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New Horizons in Pulmonary Embolectomy

Large-Bore Aspiration Thrombectomy: Catalyst for a Revolution in Treating Pulmonary Embolism

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Technological advances are setting the stage for much-needed innovations in treating pulmonary embolism (PE). Pulmonary embolism is a leading cardiovascular cause of death; the data in the medical literature are unclear, but according to some estimates, as many as 900,000 people experience PE and up to 100,000 die from it yearly in the United States. In addition, fatal PE events can be miscategorized as myocardial infarction (MI) or sudden cardiac death. Additional patients have chronic disabling symptoms after recovering from their acute PE event.

Improvements in Pulmonary Embolism Mortality Rates Trail Those in Myocardial Infarction

Whereas treatments for MI and stroke have progressed and improved patient outcomes, the same has not occurred in PE. In 1995, the mortality rate for ST- and non-ST-segment-elevation MI was >15%; by 2015, it steadily and dramatically declined to approximately 5%.[1] Better diagnostic capabilities, pharmacology, and systems of care were factors. However, the chief influence was probably the widespread adoption of angioplasty, a safe and definitive catheter-based solution. In contrast, the mortality rate for PE has not declined, and in some vulnerable populations it has increased.[2]

Why have there not been comparable improvements in PE mortality rates during the past few decades? Lytic-based therapies have long been available but have not been widely adopted, presumably because of concerns about bleeding risk. Pulmonary embolism response teams have been developed to systematically identify and initiate treatment for these patients. A safe, highly effective, widely adopted treatment like angioplasty for MI has been acutely needed for PE.

Arterial Clots and Venous Clots Differ

Arterial thrombosis usually results in acute end-organ ischemia or infarction, leading to obvious symptoms and prompt therapy. Arterial clots are small, and they are not likely to adhere to vessel walls or to transform into subacute collagen-rich clots. Conversely, venous thrombosis tends to form where vessels are injured, compressed, or inflamed. Because veins are large-capacitance vessels and because collateral vessels can easily develop, clots usually do not cause symptoms. Thrombus continues to be deposited within the lumen and to extend longitudinally, causing the vessel to become occluded. By the time deep vein thrombosis causes symptoms, it may be days or weeks old. Even if PE is treated acutely, the clot that embolized is usually partially chronic (Fig. 1).

The mass and volume of venous clots can vastly exceed those of arterial clots. Venous clots are more wall-adherent and fibrotic because of their different formation mechanism, and they can resist thrombolysis because much of their fibrin content has converted to collagen by the time of clinical presentation.

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Limitations of Current Therapies

Thrombolysis and fibrinolysis for treating acute and chronic clots have the following crucial limitations.

Bleeding Risk. Systemic thrombolysis is associated with a 2% to 4% risk of fatal and catastrophic bleeding. The risk of major bleeding can be 40%. Reducing the drug dose through local delivery has mitigated some risk, but even small doses have been associated with intracerebral hemorrhage and major bleeding. This risk is stochastic and unpredictable, and many patients with PE cannot undergo thrombolytic therapy.

Expense. Thrombolytic therapy is expensive in terms of pharmaceutical costs and hospital resources. Patients treated with thrombolytic agents must be monitored in an intensive care unit because of bleeding risk. Bleeding complications also prolong hospital stays. Patients with chronic clots often undergo prolonged therapy, during which time they remain in the intensive care unit. This issue is always relevant, but particularly so during the COVID-19 pandemic.

Ineffective Fibrinolysis of Chronic Clots. When a clot forms, a remodeling process begins. Infiltration by white blood cells, smooth muscle cells, and fibroblasts occurs as collagen replaces fibrin. Because of the time it takes for the clot to embolize from the leg to the lung, the embolus loses the substrate that would have responded to endogenous or exogenous fibrinolysis. The only way for the body to clear collagen-rich thrombus is by wall incorporation and scarification.

