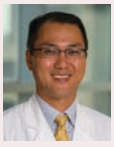
Treating Acute Limb Ischemia With Penumbra's Indigo Aspiration System

Vascular Disease Management spoke with vascular surgeon Jayer Chung, MD, Associate Professor of Surgery at Baylor College of Medicine in Houston, Texas, about treating patients with acute limb ischemia (ALI), the safety and efficacy of Penumbra's computer assisted vacuum thrombectomy technology (CAVT) such as Lightning Bolt™ 7 System to remove thrombus, and his participation in the STRIDE study, an international, multicenter, prospective, single-arm study using mechanical thrombectomy with Penumbra's Lightning technology as frontline treatment for patients with lower-extremity ALI (LE-ALI).



Jayer Chung, MD
Associate Professor of Surgery
Baylor College of Medicine
Houston, Texas

Could you talk about ALI, the disease state and current standard of care?

ALI occurs when there has been abrupt cessation of the normal blood flow to the arteries supplying the lower extremities. This can occur by 1 of 2 processes: 1) By an in situ thrombosis of an atherosclerotic plaque. 2) Alternatively, you can have an embolus, which usually originates from the heart or other areas in the aorta, that unfortunately gets lodged somewhere and thereby obstructs the flow of blood downstream to the embolus. The resultant abrupt cessation of normal circulation results in sudden ischemia to the leg, and that sudden ischemia is limb threatening. Depending on the severity of the ischemia, the risk of major amputation as a result rises significantly and can be as high in some series as 17% to 34%. The traditional treatment for ALI has been open embolectomy with, perhaps, a bypass as needed.

Starting back in the '90s, there's been a slow evolution of endovascular means to try and reopen someone's blood vessels emergently. The first attempts were via thrombolytics, which was performed via a catheter-directed thrombolysis. The way this works is that they insert a catheter across the areas of blockage using normal interventional techniques, after which they initiate a thrombolysis infusion, which nowadays is typically alteplase at a dose of 1 to 4 mg per hour. They wait after about 24 to 48 hours and then see if the vessels had reopened.

Other advances since then have included the AngioJet catheter (Boston Scientific), which uses rheolytic thrombolysis to try and mechanically remove some of the thrombus and/or embolus. These were really the only 2 devices available from about 2010 to about 2015. In the intervening 10 years, there has been an explosion of new devices that have the capability to help remove thrombus. In my opinion, the best one that's come out has been Penumbra's Lightning Bolt 7 aspiration system. It is engineered to detect the difference between blood clot and blood flow. Additionally, it is designed to identify friction within the catheter and orchestrate the rapid opening and closing of the valves to disrupt any resistance between the clot and the catheter tip. This facilitates maximum vacuum force at the catheter tip. This, in combination with the suction aspiration, has provided the largest advancement in the management of ALI.

Can you describe your preferred treatment strategy, including the decision-making process for selecting between various interventions, such as thrombectomy, thrombolysis, or surgical revascularization?

Around 2016 or 2017, we moved to a percutaneous-first approach at our institution for all ALI patients, and very rapidly we moved to a Penumbra-first approach simply because of its improved efficacy. It is to the point now that for all patients with ALI, the first thing that we do is we go to the catheterization lab, do an arteriogram, and likely use Penumbra first, regardless of the etiology, history, location, severity, or the fact that it's a stent first vs a bypass. This allows us to obtain a very rapid perfusion of the limb while still maintaining all our other endovascular options.

Can you discuss any specific challenges or considerations you encounter on addressing thrombus and ALI cases, and how do you navigate these challenges to optimize patient outcomes while minimizing risks, such as limb loss and complications?

Some of the challenges that occur are when patients have had prior interventions—that's probably the number one challenge that we face. It simply becomes a little bit more of a challenge to figure out what is where, exactly. Mitigating that requires a little bit of creativity, a lot of preoperative imaging to make sure that you have as much information about the patient ahead of time, a full history, and a physical. In terms of the history and physical, you ask the patient what procedures they've had before and look at all the incisions on their body to figure out where things are so you have an idea of exactly where things are and what you're going to need to try and reopen.

Another challenge is the team. You can't do this in isolation. It doesn't matter how good you are with your own hands

and your own skills—you need a very competent team around you. For many ALI cases, you do the angiogram, try something, and then see what you've got. There's a lot of improvising that you have to do as you proceed to try and remove the thrombus and treat the ischemia. It's vital that you have a team that's very experienced with all the wires, all the balloons, all the catheters, all the devices out there in order to minimize delays that are caused by people not knowing what they're doing. On the back end, what this requires is the assembly and training of a very good team. What that looks like at our institution is we have regular education sessions on different devices. As they come out, we train as many of the team as we can because we don't know who's going to be on call on any given night. We make sure that we provide an informative education session for them so that should something come in at 2 in the morning, for instance, they're ready.

Can you provide an overview of the STRIDE study and its primary objectives regarding the treatment of LE-ALI?

The STRIDE study is a prospective, multicenter registry that is aimed to evaluate the safety and efficacy of percutaneous aspiration thrombectomy as frontline treatment for the management of ALI. It's a single-arm prospective registry, a study format that's become very popular in device trials nowadays. The exclusion criteria are ALI from traumatic or iatrogenic causes. Inclusion criteria are very broad and include any embolic or thrombotic event that can occur in the native or stented portions or bypass portions of the lower extremities in the setting of Rutherford I to IIB ALI. It does not preclude the use of thrombolytics or other adjunctive devices or balloons. You're allowed to use whatever you'd like afterwards. But the idea was to try a Penumbra-first strategy.

