Acute Pulmonary Embolism
With an Emphasis on an Interventional Approach

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ABSTRACT

Compared with recent advances in treatment of serious cardiovascular diseases, such as myocardial infarction and stroke, the treatment and outcome of acute pulmonary embolism (PE) have remained relatively unchanged over the last few decades. This has prompted several experts to call for the formation of multidisciplinary PE response teams with a more proactive approach to the treatment of PE. In the current document, we discuss the formation of such teams and describe the available treatment options beyond anticoagulation, with a focus on the interventional approach. Acknowledging the paucity of data to support widespread adoption of such techniques, we call for the collection of outcomes data in multicenter registries and support for randomized trials to evaluate interventional treatments in patients with high-risk PE. (J Am Coll Cardiol 2016;67:991–1002) © 2016 by the American College of Cardiology Foundation.

The American Heart Association classifies pulmonary embolism (PE) into low-risk, intermediate-risk (submassive), and high-risk (massive) categories (1). Whereas massive PE is defined by the presence of persistent hypotension, submassive PE is defined as occurring in normotensive patients with evidence of right ventricular (RV) strain by echocardiogram, computed tomography (CT) scan, or cardiac biomarkers. The most recent European Society of Cardiology guidelines further divide the intermediate-risk group into intermediate-low- and intermediate-high-risk subgroups, with the latter defined by the presence of both RV dysfunction and increased cardiac biomarkers (2). Despite a high case fatality rate, most patients with massive and submassive PE continue to be treated conservatively with anticoagulation alone. This has prompted alternate, intensive treatment options, including systemic fibrinolysis, catheter-based therapy, and surgical embolectomy. Because adequate studies evaluating these therapies are scarce, and given the difficulty in managing PE patients, multiple centers have formed multidisciplinary pulmonary embolism response teams (PERT, a trademark of the National PERT Consortium) to engage specialists from different backgrounds to discuss treatment options and provide immediate advice and therapy for patients in the massive and submassive categories (3,4).

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This document summarizes current invasive treatment options beyond anticoagulation available to intermediate- and high-risk PE patients, with the understanding that data supporting any of them is either inconclusive or lacking, and therefore not covered by American and European guidelines. Most PE patients only require simple anticoagulation; patients with high-risk features deserve consideration for an invasive treatment approach.

**BUILDING AN ACUTE PE TEAM AND MANAGEMENT PATHWAY**

Intensive management of acute PE begins with formation of a PERT. Assembling a team of specialists and coordinating care through a system similar to the management of ST-segment elevation myocardial infarction (STEMI) has been described at several institutions (3,5,6). A PERT may consist of specialists from vascular medicine, pulmonary critical care, emergency medicine, interventional cardiology/radiology, hematology, vascular surgery, and cardiothoracic surgery. Not every hospital system will engage all of these subspecialists, but we recommend, at a minimum, representatives from medicine, interventional cardiology/radiology, and surgery, as the decisions to be made require an understanding of the risks and benefits of all treatment modalities.

The PERT's responsibility is to assess each case in a timely manner, examine the patient, review the available data, perform any additional testing, and then (in conjunction with the patient, family members, and care team) develop a consensus regarding the optimal treatment plan. In certain patients with massive PE and rapid deterioration, the decision to give fibrinolytic agents, go to the interventional laboratory, or proceed to the operating room will need to be made urgently by a limited number of PERT members. In such cases, prior experience assessing multiple patients with PERT colleagues will lend advantage to the on-call team members and inform their decision making. As a foundation, we recommend that the local PERT review current published reports and society guidelines (1,2,7) and establish an institutional acute PE protocol, as in the Central Illustration (6). The key to team management is activation of the PERT with a single phone call. Team members should have an easily accessible online system allowing all members to review the available medical information, including computed tomography (CT) scans, echocardiograms, electrocardiograms, and laboratory data. PE teams should leverage existing systems, such as hospital electronic medical records, imaging systems, virtual meeting rooms, and STEMI or acute stroke activation protocols. Furthermore, teams should identify the admission location best able to manage sick patients with submassive and massive PE. A defined area enables consistency and further development of expertise in management of complex PE patients. A cardiovascular intensive care unit where the surgeon, cardiovascular specialist, and critical care specialist round together is a reasonable choice. This type of team approach is a well-established Class I recommendation for management of ischemic heart disease (8).

