INTERVENTIONAL THERAPY FOR PULMONARY EMBOLISM

Alan B. Lumsden, M.D., Erik Suarez, M.D.

Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas

Abstract

Patients with pulmonary embolism (PE) present with highly variable clinical symptoms and often have accompanying comorbidities. Timely diagnosis and treatment are critical to help prevent recurrence and increased morbidity/mortality. While open surgical thrombectomy was once reserved only for those with massive PE and hemodynamic compromise, it has been reevaluated with a focus on careful patient selection and early intervention. Lately, there has been increased interest in catheter-based interventions and in combining these with an open surgical component to decrease the magnitude of the intervention—for example, direct placement of large-bore thrombectomy devices directly into the right ventricle via sternotomy or subxiphoid approaches. In addition, improved diagnostic capabilities have allowed for expedited diagnosis and treatment of patients with life-threatening PE. At our institution, a hybrid room allows patients suspected of having a massive or submassive PE to undergo on-table contrast-enhanced cone-beam computed tomography scan, thus creating a high-resolution 3-dimensional image of the arterial system that can provide immediate guidance for therapeutic intervention. This review highlights the array of therapeutic options currently used in our armamentarium at the Houston Methodist DeBakey Heart & Vascular Center and describes our development of a pulmonary angioplasty procedure that we believe will greatly facilitate selective thrombus removal in the acute PE setting.

Background

There is rapidly increasing interest in the potential of interventional or surgical therapy for the treatment of pulmonary embolism (PE). Open surgical thrombectomy has typically been reserved for patients with massive PE and hemodynamic compromise. Consequently, there has been some nihilism about the value of open surgical thrombectomy that is likely due to the high-risk nature of these patients. In the past few years, however, the role of surgical thrombectomy has been reevaluated, with emphasis now placed on careful patient selection and intervention prior to the situation becoming irreversible.[1-3] While we continue to believe there is a role for open surgical thrombectomy, we also believe that a range of therapeutic options be available to the patient and interventionalist alike. Increasingly, these will consist primarily of catheter-based interventions; however, we are more often blending these interventions with an open surgical component, thereby decreasing the magnitude of the intervention.[4] In this review, we describe all of the therapeutic options currently used in our armamentarium at the Houston Methodist DeBakey Heart & Vascular Center.

Open Surgical Thrombectomy for Pulmonary Embolism

In 1924, Kirschner published the first successful pulmonary embolectomy,[5] a surgery described and taught to him by the developer of the procedure, Friedrich Trendelenburg. The ensuing decade resulted in several further descriptions of a successful procedure; however, overall results remained wanting due to an exceptionally high mortality rate. It was not until the development of extracorporeal circulation followed by its first successful use in embolectomy by Sharp in 1962 that the current era in surgical management of acute PE developed.[6]

While the four decades following Sharp are marked by few changes in the selection of candidates for the procedure, recent emphasis has been placed on appropriate patient selection and improved mortality and outcomes.[3,7-9] In short, anticoagulation with heparin followed by Coumadin® has been the mainstay for nonsurgical intervention, whereas patients with a proven pulmonary embolus who are in hemodynamic distress despite maximal pharmacologic support have been the primary nominees for surgical intervention. The development of transesophageal echocardiography has allowed for the emergent diagnosis of pulmonary embolus for those patients rushed to the operating room with a high clinical suspicion of PE. Computed tomography pulmonary angiography reveals not only excellent resolution of central PE but also increased right ventricular (RV) enlargement, which may indicate a significantly increased 30-day mortality.[10]

In addition to improved diagnostic capabilities allowing for expedited diagnosis and treatment of patients with life-threatening PE, the development of lightweight, easily deployable inferior vena cava (IVC) filters used in conjunction with surgery has resulted in improved morbidity and mortality rates in these patients.[11,12] Risk stratification of patients after a review of surgical outcomes has determined that those experiencing preoperative cardiac arrest or who are in extremis are far less likely to survive surgical intervention.[8,13]

The modern surgery for acute pulmonary embolectomy takes advantage of normothermic bicaval cardiopulmonary bypass. Arrest of the heart is rarely needed, with most clinicians only cross-clamping the aorta if a patent foramen ovale is present and there is need to open the right atria due to an embolus in transit.

