Update on Endovascular Therapy Options for Acute Limb Ischemia

An overview of the most recent devices available to the interventionalist for the endovascular treatment of acute limb ischemia.

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Acute limb ischemia (ALI) is a devastating event that may lead to amputation or death. ALI presents as pain, pallor, pulselessness, paresthesia, poikilothermia (inability to regulate temperature and cold), and paralysis (the six "Ps"). The most commonly used classification system for ALI is the Rutherford classification system, which qualifies ALI by the degree of limb ischemia, ranging from class 1 (a nonthreatened extremity) to class 3, where ischemia has progressed and limb salvage is unlikely. Historically, open surgical thrombectomy using a Fogarty balloon catheter has been the primary treatment modality and has the advantage of restoring blood flow instantly. When performed in a hybrid operating room using an over-the-wire technique, complication rates may be reduced, and (endovascular) treatment of the culprit lesion (often the case in "acute-on-chronic" occlusions) may be performed in the same session.[1] Although surgical thrombectomy has been demonstrated to be efficacious, it is hampered by a relatively high rate of complications and mortality, with one contemporary series reporting an in-hospital mortality rate of 9.8%.[2]

Catheter-directed thrombolysis (CDT) with urokinase or recombinant tissue plasminogen activator (rtPA) has been proposed as an alternative treatment. Time to restoration of flow is longer, and because of this, CDT is not first-line treatment in some scenarios (≥ Rutherford class 2b). The most recent European Society for Vascular Surgery guidelines do not recommend CDT for treatment of patients with Rutherford class 1 ALI because of the risk of bleeding complications, but it may be considered in Rutherford class 2a ALI.[3] The use of thrombolytic therapy was further affected during the COVID-19 pandemic because it typically requires an intensive care unit (ICU) stay, and availability of ICU beds was limited during that time[4]; more recently, there have been supply chain and production issues for urokinase and rtPA as aftermath of the COVID-19 pandemic. Because of the above-mentioned limitations of surgical thrombectomy and CDT, alternative (endovascular) treatment solutions have been used, and several new devices have become available.

This article is an update to the 2010 ALI overview featured in *Endovascular Today*[5] and provides an overview of the most recent devices for the endovascular treatment of ALI, including the Ekos endovascular system (Boston Scientific Corporation), the Indigo system (Penumbra, Inc.), the Rotarex rotational excisional atherectomy system (BD Interventional), the Jeti hydrodynamic thrombectomy system (Abbott), and some newer devices coming to market.

EKOS ENDOVASCULAR SYSTEM

The Ekos endovascular system uses high-frequency, low-intensity ultrasound. It has been shown that ultrasound can speed enzymatic clot lysis in vitro by loosening fibrin strands and thereby increasing thrombus permeability and exposing more plasminogen receptors for binding.[6] The system consists of a reusable control system that powers the unit and a single-use infusion catheter system. The latter is made up of an infusion catheter with an ultrasonic core. The infusion catheter is a 5.4-F multilumen catheter with two radiopaque markers. The catheter has an 0.035-inch lumen and a working length of 106 cm. The central lumen is also

used for continuous saline infusion during the procedure (needed to cool the ultrasonic core). Drug delivery occurs through three small lumina that are positioned radially around the central lumen that end in holes present over a predefined treatment length (6, 12, 18, 24, 30, 40, or 50 cm). The ultrasonic core has a number of encapsulated radiopaque ultrasound transducers along the distal length of the shaft (corresponding to the treatment length of the infusion catheter with a spacing of 1 cm). The control system consists of a control unit and a catheter interface cable. The control unit houses the user interface, provides electrical power, and serves to monitor the power output, the connection integrity, and the temperature of the infusion catheter during the procedure, with several safety features that shut off the system in case the temperature of the catheter exceeds 43 °C, the power delivery is off limits, and when a connection failure is perceived. After advancing the infusion catheter with the treatment length of choice over the guidewire to the area to be treated, the guidewire is exchanged for the ultrasonic catheter. The ultrasonic catheter is then connected to the control system using the cable. Infusion of thrombolytic (rtPA at 1 mg/hour) is started on the drug infusion lumen, and at the same time, saline is infused through the inner central lumen.[6] Subsequently, the ultrasound power is applied, and control angiography is scheduled on a regular basis until flow is restored sufficiently. Several studies, including one randomized controlled trial, have demonstrated accelerated thrombolysis with shorter time to full flow restoration and reduction of the amount of thrombolytic agent used.[3] Given the time needed to achieve full flow restoration, this technique may be used in patients with Rutherford class 2a ALI but is less likely to be beneficial in patients with more severe grades of ischemia. For those patients, mechanical removal of the thrombotic occlusion is recommended.[3]

INDIGO SYSTEM

The first reports of the use of aspiration thromboembolectomy to treat distal emboli and peripheral arterial thrombosis described a technique using simple, large-bore guiding catheters. Aspiration was done using a 50-mL (lockable) syringe. Use of an introducer with a detachable hemostatic valve is recommended to avoid thrombotic material detaching and protruding from the tip of the aspiration catheter during withdrawal through the valve of the sheath. A disadvantage of the aspiration with a syringe is the lack of a continuous vacuum, leading to a loss of aspiration power.