In May 2015, the National PERT Consortium launch meeting, sponsored by the Massachusetts General Hospital PERT, was held in Boston, Massachusetts, and was attended by approximately 40 hospital-based PE teams. There was an important call to action to gather and share data on patients with PE. We encourage PERTs to establish institutional review board-approved databases that can be shared among like-minded institutions for further advancement of PE management, such as Research Electronic Data Capture (RedCap). Participation in a multicenter registry, such as that under development by the National PERT Consortium, will enable systematic, broad-based assessment of outcomes and further our knowledge regarding optimal care and best practices.

**PRE-INTERVENTION**

Unless contraindicated, anticoagulation should be initiated when PE is suspected, prior to additional work-up. Intravenous heparin is a good initial choice while alternative options (such as invasive therapies) are being evaluated. After confirmation, the first question is whether the PE is low risk versus submassive to massive. Massive PE is currently defined by hypotension with a systolic blood pressure (SBP) <90 mm Hg for >15 min or the requirement of inotropic support to maintain SBP >90 mm Hg. Submassive PE is defined by SBP >90 mm Hg with evidence of right heart dysfunction, as noted by a dilated RV with an RV to left ventricle ratio >0.9 in the 4-chamber view by CT or echocardiogram, or elevated biomarkers, such as troponin or B-type natriuretic peptide. The echocardiogram has the advantage of demonstrating depressed RV function and providing an estimate of pulmonary arterial systolic pressure. Other high-risk markers of submassive PE include tachycardia, tachypnea, and hypoxia, which may be less specific, and thus less helpful in management selection. Special attention
should be given to patients who had syncope, which may represent transient hemodynamic instability and the potential for higher risk (9). Hemodynamically stable patients without evidence of RV strain are considered to be at low risk, may not require PERT activation, and can be treated with anticoagulation alone. That said, the PERT might help the clinical team define the level of risk and optimal therapy for each individual patient.

Once the PERT has been activated, members typically meet, either at the patient’s bedside or virtually, and review all patient-related data. The most important data include the presenting history, with a focus on symptoms and signs of hemodynamic instability, vital signs, CT, echocardiogram, and laboratory data. Team members should discuss indications and contraindications to fibrinolytic therapy, catheter-based intervention, and surgical embolectomy, followed by discussion with the patient and family members, including the risks and benefits of each therapy proposed. A sample algorithm to help in triaging patients presenting to the emergency room of a hospital with a PERT is provided (Figure 1). The PERT should consider the degree of hemodynamic compromise and the existence of variable contraindications. The simplified PE severity index may be a useful aid when further considering the risks and benefits of interventional therapies (10).

**SYSTEMIC FIBRINOLYSIS**

Traditionally, intravenous (IV) fibrinolysis has been considered the primary intensive therapy option in patients with high-risk PE, although the data supporting its use in massive PE is poor. Most trials that randomized patients with PE to fibrinolytics versus standard anticoagulation included submassive PE only. A meta-analysis of trials including patients with massive PE showed a reduction in the composite of recurrent PE and death with use of IV fibrinolytic agents, but not in death alone (11). Univariate analysis of a large inpatient sample found that among unstable patients with PE, use of IV fibrinolytic therapy was associated with a lower mortality rate (12), but only 30% of unstable patients received such therapy.