Both longitudinal and transverse incisions of the main pulmonary artery towards or at the bifurcation have been described. Longitudinal incisions may be carried out towards the left main pulmonary artery while a separate incision may be required for the distal right main pulmonary artery. A variety of devices have also been used to retrieve emboli, including ring forceps, stone forceps, and suction using a reversed, cut, red rubber catheter. Many clinicians routinely open both pleural spaces to massage the lungs and aid in migration of a distal clot towards the proximal pulmonary arteriotomy, a maneuver with which we strongly concur. Placement of an IVC filter has become routine to the point that we recommend placement at the same surgical setting, on the table or within a few hours of the procedure.

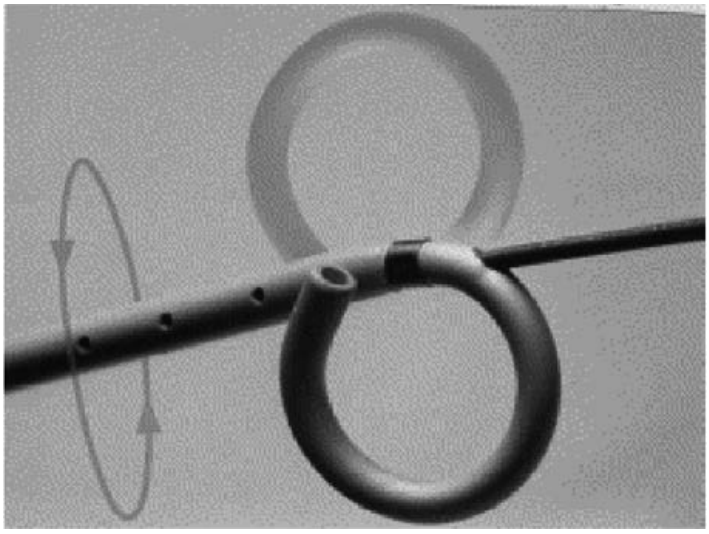

Figure 1. Pigtail catheter with maceration.

A long and proud history marks the surgical treatment for acute PE, and we agree that early detection, intervention, and appropriate patient selection in the setting of a multidisciplinary team approach will continue to be major factors in improving the success rate for such interventions. While still relatively early in development compared to surgical intervention, catheter-based and thrombolytic interventions at our institution have shown growing promise as the technology and experience with these modalities increases.

Catheter-Based Interventions for Pulmonary Embolism

A variety of techniques, some simple and some more complex, have been developed for catheter-based therapy.[14-16] Massive pulmonary emboli were approached initially with the "fragmentation technique," which involves advancing a guide wire into the thrombus, placing a pigtail over the wire and into the clot burden,[17] and reforming and manually spinning the pigtail (Figure 1). The concept was that this technique manually macerated a large proximally occlusive thrombus, allowing fragments to pass into the more distal segmental branches but relieving the proximal obstruction. A variant on this concept was placement of an angioplasty balloon into the thrombus, then inflating the balloon to reduce a large proximally occlusive thrombus into smaller components that pass distally. With both of these techniques, the underlying hypothesis is that the well-being of the patient will improve immediately since smaller occlusive thrombi are less hemodynamically significant and possibly more susceptible to spontaneous lysis.

While relatively simple in concept, this approach only attempts to relieve the upstream obstructive burden and its effect on the RV. No thrombus is removed by this technique; therefore, it has the uncertain effect of creating more distal occlusion as well as uncertain effects on hemodynamics. However, this purely mechanical technique does have the advantage of being simple and easily performed in almost any center. In addition, it does not use lytics and therefore avoids the attendant bleeding risk, which may be as high as 20% with systemic lysis although likely lower with direct catheter therapy. Despite these advantages, this basic form of mechanical intervention has not been widely utilized. We believe this is a result of two factors: First, it is used only in patients with large proximal emboli who are typically unstable, and second, the unpredictable nature of purely mechanical fragmentation in terms of efficacy means it has been applied only in dire clinical situations.

Figure 2. EKOS catheters (EKOS EndoWave Infusion Catheter System, BTG International, Inc., West Conshohocken, PA) placed into the right and left pulmonary arteries.

