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Indigo® Mechanical Thrombectomy System for Thromboembolic Disease

Experts within the endovascular community share their experiences with and perspectives on clot management protocols and the risks and benefits of the various available treatment options.

Arterial thromboembolism is a substantial health care problem. It is a cause of stroke, myocardial ischemia, mesenteric ischemia, and acute limb ischemia. Common options for treatment of a thromboembolic condition causing a threatened limb include surgical embolectomy, percutaneous thrombectomy, and/or thrombolysis. Historically, thromboembolectomy devices have shown limited efficacy. Limitations of the existing devices often include poor trackability in distal vasculature, failure to remove organized thrombus, distal embolization, and insufficient capability to revascularize vessels with large clot burdens.

This article describes the Indigo® System (Penumbra, Inc.), a new technology that became commercially available in the United States in 2014. The Indigo System is proving to be a useful tool for managing thromboembolic disease in the peripheral arteries, including visceral, upper extremity, and especially popliteal and below the knee.

The Indigo System is proving to be a useful tool for managing thromboembolic disease.

The following section contains case reports that describe the successful use of the Indigo System in the treatment of thromboembolic occlusion of peripheral arteries. Experts in the endovascular community then share perspectives on their current treatment strategies for peripheral thromboembolic disease and acute limb ischemia, including their thoughts on the costs, risks, and benefits of the different treatment options now available.

CASE 1: SUCCESSFUL SUCTION THROMBECTOMY OF ACUTE LOWER EXTREMITY THROMBOSIS AND EMBOLIZATION AFTER CARDIAC CATHETERIZATION

Ziv J. Haskal, MD, FSIR, FAHA, FACR
Professor of Interventional Radiology
University of Virginia
Charlottesville, Virginia

Nicholas Hendricks, MD
University of Virginia
Charlottesville, Virginia

A 75-year-old woman with a past medical history of coronary artery disease, diabetes, and peripheral arterial disease presented acutely after cardiac catheterization with a cold right leg. The cardiac catheterization access was achieved via the right groin. The cardiac angiogram was negative for coronary disease, and no intervention was performed. Manual compression was used for puncture-site hemostasis, and thereafter, the patient began complaining of severe right leg pain.

The interventional radiology division was urgently consulted. The patient's extremity was notably ischemic—the right leg and foot were cool to the touch,

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"This may evolve to replace surgical emboloectomy as well, especially in smaller vessels because of its angiography-guided efficiency and low risk of vessel trauma."

with marked changes in skin color, and foot pulses were no longer detectable. She had bilateral common iliac artery stents placed 5 years earlier. In retrospect, the lower extremity angiogram had demonstrated a bulky calcified plaque causing severe stenosis in the right common femoral artery at the same site as the cardiac access. The plaque was visible by grayscale sonography. Acute thrombosis and possible distal embolization related to the plaque (and subsequent compression) was presumed.

Angiography was performed from a left femoral approach and showed the iliac stents and arteries to be patent. A 6-F long vascular sheath was placed into the contralateral external iliac artery. Right lower extremity angiography demonstrated occlusion of the distal superficial femoral artery (SFA) extending into the proximal infrapopliteal arteries (Figure 1). The severe stenosis of the right common femoral artery was redemonstrated. The patient was anticoagulated with bivalirudin due to a concern for heparin-induced thrombocytopenia. We deemed tissue plasminogen activator–infusion thrombolysis to be contraindicated due to the need for rapid therapy and a notable risk of bleeding from the recent cardiac right femoral access.

Indigo thrombectomy catheters were advanced into the embolus over a 0.014-inch guidewire. A 5-F Indigo CAT5 catheter and Indigo Separator™ wire were used predominantly in the SFA and popliteal artery, and a 3-F CAT3 was used in the anterior and posterior tibial arteries. After a series of suction passes with the Indigo devices, angiography demonstrated near complete resolution of the thrombus (and possible embolus) in the SFA, popliteal, and proximal runoff vessels (Figures 2 through 4).

Approximately 200 mL of blood was aspirated into the pump canister. The patient's foot was notably warmer at the end of the procedure. A bivalirudin infusion was continued overnight, and distal right foot pulses were noted the next morning. She subsequently underwent an elective right common femoral endarterectomy 1 month later and reported no claudication symptoms at last follow-up.

DISCUSSION

In these types of cases, the Indigo System may function akin to an image-guided embolectomy, efficiently obviating (or accelerating) lysis. This may evolve to replace surgical embolectomy as well, especially in smaller vessels because of its angiography-guided efficiency and low risk of vessel trauma.

