Catheter-Based Therapy: Are We Making Progress and Is the Game Changing?

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Acute pulmonary embolism (PE) is a common and potentially fatal illness if not recognized and treated in a timely manner. Contemporary management includes systemic anticoagulation or thrombolysis, catheter-based procedures, and surgical embolectomy. Systemic thrombolysis and surgical embolectomy are not without complications. Newer catheter-based procedures allow for therapeutic benefit while minimizing complications. This article describes features of available thrombolytic and aspiration technologies and results of studies evaluating their efficacy and safety.

CATHETER-DIRECTED THROMBOLYSIS

In patients with hemodynamically significant acute PE, systemic thrombolysis improves right ventricular (RV) dysfunction, RV dilation, and reduces pulmonary artery (PA) pressures. However, systemic thrombolysis is associated with a dose-related risk of bleeding, particularly intracranial hemorrhage (ICH). An alternative to systemic thrombolysis is direct infusion into the PAs using an infusion catheter, which is appealing because it provides the therapeutic benefit of thrombus resolution with lower dose of thrombolytic drug to reduce the risk of bleeding.

There are two categories of catheters used for catheter-directed thrombolysis (CDT), multi-side-hole infusion catheters and the EkoSonic endovascular system (BTG Vascular). Ultrasound-assisted catheter-directed thrombolysis (UACDT) combines conventional CDT and high-frequency (2.2 MHz), low-power (0.5 W) ultrasound. Ultrasound accelerates fibrinolysis by disaggregating fibrin fibers, allowing greater penetration of the thrombolytic agent. The system consists of a 0.035-inch, guidewire-compatible, 5.4-F, multi-side-hole infusion catheter; an ultrasound core matched to infusion length; and a control unit. The infusion catheter is placed into the affected PA with the treatment zone embedded in the clot (Figure 1).

To date, two randomized controlled clinical trials (ULTIMA and OPTALYSE PE) and one prospective, single-arm study (SEATTLE II) have evaluated the safety and efficacy of the EkoSonic system for the treatment of acute PE and RV dilation (RV/left ventricular [LV] ratio > 0.9).

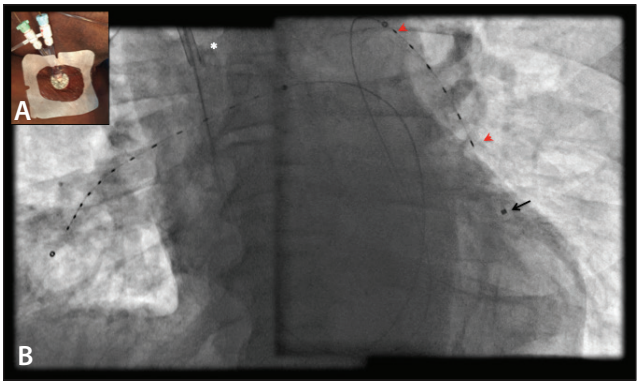

Figure 1. A 12-F Fast-Cath Duo sheath (Abbott Vascular, formerly St. Jude Medical) in the right internal jugular vein with two EkoSonic catheters inserted (A, also denoted with an asterisk in B). Bilateral placement of EkoSonic catheters in the right middle PA and the left lower PA. Infusion zone is denoted between the two red arrowheads, and the distal central lumen is denoted at the black arrow (B).

Both the ULTIMA (n = 49) and SEATTLE II (n = 150) studies showed reversal of RV dilation and reduction of PA pressures upon completion of the infusion of 10 to 20 mg tissue plasminogen activator (tPA) over 15 hours and 24 mg tPA over 12 to 24 hours, respectively. There was no occurrence of ICH in either study.[1,2] In OPTALYSE PE (n = 101), RV dilation was reversed over shorter infusion duration (2–6 hours); however, two patients experienced ICH.[3] A recent meta-analysis of 860 patients reported major bleeding or vascular injury in 4.75% and ICH in 0.35%.[4]

The PERFECT prospective multicenter registry (n = 101), which included both UACDT and multi-side-hole infusion catheters, also demonstrated improvement in RV function with a reduction in PA pressures.[5] There has not been a head-to-head comparison of UACDT to multi-side-hole catheters; however, the PERFECT registry and subsequent retrospective studies have demonstrated no difference between the two modalities.[6,7]