Clearly there is a need for more predictable, validated, catheter-based strategies that can decrease RV dilation and reduce pulmonary hypertension. In 2013 and 2015, the Ultrasound Accelerated Thrombolysis of PE (ULTIMA) and Seattle II trials reported on the use of ultrasound-assisted catheter-directed thrombolysis for PE (Figure 2). The ULTIMA trial studied 59 patients with acute main or lower-lobe PE and an RV/left ventricular (LV) dimension ratio ≥ 1.[18] Patients were randomized to receive either unfractionated heparin or ultrasound-assisted catheter-directed thrombolysis (USAT), and the primary outcome event was the difference in RV/LV ratio from baseline to 24 hours. In the USAT group, the ratio was reduced from 1.28 to 0.99, a statistically significant difference. The heparin-only group showed no difference. The authors concluded that in PE patients at intermediate risk, the USAT regimen significantly reduced RV dilatation at 24 hours with no increase in bleeding complications.[18] A similar USAT technique was used in a single-arm nonrandomized study by the Seattle II investigators. They concluded that USAT resulted in decreased RV dilation and reduced pulmonary pressures, and they further demonstrated reduced anatomic thrombus burden using the modified Miller index.[19] The ULTIMA and Seattle II trials sparked a renewed interest in catheter-based therapy for pulmonary emboli. However, this procedure still requires the use of lytic therapy.

In the last few years, mechanical suction devices such as the AngioVac system (Vortex Medical, Inc., Marlborough, MA) have been developed to remove thrombus from large vessels (Figure 3).[20] The system uses a large 22-Fr catheter with a balloon-expandable layered tip that is engaged directly in the thrombus. Aspiration is achieved by hooking the catheter to a cardiopulmonary bypass circuit, which returns after filtration to a separate venous cannula.[21] While we have found this to be very useful in the inferior vena cava, it is extremely difficult to manipulate this