Figure 1. Initial right iliac angiography demonstrates the eccentric plaque and stenosis in the common femoral artery (at the site of cardiac catheterization and manual compression).

Figure 2. Angiography of the SFA demonstrates the acute embolus (upper arrow) and thrombosis. The faintly seen popliteal artery also contains thrombus (lower arrow).

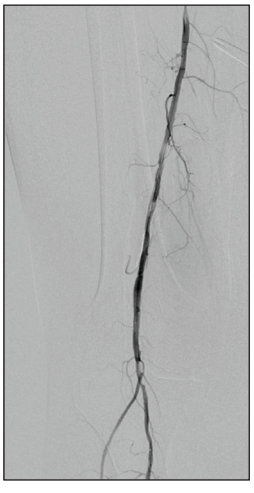

Figure 3. After aspiration thrombectomy using the Indigo System, flow is restored to the SFA and popliteal artery.

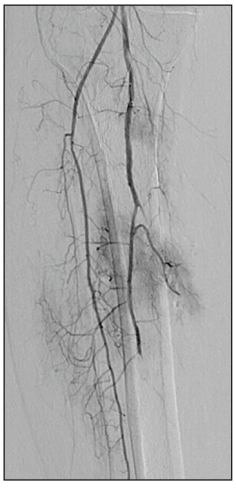

Figure 4. Angiography after use of the CAT3 catheter and Separator wire within the anterior tibial artery demonstrates restoration of flow.

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CASE 2: ENDOVASCULAR EMBOLECTOMY OF SMA EMBOLUS IN A PATIENT WITH ACUTE MESENTERIC ISCHEMIA

Rahul S. Patel, MD
Assistant Professor of Radiology and Surgery
Division of Interventional Radiology
Icahn School of Medicine at Mount Sinai
New York, New York

Patients with acute or subacute arterial occlusions have historically been treated with open surgery or thrombolytics. It is now possible to rapidly treat these patients in a single procedure, using the Indigo System. The Indigo System has been effective in aspirating thrombo-emboli in a variety of vessels, such as the superior mesenteric artery (SMA) case described here.

CASE REPORT

A 77-year-old woman presented to the emergency department with acute onset of abdominal pain. She had a history of type II diabetes mellitus, hypertension, coronary artery disease, and atrial fibrillation. Her surgical history was significant, including coronary artery bypass grafting, TAH-BSO, and open cholecystectomy. Her INR at presentation was 1.4, with a lactate of 2. CT angiography was performed (Figure 1), which demonstrated a filling defect in the mid portion of the SMA without evidence of bowel wall thickening or free air. There was also an anterior abdominal wall hernia containing bowel and omentum.

Given her relative stability, the decision was made to attempt a rapid endovascular solution first.

From a right common femoral approach, the SMA was cannulated, and angiography was performed, demonstrating the embolus at the mid portion of the SMA (Figure 2). A 6-F guide sheath was placed at the orifice of the SMA, and the Indigo CAT5 catheter easily tracked to the occlusion. The Indigo System rapidly and effectively removed the clot (Figure 3) and embolus. Angiography post-Indigo demonstrated restoration of flow through the SMA and all of its branches (Figure 4), thus avoiding the need for tissue plasminogen activator use or open surgery. The patient was placed on a heparin drip and was restarted on warfarin with a goal INR of 2 to 2.5.

Prior to the Indigo System, the only option to treat a visceral vessel emergently was surgical embolectomy. Now with the Indigo device, we have the option to treat these using an endovascular technique with a highly trackable catheter, and extract the clot much more rapidly.

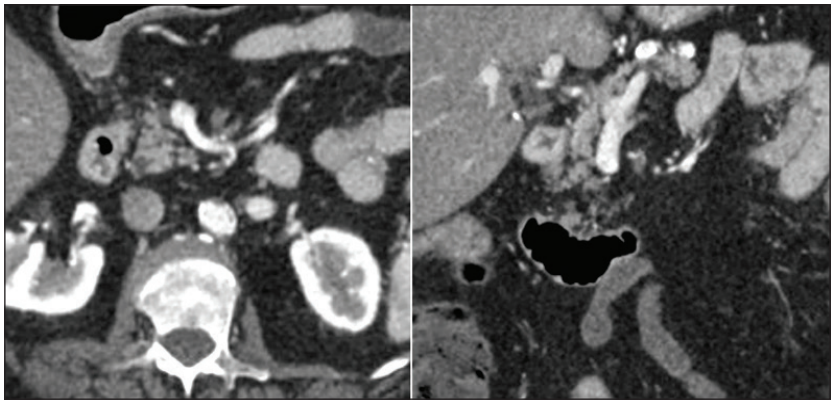

Figure 1. Preprocedural CT angiography showing a filling defect in the mid portion of the SMA.