CATHETER ASPIRATION

Percutaneous mechanical removal of the PE has always been an attractive concept, with the theoretical benefits of immediate resolution of the pulmonary vascular obstruction, avoidance of thrombolytic use, and reduction of clot

burden as nidus for potential chronic obstruction. Although technologic advances have allowed successful percutaneous retrieval or aspiration of most coronary and cerebral arterial thrombi, borrowing similar technologies to treat venous thromboembolic clots has been far less successful. Regardless of the catheter size, the strength of the applied aspiration, or the innovation of the clot capture mechanism, the basic procedural challenges remain the same: very large and organized thrombus, tortuosity and unfavorable angulations, a difficult-to-navigate tapering, and rapidly branching pulmonary arterial structure.

Despite these difficulties, recent technologic advances and collective experience have yielded better results and renewed hope in venous thromboembolic aspiration. Most notable in this field is the newly FDA-approved FlowTriever catheter (Inari Medical; Figure 2). This catheter is a 20-F, 90-cm aspiration guiding catheter equipped with a large-bore side port and an aspiration syringe. Typically introduced in the femoral vein through a 22-F sheath, the catheter and its removable dilator are advanced over a stiff wire into the desired pulmonary branch until they reach the thrombus. Initial crossing of the right heart into the PA has to be done first with a balloon-tipped catheter to avoid entrapment behind a tricuspid valve cord, before the wire exchange happens. Individual interlobar or lobar branches can be selected using a standard coronary catheter. Once the FlowTriever catheter is in position, the dilator is removed and suction is applied through the provided aspiration syringe. Catheter engagement of the clot is crucial for successful aspiration. If needed, self-expanding nitinol discs can be deployed distally and retrieved into the catheter to help drag thrombi proximally while aspiration is performed. Longer, smaller (16 F) aspiration catheters may also be used, intussuscepted into the larger catheter for more distal aspiration.

Courtesy of Inari Medical.

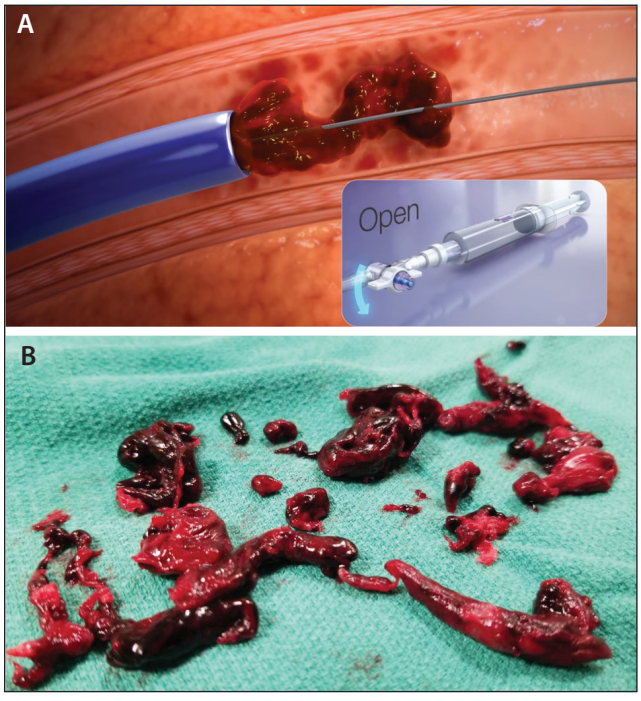

Figure 2. Image of the FlowTriever catheter advanced into the thrombus. The aspiration syringe is turned on when the catheter engages the thrombus (A). Example of aspirated thromboemboli using the FlowTriever (B).

The efficacy and safety of the FlowTriever catheter were studied in the single-arm, prospective FLARE trial, which showed significant improvement in RV/LV ratio at 48 hours postprocedure in patients with intermediate-risk acute PE (RV/LV ratio > 0.9).[8] Three patients had procedure-related (but not catheter-related) complications. In our experience, if adequate aspiration is performed, significant improvement in hemodynamic numbers and patient symptoms can be observed immediately.