Patients with submassive PE were better represented in randomized trials. The MAPPET (Management, Strategies and Prognosis of Pulmonary Embolism)-3 trial (13) randomized 256 patients with PE and pulmonary hypertension or RV dysfunction to 100 mg of IV alteplase or placebo infused over 2 h plus anticoagulation. IV alteplase was associated with a lower risk of further need to escalate the treatment and with a similar risk of death. Mortality was lower than expected in both groups (3.4% in the alteplase and 2.2% in the placebo group; p = 0.71). More recently, the PEITHO (Pulmonary Embolism Thrombolysis) trial (14) randomized 1,006 patients with submassive PE (normal blood pressure, RV enlargement, and increased troponin level) to tenecteplase or placebo. The PEITHO trial showed a reduction in the primary endpoint of hemodynamic collapse at 7 days with tenecteplase, but a significant increase in hemorrhagic stroke (most in patients older than 75 years of age), with similar mortality in both groups. The smaller MOPETT (Moderate Pulmonary Embolism Treated With Thrombolysis) trial (15) randomized 121 patients with moderate-risk PE to half-dose alteplase (maximum 50 mg over 2 h) with anticoagulation versus anticoagulation alone. Low-dose alteplase was associated with lower pulmonary pressure at 28 months and no major bleeding. A 1,700 patient meta-analysis...
of all fibrinolysis trials, including patients with catheter-directed fibrinolysis (CDF), demonstrated a statistically significant mortality benefit from fibrinolysis in patients with intermediate-risk PE (16). There was a significantly increased risk of hemorrhage, but the benefit appeared to outweigh the risk when the analysis excluded patients older than 65 years of age. Importantly, subanalyses of patients younger than 65 years of age were performed post hoc in the trials included in the meta-analysis.

Taken together, these studies show that the use of IV fibrinolytic therapy in patients with massive or submassive PE leads to improved hemodynamic stabilization and, possibly, a lower risk of recurrent PE and PE-attributed death. However, this benefit comes with an increased risk of severe bleeding and intracranial hemorrhage (14).

**CATHETER-BASED THERAPIES**

Catheter-based therapies aim to relieve obstruction quickly and restore pulmonary blood flow, thus improving cardiac output and converting a hemodynamically unstable situation into a stable one. This is accomplished with reduced or no doses of fibrinolytic agents. Catheter-directed therapies (CDT) might include clot fragmentation, aspiration, and low-dose fibrinolytic injection. The American Heart Association and American College of Chest Physicians guidelines address catheter-based management of
acute PE, giving advanced therapies a limited recommendation because of a lack of randomized control data (1,7).

Multiple percutaneous techniques have been described for treatment of unstable patients with PE (Table 1). They aim at relieving the obstruction in the pulmonary circulation, thus immediately improving the patient's hemodynamics and potentially reducing the long-term risk of pulmonary hypertension (17). These techniques have been poorly studied, and they face the challenge of trying to remove large, sometimes organized thrombi from a large space with numerous 3-dimensional branches and multiple angles. The simplest and most commonly performed catheter-based therapy is a local, slow infusion of a fibrinolytic agent through low-profile catheters placed in the obstructed pulmonary artery (PA). CDF is best suited for more stable patients or those who have been hemodynamically stabilized, as thrombus resolution may take several hours.

For unstable patients who require immediate intervention and/or those with contraindication to fibrinolysis, mechanical thrombus fragmentation, debulking, or aspiration of occlusive thrombi may be attempted.

Potential complications of any catheter-based therapy may include pulmonary arterial injury, pericardial tamponade, major bleeding, hemodynamic deterioration, distal embolization and “no-reflow” phenomenon, and access site bleeding. A meta-analysis of CDT using ≤10-F low-profile devices reported minor and major procedural complications of 7.9% and 2.4%, respectively (18). Minor complications included: groin hematomas not requiring transfusion, transient bradycardia, heart block, hemoglobinuria, mild hemoptysis, temporary renal insufficiency, embolus dislocation (n = 1), and PA dissection (n = 1). Major complications included: groin hematomas requiring transfusion, massive hemoptysis requiring transfusion, renal failure requiring hemodialysis, cardiac tamponade (n = 1), and death (n = 5; 1 each from bradycardia and apnea, distal embolization, and cerebral vascular hemorrhage, plus 2 procedure-related deaths not otherwise specified) (18).