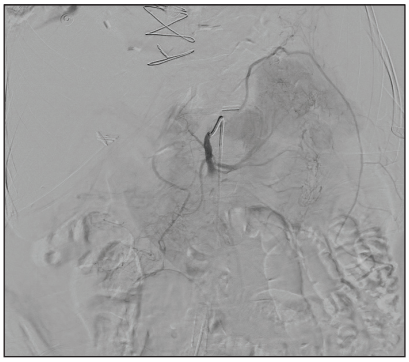

Figure 2. Angiography showing the embolus at the mid portion of the SMA.

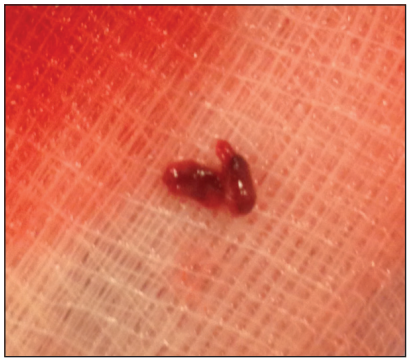

Figure 3. Clot removed by the Indigo System.

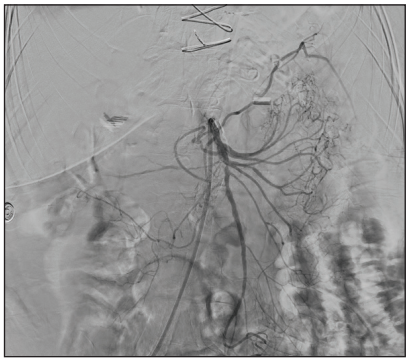

Figure 4. Angiography post-Indigo showing restoration of flow through the SMA and all of its branches.

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CASE 3: MECHANICAL THROMBECTOMY AFTER ANGIOPLASTY OF A LONG SFA OCCLUSION

George L. Adams, MD, MHS
Rex Health Care
University of North Carolina Health System
Raleigh, North Carolina

Vinayak Subramanian, BS
Department of Biomedical Engineering
North Carolina State University
Raleigh, North Carolina

Chronic total occlusions (CTOs) are encountered in 40% of all peripheral vascular interventions.[1] These lesions are technically challenging and successful treatment is largely dependent on having a variety of endovascular tools and on the skill set of the interventionist.[2-4] The plaque morphology dictates the tools required to successfully treat the patient. The plaque morphology of CTOs typically contains areas laden with thrombus.[5] Treatment of such lesions with conventional balloon angioplasty and/or stent may result in distal embolization, complicating the course of treatment. A mechanical thrombectomy device such as the Indigo System can be used to aspirate the thrombus, reducing the risk of distal embolization.

CASE REPORT

A 58-year-old man with a history of hypertension, dyslipidemia, and tobacco abuse presented with left lower extremity claudication. Left lower extremity ankle-brachial index measurement was diminished and duplex ultrasound revealed an SFA occlusion with thrombotic-appearing plaque. Angiography of the left lower extremity revealed a CTO of the left SFA, with three-vessel outflow (Figure 1).

The CTO in the left SFA was approximately 30 cm in length and was successfully crossed with an 18-g CTO wire followed by a support catheter. The wire and support catheter went smoothly, with no significant impairment, suggesting that this may be thrombus. Intravascular ultrasound was performed, which confirmed this suspicion. A 2- X 200-mm balloon was used to perform percutaneous transluminal angioplasty of the SFA to make a pilot channel. The Indigo System was used to successfully aspirate white clot. Percutaneous transluminal angioplasty of the SFA was repeated with a 5- X 150-mm balloon (Figure 2A), and a 50% residual stenosis with obvious thrombus in the vessel was revealed (Figure 2B). The Indigo System was again used to successfully aspirate white clot from a long segment of the SFA (Figure 3). Four 6- X 80-mm Zilver PTX drug-eluting stents (Cook Medical) were then placed, followed by post-dilatation with a 5- X 200-mm balloon, which resulted in 10% residual stenosis (Figure 4).

