ■

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