**Fragmentation and Aspiration.** Fragmentation and aspiration of PE may be helpful in stabilizing patients with massive PE, especially when systemic fibrinolysis is contraindicated or has failed. Multiple techniques have been tried with some success (19). By rotating a pigtail catheter in the PA, the PE can be fragmented (20). The aim is to reduce the load on the RV by partially relieving the obstruction in the main PA branches. Fragmentation alone may cause distal embolization and potentially worsen distal branch obstruction (21). Fragmentation is frequently combined with local infusion of small-dose fibrinolytic agents (e.g., 4 to 10 mg of tissue-type plasminogen activator [t-PA]), delivered either at the time of the procedure or subsequently via an infusion catheter left in place. Concomitant aspiration can reduce the risk of worsening obstruction (21). Fragmentation can also be performed by inflation of an angioplasty balloon, with care to keep inflation in larger vessels and to choose a balloon smaller than the artery diameter. Injection through a diagnostic catheter (e.g., a multipurpose catheter) placed distal to the intended inflation site can help determine the size of the distal artery before selecting a balloon catheter.

Aspiration can be attempted using regular 8-F guide catheters or specialized catheters. One of the first aspiration catheters was the Greenfield embolectomy catheter (22), which consisted of a suction cup at the tip of a straight catheter. Its complexity and the requirement for a surgical cutdown for access prevented it from being widely adopted. Other specialized devices used to treat peripheral thrombi have also been used off-label to treat PE. These include the 10-F Aspirex thrombectomy catheter (Straub Medical, Wangs, Switzerland), currently unavailable in the United States, which combines rotational thrombus fragmentation with aspiration (23); the 7-F Helix Clot Buster (ev3, Plymouth, Minnesota), approved for dialysis graft thrombosis treatment (24); and 8- to 14-F Pronto XL manual extraction catheters (Vascular Solutions, Minneapolis, Minnesota).

The Angiojet Rheolytic Thrombectomy System (Possis, Minneapolis, Minnesota) deserves special mention. This 8-F peripheral catheter utilizes the

### Table 1: Catheter-Based Therapies

<table>
<thead>
<tr>
<th>Device</th>
<th>Size</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pigtail catheter</td>
<td>6- to 8-F</td>
<td>Fragmentation</td>
</tr>
<tr>
<td>Peripheral balloon</td>
<td>5 to 10 mm</td>
<td>Fragmentation</td>
</tr>
<tr>
<td>Catheter-directed fibrinolysis</td>
<td>4- to 6-F</td>
<td>Direct infusion of fibrinolytic agent</td>
</tr>
<tr>
<td>Ultrasound-accelerated thrombolysis</td>
<td>6-F</td>
<td>Direct infusion of fibrinolytic agent plus ultrasound for clot separation. Currently the only catheter-based therapy FDA-approved for PE treatment.</td>
</tr>
<tr>
<td>Guide catheter</td>
<td>6- to 10-F</td>
<td>Manual aspiration</td>
</tr>
<tr>
<td>Pronto XL catheter</td>
<td>6- to 14-F</td>
<td>Manual aspiration</td>
</tr>
<tr>
<td>Penumbra Indigo system</td>
<td>6- to 8-F</td>
<td>Suction pump aspiration</td>
</tr>
<tr>
<td>Inari FlowTrieve</td>
<td>22-F sheath</td>
<td>Disruption, retraction, and aspiration of clot</td>
</tr>
<tr>
<td>AngioVac</td>
<td>26-F sheath and 18-F cannula</td>
<td>Large-volume aspiration with return of filtered blood utilizing a centrifugal pump</td>
</tr>
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FDA = Food and Drug Administration; PE = pulmonary embolism.
Venturi-Bernoulli effect, using multiple high-velocity saline jets introduced through the distal tip, creating a low-pressure vacuum through small slits in the catheter that can entrain and fragment thrombi. A meta-analysis reported higher mortality and morbidity, including massive hemoptysis, renal failure, and death from bradycardia and apnea or from widespread distal embolization (18), which resulted in a black-box warning from the Food and Drug Administration (FDA) for use of Angiojet in acute PE.

Additional embolectomy devices are discussed in the following sections.