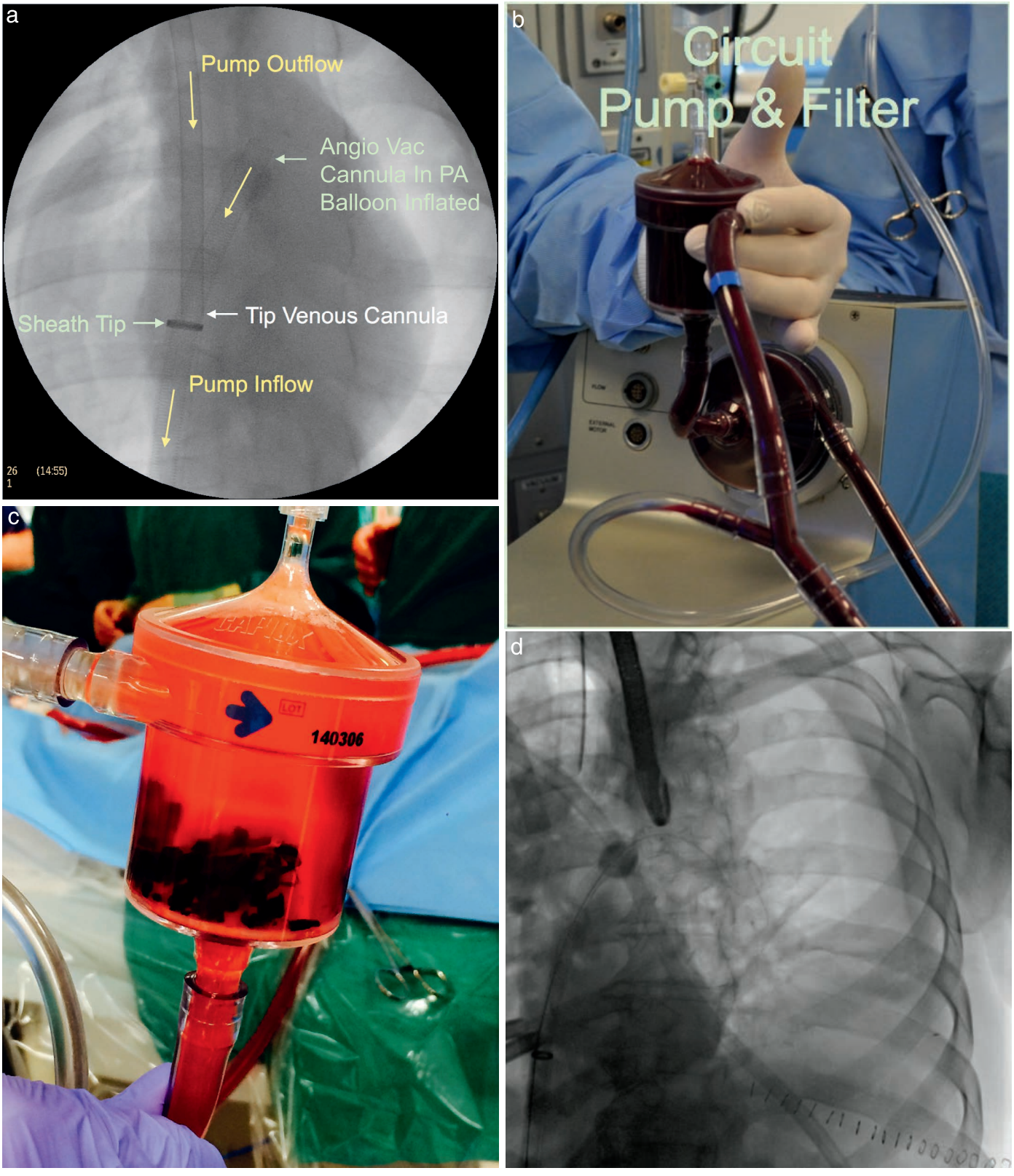

Figure 3. AngioVac system. (a) AngioVac set-up; (b) AngioVac circuit pump and filter; (c) thrombus in AngioVac canister; (d) AngioVac left pulmonary artery.

catheter through the right side of the heart and then to the pulmonary arteries. The literature shows very little data of its efficacy in the pulmonary system, and most of it consists of isolated PE cases within much larger series of IVC and iliac vein thromboses. More recently, an angulated catheter has been developed to try and facilitate navigation and steering of this device, but there is still minimal experience with this new modification.

At our institution, we have used the AngioVac in a somewhat unorthodox manner. We acknowledge that the system is very effective at thrombus removal when in contact with large thrombi,

but its use in the pulmonary system is limited due to the extreme difficulty navigating through the heart to the target. In patients with massive pulmonary emboli who are otherwise considered open-surgical thrombectomy candidates, we have delivered the AngioVac directly into the RV. This can be done in some cases using a subxiphoid approach, thereby completely avoiding a sternotomy. In cases where the distance between the subxiphoid incision and the under surface of the RV precludes safe insertion of a purse string, a sternotomy is performed. A purse-string suture is then placed in the anterior aspect of the RV, access is gained using the standard Seldinger technique, a stiff wire is placed in the target pulmonary artery, and a 24-Fr sheath is inserted through the RV and into the pulmonary trunk. The AngioVac system is then used in fairly standard fashion and can easily be directed into the right and left main pulmonary arteries. Although still a somewhat complicated procedure, this technique does not require the patient to be placed on full cardiopulmonary bypass. Open surgical thrombectomy then remains a clear next step if the thrombus is not successfully removed.

Next-Generation Approaches

It is our belief that the pulmonary arterial system represents the next big vascular bed that can be effectively treated by next-generation devices. However, many physicians are not trained in the anatomy of pulmonary arterial segments or to navigate selectively between those segments to safely remove a pulmonary thrombus. Our group has been developing a pulmonary angioplasty procedure for chronic thromboembolic pulmonary hypertension that refines the techniques for rapid sequence navigation from one pulmonary segment to the other. We believe this expertise will greatly facilitate selective thrombus removal in the acute PE situation.

Accurate imaging and localization of a thrombus within the pulmonary arterial system forms the basis for planning the intervention. In our opinion, this will require either fused pulmonary computed tomography angiography (CTA) images or the acquisition of on-table cone-beam CT angiograms.[22] Precise localization and navigation to these targets is vital. Next-generation devices for acute thrombus removal must be easily navigated among these pulmonary segments, effectively remove the thrombus burden in one step, and avoid the use of lytics. This would greatly increase the applicability of catheter-based therapy for patients with pulmonary emboli. We have developed several models that allow us to objectively quantitate the efficacy of mechanical thrombectomy catheters and test thrombus burden measurement techniques (Figures 4, 5). A porcine heart-lung explant model is used to test mechanical thrombectomy catheters in a highly reproducible setting. On-table cone-beam CT scanning is used to make a diagnosis in both the hybrid operating room and unstable patients (Figure 6) and can be used with the ex vivo flow model for both diagnosis and quantitation of thrombus burden.[17] We have also used this model to validate the efficacy of robotic catheter navigation in this complex arterial system. In addition, we have a 3-dimensional (3D) printed floor model of the pulmonary arterial tree that also allows us to practice navigation strategies and test thrombectomy strategies in a highly relevant clinical system.