The Indigo system consists of an Indigo aspiration catheter (available in sizes of 3, 5, 6, and 8 F), a separator (in a matching size range), reinforced tubing, and a continuous vacuum pump (Pump Max). The pump allows for a continuous vacuum, and the catheters have a reinforced tip that does not collapse during maintained suction. The purpose of the separator is to break up thrombus that may block the catheter tip, thus preventing occlusion of the catheter and obviating the need for removal of the catheter to be cleared of occluding thrombotic material. The catheter design potentially reduces damage to the vessel wall, hemolysis, and distal embolization. When using the device, it is important not to pass the distal edge of the occlusion and "break through" only after (complete) removal of the proximal part of the thrombus/embolus. Adjunctive procedures are oftentimes necessary and include angioplasty and stenting (for treatment of the culprit lesion in acute-on-chronic occlusions), thrombolysis, and/or surgical embolectomy.[7-9] The most frequent cause of incomplete clot removal is a mismatch between the arterial diameter and the size of the device. Typically, aspiration techniques work better in acute thrombus (< 14 days old).

One of the disadvantages of the continuous suction is the potential risk of aspiration of blood instead of thrombotic material. To overcome this potentially devastating problem, a computer-aided mechanical aspiration system has been developed: the Indigo system with Lightning aspiration tubing, powered by the Penumbra Engine. The Lightning aspiration tubing has dual-pressure sensors that can monitor real-time blood flow. A built-in microprocessor features a proprietary algorithm that controls a valve in the tubing, allowing continuous aspiration when the catheter is located in the thrombus and only intermittent aspiration when the tip is in a segment with flow. This device can limit the amount of blood aspirated and still efficiently remove thrombotic material.[10]

ROTAREX ROTATIONAL EXCISIONAL ATHERECTOMY SYSTEM

The Rotarex rotational excisional atherectomy system consists of an external electronic unit, a motor that serves simultaneously as a handle, and the Rotarex catheter.[11] The catheter has chisel-like facets at the tip that serve to break up the thrombotic material. The facets are connected to a spiral that rotates at a speed of 40,000 to 60,000 rpm, and this motion is achieved by magnetic coupling with the motor unit. The catheter is slowly advanced over a specifically designed guidewire, and detached fragments are hurled against the vessel wall by the strong vortex caused by the rotating head. This loosens additional thrombotic material attached

to the vessel wall without the rotating head of the catheter coming into contact with the vessel wall. A helix within the catheter serves as an Archimedes screw, and the rapid rotation of the helix generates a permanent negative pressure inside the catheter. This vacuum causes thrombotic material in the target lesion to be suctioned and conveyed into a collection bag at the end of the catheter.[12] Several registries have demonstrated a high technical success rate with the Rotarex system and have shown that this technology can reduce the need for additional CDT.[3] Despite the strong aspiration power, distal embolization can still occur. Perforation has also been described and is related to its use in the presence of vasospasm. The device cannot be used in smaller below-the-knee arteries.

JETI HYDRODYNAMIC THROMBECTOMY SYSTEM

The Jeti hydrodynamic thrombectomy system uses a focused, high-pulse saline jet to break up the clot and remove the crushed material. The jet is used to prevent catheter clogging by fragmenting and lubricating the clot during aspiration. The location of the saline jet within the catheter lumen avoids exposing the patient to any hemolytic compounds during thrombectomy, as these contents are immediately aspirated from the body. In a small series of patients with class 2a and 2b ALI, the Jeti system was used successfully as standalone therapy in 26% of patients, and adjunctive procedures (eg, angioplasty, stenting, open thrombectomy) were necessary in 59% of cases.[13]

POUNCE THROMBECTOMY SYSTEM

The Pounce thrombectomy system (Surmodics, Inc.) includes three components: a 5-F delivery catheter, a basket wire (with two baskets), and a funnel catheter. The basket wire is advanced through the delivery catheter beyond the distal location of the thrombus, and the two nitinol self-expanding baskets are deployed by retracting the delivery catheter while keeping the basket wire in place. The baskets capture the clot and are retracted into the nitinol collection funnel, which has a diameter of 7 mm and a length of 6.5 cm. An integrated handle with a slider button serves to unsheath and sheath the funnel. With the clot entrained, the system is withdrawn into a minimum 7-F guide sheath through which the clot is removed from the body. During removal, a wire lock avoids movement of the basket wire within the funnel.

The Pounce system received FDA 501(k) clearance in September 2020 and is available for use in the United States. Several case reports have been published, and data from the first consecutive 20 patients treated in the first-in-human study were presented at Charing Cross 2022, demonstrating a 100% target lesion success rate (mean procedure time, < 90 minutes), with no adjunctive thrombectomy treatments required.[14] PROWL, an open-label, retrospective, multicenter, United States registry of the Pounce system will involve 500 patients and has recently enrolled the first patient.

PRODIGY THROMBECTOMY SYSTEM

The Prodigy thrombectomy system (Imperative Care Vascular, formerly Truvic Medical) is composed of several components, including the Prodigy catheter (available in sizes of 5, 6, and 8 F), the Prodigy Twist (in a matching size range), the Prodigy Hotshot controller, a generator, a canister, and a tube set. The single-lumen Prodigy catheter targets aspiration from the Truvic generator directly to the thrombus. The Prodigy Hotshot controller connects the Prodigy catheter to the Truvic generator and provides the user with the ability to control flow and visualize the extracted thrombus. The wire-based Prodigy Twist utilizes a soft, flexible polymeric tip to facilitate thrombus removal through the Prodigy catheter as needed. The Prodigy catheter is available in multiple diameters, and both the Prodigy catheter and Prodigy Twist are available in multiple effective lengths and are visible under fluoroscopy via radiopaque marker bands. Current clinical experience has been described in case reports only. The Prodigy system received FDA 501(k) clearance in April 2022 and is currently available in the United States only.

CONCLUSION

Multiple endovascular devices are currently available for the minimally invasive treatment of ALI. The body of clinical evidence for these devices is rapidly growing, which has led to increased use of these devices in the treatment of patients with ALI. ■

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