**AngioVac thrombectomy device.** The AngioVac Cannula (Angiodynamics, Latham, New York), a 22-F venous catheter that can remove soft thrombi utilizing the centrifugal pump and venous reinfusion cannula used in cardiopulmonary bypass (Figure 2), is FDA approved for the removal of undesirable intravascular material, including fresh, soft thrombi or emboli. The AngioVac catheter consists of a balloon-expandable, funnel-shaped distal tip, which improves removal of large clots en masse. Patients are prepped in 2 body locations that will allow for large venous sheath placements (common femoral or internal jugular veins). A 26-F sheath is placed in 1 vein and an 18-F reinfusion cannula is placed in another vein. The AngioVac cannula is then attached to the inflow tubing of the centrifuge pump and the outflow tubing connected to the 18-F reinfusion cannula, creating a “veno-veno” bypass circuit. The cannula is inserted into the 26-F sheath and is advanced to the thrombus, which is suctioned out and captured by a filtration canister inserted proximal to the centrifuge pump; filtered blood is returned continuously via the reinfusion cannula. Limitations of this device include the large dual sheaths required for access, leading to a higher likelihood of bleeding complications, and the relatively stiff suction catheter, which is difficult to maneuver into the RV and PA. Furthermore, the active participation of an experienced perfusionist is required for AngioVac setup and operation, as there is a learning curve for its use. AngioVac has been utilized in PE, although it is more commonly used to retrieve thrombi from the vena cava and right atrium (25). The rapidity of initiation may limit its use in massive PE situations; future iterations may render it more useful for PE.

**FlowTriever device.** The FlowTriever catheter (Inari Medical, Irvine, California) is a recently released device that has FDA 510(k) approval for removal of emboli and thrombi from blood vessels (Figure 3). The FlowTriever Infusion Aspiration System requires a 22-F venous sheath and consists of 3 parts: the Flow Restoration Catheter, which is made up of 3 self-expanding nitinol disks; the Aspiration Guide Catheter; and the Retraction Aspirator Device. The FlowTriever device is advanced over the wire and into the thrombus, where the expandable disks are deployed using a pin and pull method. The disks and disrupted thrombus are then retracted and removed through the aspiration catheter. Set-up is rapid, and there is a modest learning curve for device utilization. Limitations include the large size requirement of the access sheath, and manipulation of the large-bore catheter into the PA.

**Penumbra Indigo thrombectomy system.** The Indigo mechanical thrombectomy system (Penumbra, Inc., Alameda, California) consists of a pump, 6- to 8-F straight or angled catheters, and a Separator device (Figure 4). It is approved for thrombus removal in both peripheral arterial and venous systems. An advantage is that it only requires an 8-F venous
sheath and can be placed into the PA system quickly, in an over-the-wire technique. Once placed proximal to the clot, the thrombectomy catheter is advanced while suction is supplied with the ACER pump. The provided Separator wire is used to clear the system of thrombus as the catheter is manipulated inside the artery.

A distinct limitation of these last 3 devices is the absence of published data on their overall success and safety.

**CATHETER-DIRECTED FIBRINOLYSIS. General considerations.** Given that full-dose systemic fibrinolysis is helpful in stabilizing high-risk PE patients and reducing pulmonary pressure, but at the cost of increased systemic bleeding, interest has risen in local delivery of low-dose fibrinolytics close to or into the PA thrombus. Unfortunately, data supporting such therapy is limited and mostly from small case series (18,26–28). One small trial randomized 34 patients with angiographically large PE to IV- or catheter-based infusion of t-PA at a dose of 50 mg over 2 h (29), and showed similar safety and angiographic and hemodynamic results by both techniques. However, the local fibrinolytic dose used in this older trial was much higher than what is currently used. In a more recent prospective registry of 101 massive and submassive PE patients treated with catheter-based therapy (mostly local fibrinolysis), there was a significant decrease in PA pressure and improvement in RV function, with no reported major complications, major bleeding, or strokes (26). Given the low risk for major complications, it is reasonable to consider CDF in patients with already stabilized massive PE who have contraindications to systemic fibrinolysis and in patients with intermediate-high-risk PE (those with RV dysfunction and increased biomarkers), particularly those deemed at increased bleeding risk with full-dose systemic fibrinolysis. In a series of 52 PE patients treated with CDF, a more prominent hemodynamic benefit was obtained in patients with symptom duration <14 days, as compared with those with a longer symptom duration (28).