New Interventional Imaging Techniques for Pulmonary Embolism

With their increasing capabilities, hybrid rooms can be used for both diagnosis of PE and treatment using the most appropriate technique. For example, patients in our cardiovascular intensive care unit suspected of having a massive or submassive PE are taken directly to the hybrid room, where a pigtail catheter is placed in the main pulmonary artery and an on-table contrast-enhanced cone-beam CT scan is performed (Figure 6). This results in a high-resolution 3D image of the arterial system that can provide immediate guidance for therapeutic intervention. We believe this is the single most efficacious approach for unstable patients with massive and submassive pulmonary emboli.

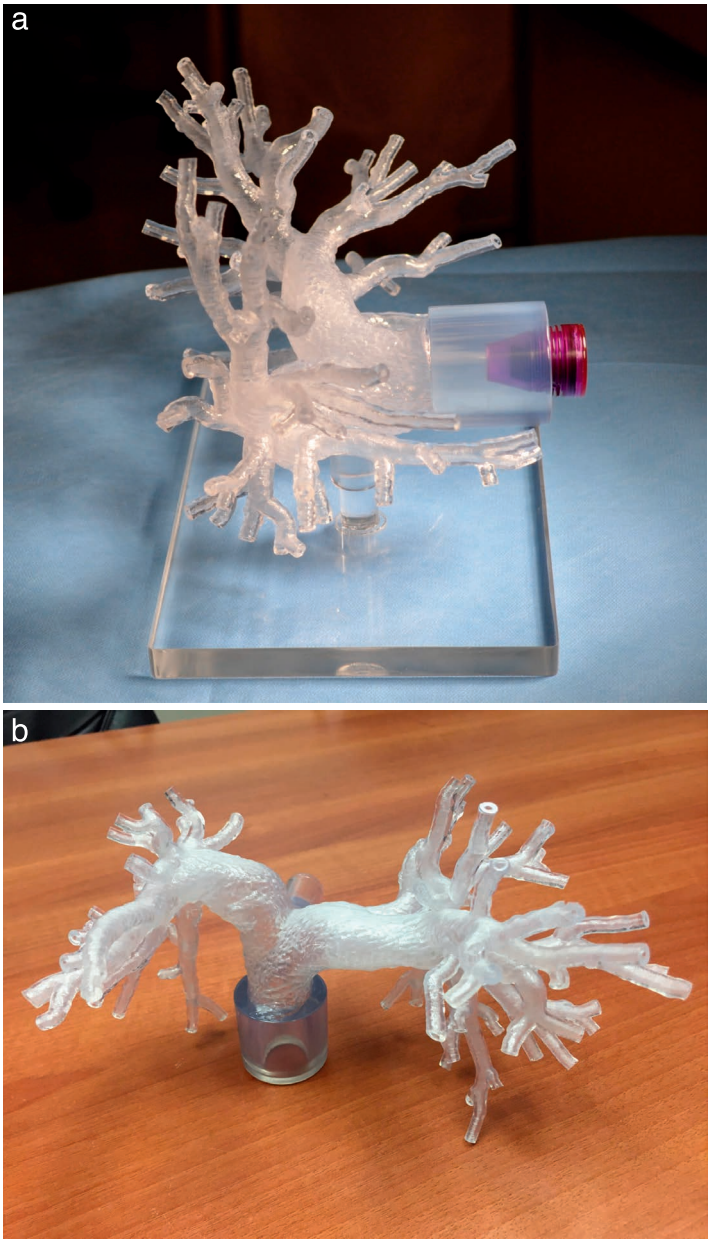

Figure 4. Three-dimensional (3D) printed arterial system. (a) Lateral view of 3D printed model. (b) 3D printed pulmonary artery model.