A couple of things drew me to this trial. One is that when they approached me to participate, a "Penumbra-first" approach was already becoming my practice anyway. One of my best friends is a neurointerventional radiologist, and he'd been talking about Penumbra when it first started in the cerebrovascular space for years, and he said, "….You're going to love it when it finally comes out in the periphery…." So I was excited as one of the early adopters because of that, but also, I like the fact that they didn't try to just ram the device down your throat and say you're only allowed to use our device; if ultimately what the patient needs is something else, they want you to use it. That's important because I think that reflects a person's true practice, so this turned out to be a very real-world registry of how to manage ALI with a Penumbra-first strategy.

What were the key findings regarding safety and efficacy?

The key finding is that a Penumbra-first strategy is both safe and efficacious with excellent 30-day limb salvage rates and low mortality. The initial findings showed that we can save a patient's limb more than 98% of time, which is very high with minimal complications. When you look at traditional open vascular surgery to perform an embolectomy, the data suggest an 83% 30-day limb salvage rate. We also recently presented data from a subgroup analysis of the STRIDE study that showed Penumbra's Indigo Aspiration System used in a single session without the need for overnight tPA is safe and effective for patients with LE-ALI. This was an interesting find because thrombolysis carries with it the risk of hemorrhagic complications, and it requires more intensive monitoring in an ICU setting because of this risk. Point of fact, for some patients, we treat with the Penumbra, we maybe balloon something, and after that, they're able to go home that same day.

Were there any unexpected findings or challenges encountered during the STRIDE study? If so, how were they addressed?

I was a little bit surprised at how well it worked. I was a little bit dubious when I first started. My practice was heading that way, but I was still thinking, "Well, you're still going to need to do a lot of adjunctive thrombolysis or additional procedures." And what I found over time during my participation in the study was that the more you familiarize yourself with the device, the better you are at it, and it lessens the need for further interventions going forward. So I was pleasantly surprised and very grateful that I participated in the trial because it worked very well.

My favorite thing about it is that the whole family of catheters has a role. So for instance, let's say you're doing an aspiration in the superficial femoral artery and you get most of it, but take an angiogram and uh-oh, it is a multilevel ALI case. Well, guess what? Now you have another catheter and you can go down there and get it. It allows you to manage ALI for a variety of indications, obtain immediate perfusion, and go chase things even if something goes wrong.

In your opinion, how might the findings of the study influence current clinical practices and treatment algorithms for LE-ALI?

I think it certainly promotes the idea that a percutaneous-first strategy works for ALI. A requirement for embolectomy or bypass for, say, Rutherford class 2B, ie, a more urgent ischemia, or requirement for doing embolectomy or bypass for an embolus. I think with the prior devices, or perhaps if

you were limited to some of the other devices, you might think about that. But with Lightning Bolt 7, you're able to get out embolus equally as well as you can with an open embolectomy. We published another series outside of STRIDE that showed that in our own center, regardless of the etiology, embolus, or thrombosis, you're able to get it out. And the second thing is you're able to achieve rapid reperfusion—so that reason for doing an open-first approach no longer exists. I think the biggest take-home from this study is that Penumbra's innovations work really well, and an endovascular approach works really well, for ALI.

What is the latest innovation to treat ALI? What is CAVT? How does it differ from other mechanical thrombectomy systems?

There are a multitude of devices that are coming to market, it's not just Penumbra, but what Penumbra has done is very clever. First, their catheters are designed to be very atraumatic with different angles that address the various anatomies. For example, you can get a wide sweep with the catheter and engage clot in a way that's atraumatic to the vessel wall. Unlike stent retriever-like baskets that scrape along the vessel wall, CAVT can capture clot without causing damage to the endothelium. They've also recognized that one of the main drawbacks of aspiration thrombectomy was excessive blood loss. So rather than teach the operators when to turn suction off, they developed an algorithm that can detect whether the catheter tip is in a thrombus or an embolus vs free-flowing blood. It can also modulate the aspiration so it works better in acute thrombus, as well as mitigate blood loss.

I think for anybody who treats ALI, it's probably important to know all the devices, but I do think CAVT has probably been the greatest advancement in the last couple years.

How will this technology affect the treatment protocol for ALI patients? What are you hoping to see in the next 3 to 5 years for ALI treatment?

I'm hoping to see more people move toward a percutaneous-first approach. The STRIDE study, as well as others, shows that it's equally effective and efficacious regardless of the etiology and regardless of the patient subgroup. There have been certain subgroups of ALI that have fared worse in the past with traditional techniques, and the one that's most notable is females with ALI, who in the past have done more poorly. They've had higher major amputation rates, higher mortality, lower patency rates, and lower technical success rates. In the STRIDE study, we didn't see that. And in our own series, where we looked at mostly a percutaneous-first approach, we were able to mitigate the sex-based disparities. I think that is one of the greatest take-homes of a percutaneous-first approach. You're allowed to achieve all the things that you can with open surgery without the morbidity associated with it. You're allowed to see the anatomy. You can treat much of the underlying stenosis that may have contributed to some of the ischemia as well. And in so doing, you're able to mitigate many of the disparities that we've seen before. I hope that that's what we see as more of the therapies progress. Outcomes just continue to get better, and hopefully, we can alleviate some of the disparities in healthcare as well. ■

Interview sponsored by Penumbra, Inc. Dr. Jayer Chung is a consultant for Penumbra, Inc.