Another aspiration catheter currently on the market but not yet FDA approved for acute PE is the 8-F Indigo catheter (Penumbra, Inc.). Typically advanced to the PA through a 10-F, 80-cm sheath, the catheter with a slightly angulated tip is advanced over a wire until it engages thrombi. The guidewire is then pulled and a separator wire introduced to keep clearing the tip from obstructive thrombi while a pump applies continuous mechanical suction through the back of the catheter. This device is currently under investigation in the now completed EXTRACT PE trial, a single-arm prospective trial; results have not yet been presented or published (NCT03218566.)

THE ANGIOVAC SYSTEM

An option for large-bore catheter removal of intravascular material is the AngioVac system (AngioDynamics). The AngioVac system consists of a venovenous bypass circuit, filter, and proprietary 22-F aspiration cannula. The cannula has a coil-reinforced shaft, preventing collapse with the high suction forces generated, and a balloon-actuated, expandable, funnel-shaped distal tip. This tip enhances venous drainage flow when the balloon is inflated, which helps prevent clogging of the cannula with large clots. The cannula is inserted through a 26-F sheath and then connected to an extracorporeal bypass circuit, which passes through a filter. The filtered blood is then returned to the venous system through either a 16- or 18-F reperfusion catheter.

A closed-circuit aspiration system is particularly beneficial in the management of right heart thrombi (RHT). RHT are found in 4% of all PE according to the International Cooperative Pulmonary Embolism

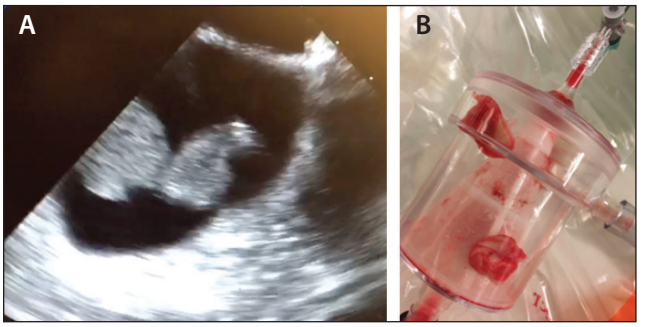

Figure 3. A transesophageal echocardiogram demonstrating a mobile "ball-like" thrombi within the right atrium in a patient with submassive PE (A). After AngioVac aspiration, the masses could be seen as organized thrombi (B).

Registry data[9] and in up to 16% of high-risk PE.[9] The most common morphology is a cast of femoral or iliac vein thrombus in motion in the right atrium. Previously, pharmacologic and open surgical thrombectomy were the only recognized treatment options. The AngioVac system allows for a minimally invasive endovascular option now favored in many centers (Figure 3). Several publications have demonstrated efficacy with low complications. In particular, the ability to rapidly remove RHT, theoretically preventing the future risk of PE and cardiovascular collapse, with a single procedure is enticing because it allows preservation of all other options for PE management such as CDT. An area of particular interest is the role of AngioVac aspiration of RHT in the setting of a patent foramen ovale (PFO). Recent data have shown the high prevalence of paradoxical embolism in PE patients,[10] and although there is no large series of AngioVac usage in the presence of a shunt, several case reports have shown safe removal of thrombi that have partially traversed a PFO.

Compared to RHT, use of AngioVac for removal of PA thrombus has been slow to gain widespread favor. This is largely due to two factors: (1) the rigidity of the 22-F aspiration cannula can make it difficult to pass the cannula through the right heart to the PA, placing more stress on the RV outflow tract and leading to either arrhythmia or bleeding; and (2) the hemodynamic effects of aspirating up to 3.5 L/min directly from the PAs, especially in the setting of an already compromised pulmonary perfusion, can precipitate hypotension and right heart failure. Although there have been anecdotal reports of good success of PE aspiration with the AngioVac system at high-volume centers, this should be considered a second-line or bailout option.

SUMMARY

Although there are limited clinical trial data, catheter-based treatment of acute PE is promising. Small studies have demonstrated CDT to be safe and effective in reversing RV dilation and reducing PA pressures. The risk of bleeding complications, particularly ICH, is much lower compared to systemic thrombolysis. Aspiration using the FlowTriever catheter allows for thrombus removal without the need for thrombolysis and the associated risk of bleeding. Although the Indigo catheter is currently under investigation and is not FDA approved, it appears to be promising for clot removal, particularly for more distal smaller PAs. The AngioVac system has not proven to be a viable option for extraction of PE but can be useful for treating RHT or clot in transit in the setting of acute PE. ■

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