Summary

The complexity of these patients—many of whom have comorbidities, have undergone recent surgery, or are hypercoagulable—demonstrates that there is no one treatment solution. We believe that the most minimally invasive effective technique should be employed to relieve the hemodynamic effects of the thrombus burden. However, the emphasis is on effective hemodynamic unload-

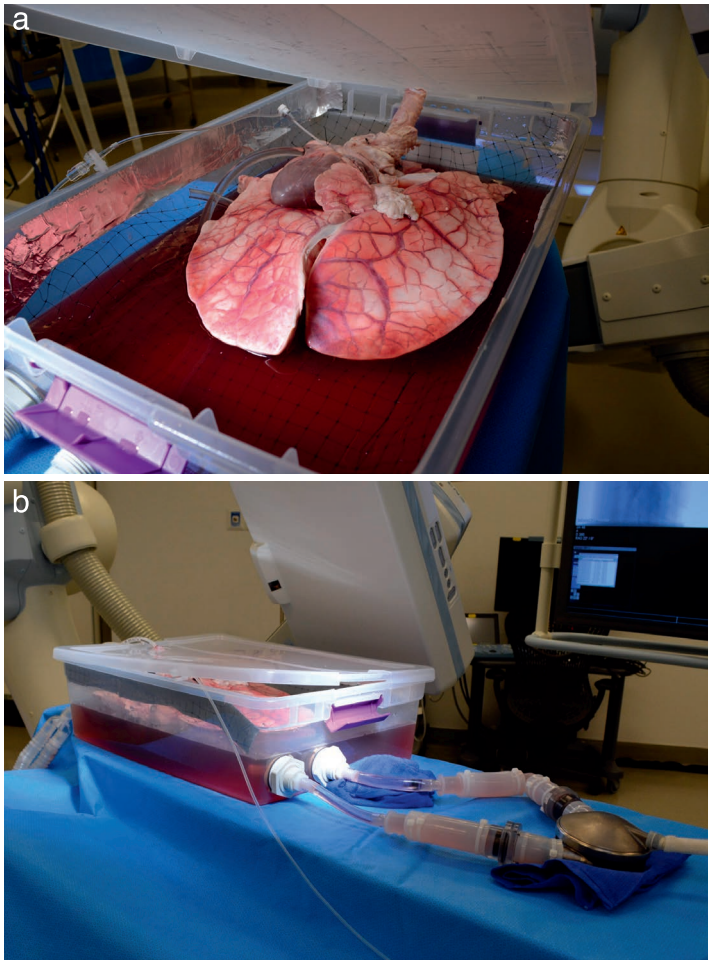

Figure 5. Direct access to right ventricle. (a) Isolated porcine heart-lung model. (b) Heart-lung model with left ventricular perfusion device to provide flow.

ing of the right ventricle.[23] To this end, we employ escalating levels of intervention depending on the case, starting with ultrasound-assisted catheter-directed thrombolysis escalating to AngioVac, delivered via a subxiphoid or direct RV access approach, followed by open surgical thrombectomy.

It is highly likely that catheter-based thrombus removal devices will evolve to allow for earlier intervention and on more high-acuity patients. Appropriate deployment of these devices will depend on refined imaging and navigation strategies. The interventional physician workforce will need significant additional training to effectively navigate and utilize these devices.

Key Points:

- Early detection, intervention, and appropriate patient selection are major factors in improving the outcomes for patients with pulmonary embolism.
- Anticoagulation with heparin followed by Coumadin® has been the mainstay for nonsurgical intervention, whereas surgical intervention has been reserved for patients with a proven pulmonary embolus who are in hemodynamic distress despite maximal pharmacologic support.
- Next-generation devices for acute thrombus removal must be easily navigated among pulmonary segments, effectively remove the thrombus in one step, and avoid the use of lytics to increase the applicability of catheter-based therapy.

Figure 6. On-table cone-beam pulmonary computed tomography angiography showing embolus in segments A 5, 6.

- The more widespread availability of hybrid rooms permits diagnosis and endovascular and/or open therapy in one setting.