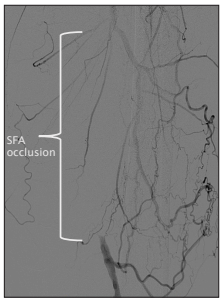

Figure 1. Preintervention angiography showing a CTO of the SFA.

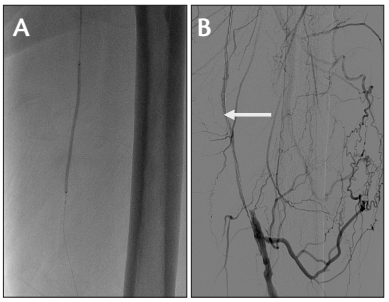

Figure 2. Initial percutaneous transluminal angioplasty of the SFA (A). Thrombus formation in the SFA (arrow, B).

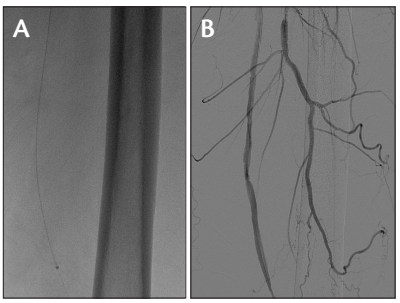

Figure 3. Mechanical thrombectomy using the Indigo System in the left SFA (A). Selective angiography of the left SFA after thrombectomy (B).

Figure 4. Postintervention angiogram showing multiple drug-eluting stents placed in the left SFA.

In this patient who had a long SFA occlusion, the plaque morphology was determined to be soft and thrombogenic based on the initial duplex ultrasound, feel of the crossing wire and catheter, and intravascular ultrasound images. These findings prompted the need for mechanical thrombectomy. Utilization of the Indigo System helped reduce the risk of distal embolization following balloon angioplasty and prior to stent placement. Formation of thrombus is common when treating the long CTOs that are commonly seen in patients with peripheral arterial disease. The Indigo System is valuable to have in the interventionist's toolkit in order to treat these technically challenging lesions.

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Q&A SESSION WITH EXPERTS IN THE FIELD ON THE INDIGO SYSTEM

PARTICIPANTS

James F. Benenati, MD
Fellowship Program Director
Medical Director, Noninvasive Vascular Lab
Miami Cardiac & Vascular Institute
Miami, Florida

Frank R. Arko III, MD
Co-Director, Aortic Institute
Professor of Cardiovascular Surgery
Sanger Heart and Vascular Institute
Carolinas Healthcare System
Charlotte, North Carolina

Richard R. Saxon, MD, FSIR
San Diego Cardiac and Vascular Institute and
San Diego Imaging Medical Group
San Diego, California

Mahmood K. Razavi, MD, FSIR
Director of the Department of Clinical Trials
Vascular and Interventional Specialists of Orange County
St. Joseph Heart & Vascular Center
Orange, California

What would you describe as your workload with respect to arterial clot management? In what types of situations are you dealing with clot?

Dr. Benenati: We have a very busy arterial practice that includes a large number of critical limb ischemia and acute limb ischemia cases. We are dealing with thrombosis from native vessels as well as cardiogenic emboli. We are also faced with distal emboli during complex revascularization cases.

Dr. Arko: We have a large practice in the Carolinas that deals with both arterial and venous thrombosis. Within our patient population, we have patients who present with acute arterial ischemia from critical limb ischemia, as well as our own group of patients who have undergone either percutaneous or open surgical revascularization. These patients often present emergently and require urgent intervention.

Dr. Saxon: Clot management is ubiquitous throughout interventional radiology. From reopening thrombosed dialysis fistulas, deep vein thrombosis treatment, pulmonary embolism management, and arterial occlusions, we deal with thrombus on a daily basis. Specifically, with respect to arterial thrombi and emboli, there are multiple vascular beds and clinical situations that come to mind, which include stroke, acute mesenteric ischemia, renal ischemia, and acute limb ischemia.

From a vascular surgery perspective, how would you describe your treatment protocol when a patient presents with an acutely ischemic foot?

Dr. Arko: When a patient presents with an acutely ischemic foot, we begin with anticoagulation and then proceed to the angio suite for further evaluation. We attempt to proceed with an endovascular solution with newer mechanical aspiration catheters in the majority of these patients, especially in the distal and visceral vasculature.