**Technique.** CT images, if available, are the basis for planning the CDT procedure. Most high-risk patients have bilateral PE, although some have a major thrombus in 1 PA and only require unilateral treatment. Internal jugular or femoral venous access with ultrasound guidance is obtained. For femoral access, ultrasound is used to rule out iliofemoral thrombus. A catheter (e.g., balloon-tipped, pigtail, or multipurpose) is carefully advanced to the main PA, where pressure and blood oxygen saturation sampling are obtained. Contrast injection into the main PA or selectively into each PA can be performed to identify the location of the thrombi; these are typically in the main and/or lower main PA branch (Figure 5). If the location of the thrombi is not clear by manual injection, or the anatomy has not been previously established by CT, and if the pulmonary pressure is not severely elevated, a power injection may be necessary (e.g., at 15 to 20 m/s for a total of 30 ml selectively in each main PA, with a 15° to 20° left anterior oblique projection for the left PA and 0° to 20° right anterior oblique projection for right PA). The volume of contrast injected can be adjusted on the basis of the CT findings. An exchange-length soft- or j-tipped wire is placed in the lower PA branch, and the diagnostic catheter is exchanged for an infusion catheter, which has a treatment zone of 6 to 12 cm through which t-PA may be infused into the clot. A second infusion catheter may be placed in the
contralateral PA through a second venous sheath, if needed, using the same technique. Alternatively, a 10- to 12-F sheath may be placed at the beginning of the procedure and both catheters placed through the larger sheath. A commonly used t-PA dose is 0.5 to 1.0 mg/h per catheter. The total t-PA dose is typically between 12 and 24 mg, delivered over 6 to 24 h. Low-dose, weight-adjusted heparin infusion is usually continued during t-PA infusion, with a target partial thromboplastin time on the low end of the therapeutic range (e.g., 40 to 60 s).

Commonly available infusion catheters used off-label for PE include the Cragg-McNamera catheter (ev3 Endovascular Inc.), the Fountain catheter (Merit Medical, South Jordan, Utah), and the Unifuse catheter (Angiodynamics). The EkoSonic catheter, discussed later, is currently the only catheter specifically approved by FDA for the treatment of high-risk PE.

The risk of serious complications, including major hemorrhage, using CDT has been low in published studies. The risk of intracranial hemorrhage is <0.2% (18,26–28).

**Ultrasound accelerated fibrinolysis.** The EkoSonic catheter (Figure 6) consists of a 5.2-F conventional infusion catheter with an inner cable that transmits high-frequency, low-power ultrasound signals, designed to loosen the fibrin strands and enhance thrombus penetration of the fibrinolytic agent, hence theoretically achieving a faster thrombus breakdown (30). The technique used for in vivo insertion is similar to other infusion catheters, as described earlier. Once the catheter is in position over the 0.035-inch guidewire, the guidewire is replaced with the microsonic cable, which is then locked into place. The catheter has 2 infusion ports: 1 for the fibrinolytic infusion, and the other for a coolant solution (normal saline at ≥35 ml/h).

Limited evidence supports the use of ultrasound-accelerated thrombolysis (discussed in detail by Konstantinides et al. [31]). It is uncertain whether this treatment is suitable for patients who are hemodynamically unstable and need faster resolution of the PE or if there is long-term benefit of the prolonged treatment in prevention of future pulmonary hypertension, underscoring the need for more evidence.

**EXTRACORPOREAL MEchanical Oxygenation And Rv Assist DEvices**

Extracorporeal membrane oxygenator (ECMO) placement has been described in case reports of patients with massive PE, as it has the potential to unload the RV and, importantly, provides oxygenation during massive PE to allow for RV recovery (32,33). The ability of the interventional team to place the ECMO underscores the importance of a multidisciplinary approach. In many institutions, PERT members are also ECMO service members.

Technologies such as the percutaneous RV assist device (Impella RP, Abiomed, Danvers, Massachusetts) may one day be considered for use in massive PE, either as a bridge to definitive therapy, or to support RV recovery after thrombus removal.