Characteristics of Ideal Pulmonary Embolism Therapy

Ideal PE therapy should be safe, particularly in regard to bleeding and vascular complications. It should effectively remove as much thrombus as possible and rapidly reduce right-sided heart strain. In turn, these clinical improvements should improve oxygenation, tachycardia, and symptoms. Eventually, the therapy should reliably reduce short- and medium-term mortality rates and, optimally, improve recovery time and quality of life. The technique should be simple and cost effective, with limited impact on healthcare resources.

Multiple devices have been developed for arterial thrombectomy. However, similar results cannot be expected when using them to treat venous clots. To be effective in the venous space, devices with specific properties are needed.

The FlowTriever System

The FlowTriever system (Inari Medical) features the large-bore Triever Aspiration Catheter (Fig. 2). The catheter (diameter, 20F or 24F) can be readily navigated through the right side of the heart to the pulmonary arteries from multiple venous approaches. When it is in position, rapid aspiration can be performed with use of a proprietary large-bore 60-cc syringe. The FlowTriever has 3 self-expanding nitinol mesh discs that can be deployed within resistant thrombus to dislodge it from the vessel wall and enable aspiration.

Why "Bigger Is Better" for Treating Pulmonary Embolism

In treating PE, using a large catheter provides 2 major advantages. First, a large-mouthed catheter enables massive clots to be captured and removed completely, whereas a smaller lumen can clog and necessitate macerating the thrombus into pieces. Second, aspirational force is crucial to dislodging and removing adherent thrombus. The force on a clot is related to the aspirational flow rate, in accordance with Poiseuille's law. Flow is proportional to the tube radius to the 4th power, meaning that small increases in tube size bring dramatic increases in flow rate. Powerful suction from the FlowTriever system, applied for a fraction of a second, rapidly and effectively removes clots with minimal blood loss (Fig. 3).

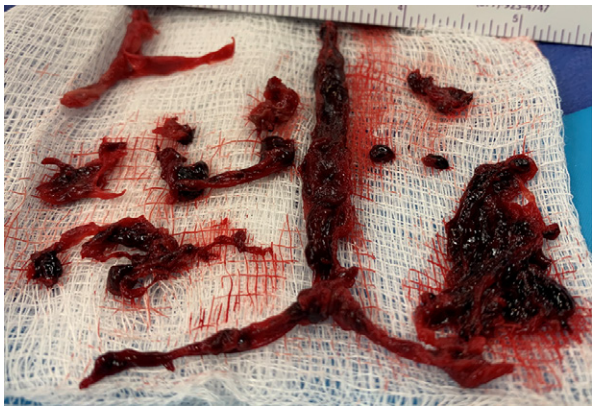

Fig. 1 *Photograph of aspirated pulmonary embolism sample shows acute (darker) and chronic (lighter) thrombus.*

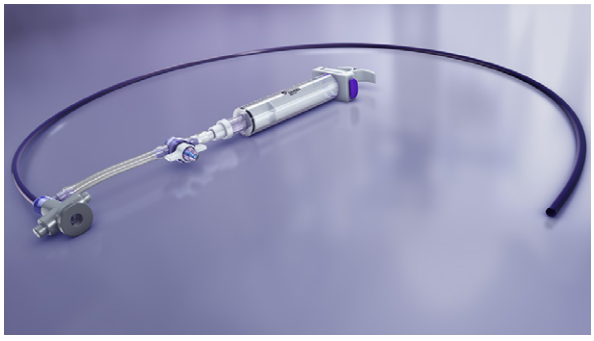

Fig. 2 *The FlowTriever system consists of the Triever aspiration catheter and a proprietary large-bore syringe.*

(Photograph courtesy of Inari Medical)