Conflict of Interest Disclosure: The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Keywords: pulmonary embolism, open surgical thrombectomy, ultrasound-assisted catheter-directed thrombolysis, AngioVac system

References

1. Golhaber SZ. Surgical pulmonary embolectomy: the resurrection of an almost discarded operation. Tex Heart Inst J. 2013;40(1):5-8.
2. Aklog L, Williams CS, Byrne JG, Goldhaber SZ. Acute pulmonary embolectomy: a contemporary approach. Circulation. 2002 Mar 26;105(12):1416-9.
3. Dauphine C, Omari B. Pulmonary embolectomy for acute massive pulmonary embolism. Ann Thorac Surg. 2005 Apr;79(4):1240-4.
4. Sabri SS, Saad WEA, Turba UC, Park AW, Angle JF, Matsumoto AH. Percutaneous pulmonary embolectomy: indications, techniques and outcomes. Vasc Dis Manage. 2010 Nov;7(11):E223-9.
5. Kirschner M. Ein durch die trendelenburgsche operation geheilter fall von bolie der arterien pulmonalis. Arch Klin Chir. 1924;133:312.
6. Sharp EH. Pulmonary embolectomy: successful removal of a massive pulmonary embolus with the support of cardiopulmonary bypass. Case report. Ann Surg. 1962 Jul;156:1-4.
7. Stein PD, Alnas M, Beemath A, Patel NR. Outcome of pulmonary embolectomy. Am J Cardiol. 2007 Feb 1;99(3):421-3.

8. Leacche M, Unic D, Goldhaber SZ, et al. Modern surgical treatment of massive pulmonary embolism: results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach. J Thorac Cardiovasc Surg. 2005 May;129(5):1018-23.
9. Meyer G, Tamisier D, Sors H, et al. Pulmonary embolectomy: a 20-year experience at one center. Ann Thorac Surg. 1991 Feb;51(2):232-6.
10. Quiroz R, Kucher N, Schoepf UJ, et al. Right ventricular enlargement on chest computed tomography: prognostic role in acute pulmonary embolism. Circulation. 2004 May 25;109(20):2401-4.
11. Simon M, Athanasoulis CA, Kim D, et al. Simon nitinol inferior vena cava filter: initial clinical experience. Work in progress. Radiology. 1989 Jul;172(1):99-103.
12. Sareyyupoglu B, Greason KL, Suri RM, Keegan MT, Dearani JA, Sundt TM 3rd. A more aggressive approach to emergency embolectomy for acute pulmonary embolism. Mayo Clin Proc. 2010 Sep;85(9):785-90.
13. Clarke DB, Abrams LD. Pulmonary embolectomy: a 25 year experience. J Thorac Cardiovasc Surg. 1986 Sep;92(3 Pt 1):442-5.
14. Kim P. Current studies in endovascular therapy for pulmonary embolism. Endovasc Today. 2013 Jul;56-9.
15. Kucher N. Catheter embolectomy for acute pulmonary embolism. Chest. 2007 Aug;132(2):657-63.
16. Engelberger RP, Kucher N. Catheter-based reperfusion treatment of pulmonary embolism. Circulation. 2011 Nov 8;124(19):2139-44.
17. Furlan A, Patil A, Park B, Chang CC, Roberts MS, Bae KT. Accuracy and reproducibility of blood clot burden quantification with pulmonary CT angiography. AJR Am J Roentoenol. 2011 Mar;196(3):516-23.
18. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014 Jan 28;129(4):479-86.
19. Piazza G, Hohlfelder B, Jaff MR, et al.; SEATTLE II Investigators. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: The SEATTLE II Study. JACC Cardiovasc Interv. 2015 Aug 24;8(10):1382-92.
20. Dudiy Y, Kronzon I, Cohen HA, Ruiz CE. Vacuum thrombectomy of large right atrial thrombus. Catheter Cardiovasc Interv. 2012 Feb 1;79(2):344-7.
21. Tsuji A, Ogo T, Demachi J, et al. Rescue balloon pulmonary angioplasty in a rapidly deteriorating chronic thromboembolic pulmonary hypertension patient with liver failure and refractory infection. Pulm Circ. 2014 Mar;4(1):142-7.
22. Wu AS, Pezzullo JA, Cronan JJ, Hou DD, Mayo-Smith WW. CT pulmonary angiography: quantification of pulmonary embolus as a predictor of patient outcome—initial experience. Radiology. 2004 Mar;230(3):831-5.
23. Gerges C, Skoro-Sajer N, Lang IM, Right ventricle in acute and chronic pulmonary embolism (2013 Grover Conference series). Pulm Circ. 2014 Sep;4(3):378-86.