> ...the risks of lytics are bleeding and intracranial hemorrhage. These can be avoided with the use of newer mechanical thrombectomy devices that are extremely trackable.
> — Dr. Arko

And what is the protocol from an IR perspective?

Dr. Saxon: When a patient presents with acute limb ischemia, we have to first decide if the ischemia is critical enough that immediate revascularization is required—generally, those with loss of sensation or muscle strength versus those who have less critical ischemia who can tolerate the time required for thrombolytics, which is often first-line therapy. In those who have distal vascular bed occlusions (distal popliteal arteries and below), surgical techniques can be suboptimal. Endovascular mechanical revascularization using newer, more trackable aspiration catheters has become a routine part of our toolbox for patients with popliteal and tibial occlusions who don't have time for lytics, have failed to improve with lytics, or who have contraindications to lytics.

Dr. Razavi: I believe that the management of patients with acute limb ischemia is fairly standardized, regardless of the specialty of the treating physician. Practically, however, local expertise and referral patterns tend to determine how

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> The benefits of newer mechanical clot removal devices are that you can achieve a successful result quicker, which in turn saves time and money.
>
> — Dr. Benenati

a patient is treated. In patients with acute limb ischemia stage I to IIa, we usually treat them by catheter-directed therapies (lysis, aspiration, thrombectomy, etc.). Patients with stage IIb presentation may go to the operating room for surgical thrombectomy or to the angio lab for percutaneous thrombectomy. Advancements in tools and technologies nowadays allow us to treat many such patients using percutaneously in a single session.

What would you say is the established treatment paradigm for acute limb ischemia? Are you seeing a shift in this paradigm toward single-setting management?

Dr. Benenati: If the foot is viable, the current standard is to initiate thrombolysis, unless the leg is so threatened that it mandates immediate surgical intervention. More recently, our paradigm has been changing for focal or shorter segments of clot using the Penumbra Indigo System as a first-line therapy.

Dr. Arko: My own practice continues to evolve. Early in my career, I often used a variety of percutaneous mechanical thrombectomy devices in an attempt to clear the clot and revascularize the foot. However, I have since gone more to a lytic-first approach for most of these patients, as I believed that the results of early devices were often limited in their efficacy. However, with newer devices, I am hopeful that a single setting may still be possible.

Dr. Saxon: Our paradigm is shifting to a greater use of mechanical endovascular removal of thrombi, emboli, and intraprocedural emboli. Use of the Indigo System has been almost universally successful at quickly removing these emboli and can even be tracked down into the pedal vessels.

What about the visceral arteries or when a patient is contraindicated to lytics and the clot is either focal or in the popliteal and distal vessels? How do you treat these patients?

Dr. Arko: As a surgeon, visceral embolectomy is typically performed when a patient presents with acute mesenteric ischemia. If we are able and have time, we have started using the Indigo System in these cases. I have experience with two patients in which we have utilized this system successfully in order to prevent a laparotomy. Furthermore, we have successfully utilized this system in the popliteal and tibial arteries, as well as in the radial and ulnar arteries in patients with hand ischemia. To date, we have seen good results and have been able to avoid the use of lytics.

Dr. Benenati: Up until recently, visceral emboli were dealt with primarily with surgical intervention or thrombolysis, depending on the location of the clot and the severity of the patient's symptoms. Currently, I choose newer aspiration catheters as my go-to for treating visceral emboli. With some more refinement of the Penumbra catheters, there is potential for this technology to become first-line therapy for acute arterial clot management anywhere in the peripheral vasculature.

How often are you dealing with intraprocedural complications? Is the Indigo System a good option for these types of cases? Are certain lesions more prone to resulting in an intraprocedural complication?

Dr. Saxon: Although intraprocedural distal emboli are rare, they are far more common during some of the more complicated revascularizations (eg, atherectomy). They are also common when trying to reopen somewhat more chronically thrombosed, failed femoropopliteal stents or stent grafts. The Indigo System has made these emboli far easier to manage.

Dr. Arko: We try to limit the number of intraprocedural complications that we have, but they certainly do occur. One of the more dreaded complications is distal embolization. When this happens, it can be difficult to achieve a successful outcome. Certainly, the Indigo System is a value-added device that can assist with this complication both quickly and successfully. This device tracks well to the lesion, even in very small vessels with no risk of damaging the vessel based on its design.