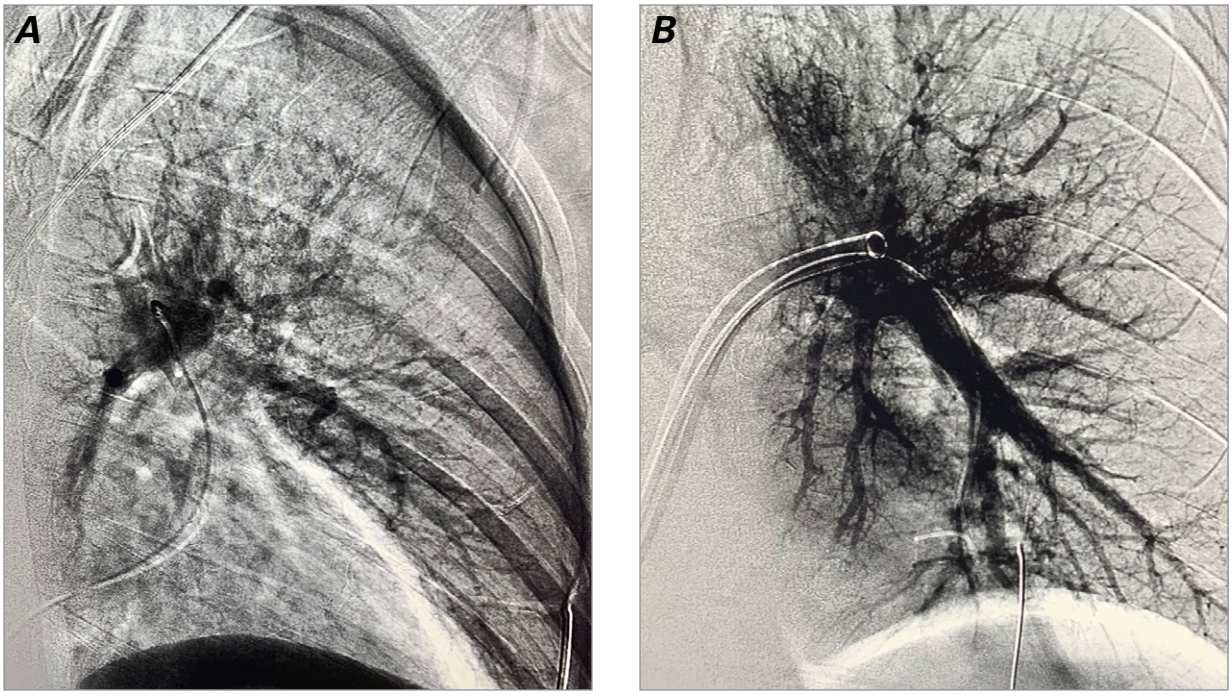

Fig. 3 *Pulmonary angiograms show* ***A****) poor pulmonary artery filling due to thrombus and* ***B****) resolution after FlowTriever thrombectomy.*

FlowTriever Clinical Data

The FlowTriever was initially evaluated in the FlowTriever Pulmonary Embolectomy Clinical Study (FLARE), a single-arm prospective multicenter trial of the device in intermediate-risk PE patients.[3] The main findings were excellent safety and a significantly reduced right ventricular-to-left ventricular ratio at 48 hours. Consequently, the U.S. Food and Drug Administration approved PE as an indication for using the FlowTriever, making it the first mechanical thrombectomy device thus approved. Results of several single-center, real-world studies have since validated its safety and revealed substantial on-table reductions in mean pulmonary artery pressure. A multicenter retrospective study of FlowTriever use in patients critically ill with massive and high-risk submassive PE revealed a markedly low mortality rate and excellent technical success.[4] Finally, an interim analysis of the first 230 patients in a real-world, all-comers registry revealed minimal 48-hour[5] and 30-day[6] mortality rates, excellent safety, and acute hemodynamic improvements.

Conclusion

We are on the cusp of a revolution in treating PE. Technological advances have enabled new approaches to risk stratification and therapy for PE patients. Therapeutic goals have moved beyond merely avoiding in-hospital death and now include immediately improved hemodynamic status, reduced patient acuity, lower consumption of hospital resources, longer survival times, and good quality-of-life outcomes. The development of large-bore suction thrombectomy is a sea change, as catheter-based therapy was for acute MI and stroke. In those diseases, treatment progressed from conservative measures to thrombolysis, and then to definitive catheter-based solutions, initially in patients at highest risk and eventually in a much wider population. This same paradigm shift needs to occur in PE treatment, to improve outcomes in patients with this potentially fatal disease.

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