Dr. Razavi: Intraprocedural thromboembolism is on the rise due to the greater complexity of the lesions treated percutaneously and the increased use of debulking devices. Recanalization of chronic total occlusions, interventions immediately following catheter-directed thrombolysis, and the use of certain atherectomy devices have all been shown to be associated with a higher risk of atheroembolization. Although the risk is still quite low, operators should be familiar with the strategies to reduce that risk and newer tools that allow effective treatment. Better and more trackable aspiration catheters have made this task easier.

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Dr. Benenati: Occasionally, intraprocedural thrombus or emboli can be a result of the intervention. When we have those, we try to manage it immediately. The Indigo System is our primary tool for managing these complications due to the trackability of the catheter, as well as the ability to maintain continuous vacuum allowing for continuous large-bore aspiration, even in the distal vessels. We have, in fact, tracked the CAT 3 Indigo catheter down to the plantar arch and have successfully extracted emboli.

What are the benefits and risks of mechanical clot removal versus thrombolysis?

Dr. Arko: Certainly, most people would say that the risks of lytics are bleeding and intracranial hemorrhage. These can be avoided with the use of newer mechanical thrombectomy devices that are extremely trackable, and due to continuous vacuum, are highly effective at extracting clot. Furthermore, if lytics are used, the patient will require either a telemetry bed or an intensive care unit bed, depending on the institution. The use of a mechanical thrombectomy device can eliminate these complications and costs when it is successful.

Dr. Benenati: The benefits of newer mechanical clot removal devices are that you can achieve a successful result quicker, which in turn saves time and money. Not all emboli are fresh or lysable. If you embolize plaque, mechanical aspiration is ideal because plaque cannot be lysed or fragmented with other mechanical devices. One of the risks of mechanical devices is that you can worsen the situation and traumatize the vessel. There is always a risk that you can only get partial restoration of flow and may still have to perform thrombolysis with a mechanical device. The good news is that, usually, mechanical aspiration catheters do not create distal emboli that worsens the clinical situation and do not cause problems that may contraindicate thrombolysis later.

Dr. Razavi: There is a paucity of data on percutaneous single-session treatment of patients with acute limb ischemia. Hence, operators or institutions will have to rely on their own experiences to determine the risk/benefit ratio of such an approach versus catheter-directed thrombolysis or surgery. One obvious benefit is the potential reduced risk of bleeding associated with lytic agents. Others include possible reduced hospital stay and cost.

What factors would indicate that a patient is ideal for a first-line Indigo System approach? In what situations would it make sense to supplement a mechanical approach with lytic or surgery?

Dr. Benenati: Patients who are ideal for the Indigo System approach are those who have clot in any of the visceral arteries or renal arteries, is isolated to the infrapopliteal vessels, or clot that is in the femoral/popliteal/upper extremity segments (ie, focal or short segments). The early data analysis of the PRISM trial shows a high technical success rate at restoring normal flow and a very low complication rate related to the device. This study is still ongoing, and we should have more data over the next year.

> …using this device may ultimately drive costs down while still keeping all of your options open.
> — Dr. Benenati

Dr. Saxon: Our approach is evolving as the devices available for performing mechanical thrombectomy evolve. We are now fairly confident in reopening tibial vessels, and we might try this technique first for these size vessels or in acute renal and mesenteric ischemia. We reserve thrombolysis or surgery for failure of mechanical aspiration thrombectomy. On the other hand, larger thrombus burdens associated with iliofemoral or SFA thrombosis are much more difficult to deal with, and we would prefer surgical or lytic therapy as the first line, with mechanical means reserved for failure of other techniques.

How does cost factor into the discussion of the management of acute limb ischemia?

Dr. Arko: In today's environment, cost, as well as quality, is an important issue. Removing thrombus quickly is important, while limiting the risks and costs to the patient and system is important. Certainly, an effective percutaneous thrombectomy device can do this by eliminating or decreasing the amount of lytics used and avoiding a prolonged stay in the intensive care unit.

Dr. Benenati: Managing acute limb ischemia is costly because of the devices, the drug involvement, and the monitored care beds that are often necessary for overnight infusions. If we can avoid longer procedures and overnight infusions in appropriate clinical scenarios, we can help drive the cost way down. Because the cost of complications are potentially lower with the Indigo System, using this device may ultimately drive costs down while still keeping all of your options open.

Dr. Saxon: An analysis of the cost of starting with mechanical thromboembolectomy and proceeding to thrombolysis only if mechanical means fail shows that this might be a far more cost-effective approach than initial use of overnight thrombolytic therapy in all comers. ■