**SURGICAL EMboLECTOMY**

Currently, surgical therapy is considered a last resort for acute PE and is offered only to patients in extremis. This concept is on the basis of data from the 1960s, when the surgical pulmonary embolectomy mortality rate was in excess of 50% (34). This may have been due, in part, to selection bias, as only patients with very poor prognosis were brought to the operating room. Significant advances in cardiac surgical techniques have led to an impressive reduction in operative mortality, which is as low as 6% in the current era (35,36). Furthermore, there is evidence to support reduced long-term mortality in patients undergoing pulmonary embolectomy (37,38). In a 2013 report on 27 consecutive surgical pulmonary embolectomy patients, there was no
in-hospital mortality and a 10-year actuarial survival rate of 93%; both late mortalities were unrelated to PE or related therapy (39).

**SURGICAL TECHNIQUE.** After median sternotomy, patients are anticoagulated with heparin and placed on cardiopulmonary bypass. Dual venous cannulation allows excellent venous drainage and full access to the right heart. The PA is typically opened longitudinally, distal to the pulmonic valve, to a length of approximately 5 cm. Sponge forceps are used to grasp and remove visible clots. Small clot fragments may be extracted using targeted gentle suction. The aorta may be circumferentially freed and gently retracted to allow “deeper” visualization of the right PA. Occasionally, a secondary distal incision of the right PA is made to allow even more distal access. Clots are typically not adhered to the artery wall, and thus are easily removable in acute PE cases.

**VENA CAVA FILTER**

Placement of an inferior vena cava (IVC) filter is indicated in patients with acute PE who have absolute contraindications to anticoagulation or in patients who have recurrent PE, despite adequate anticoagulation (1,2). The position of the filter below or above the renal veins depends on the absence or presence of renal vein thrombus, respectively. Retrievable filters are preferable because they are associated with lower complication rates (40). Both the American and the European guidelines do not recommend routine use of IVC filters in patients with PE (1,2). These recommendations are supported
by the PREPIC2 (Prevention of Recurrent Pulmonary Embolism by Vena Cava Interruption 2) study, recently conducted in intermediate- and low-risk patients (41). However, 3 large analyses, including a U.S. nationwide hospital sample (42) and a study from Japan (43), suggest that IVC filters may result in better outcomes in patients with massive or intermediate-high-risk PE. In the International Cooperative Pulmonary Embolism registry, IVC filter use in patients with massive PE was associated with reduced rates of recurrent PE and mortality at 90 days (44).

**POST-INTERVENTION**

Maintenance of anticoagulation post-intervention is critical to prevent recurrent clot formation. However, patients who have had a recent catheter-based intervention are at risk of access site bleeding. One strategy to potentially reduce bleeding risk is to hold the heparin drip for 1 to 2 h after sheath removal, then restart without a bolus. Warfarin is administered on the night of the procedure, and parenteral anticoagulation and warfarin are overlapped until the international normalized ratio is 2 to 3 for at least 24 h, as per American College of Chest Physicians guidelines (7).

Low molecular weight heparin can be utilized in lieu of IV heparin. Alternatively, novel oral anticoagulants, including rivaroxaban, dabigatran, apixaban, and edoxaban, can be used (45-48). However, no guidelines indicate when or how these agents should be initiated post-CDT, especially if fibrinolytic agents have been administered. If an alternative anticoagulant agent is utilized, we suggest heparin alone for the first 24 to 48 h post-intervention and then discontinuation of the heparin at the time of the first alternative anticoagulant agent dosing. This strategy does not include dabigatran or edoxaban usage, which require at least 5 days of parenteral therapy before initiation.

Appropriate transition of the patient from the inpatient to the outpatient setting is important. This includes assessment of adequacy of anticoagulation or affordability of novel anticoagulant agents, if prescribed. Outpatient follow-up with a medical provider familiar with PE care is imperative; several institutions incorporate a PE follow-up clinic as part of the PERT program. To be addressed at follow-up are: monitoring of anticoagulation; assessment of length of anticoagulation and bleeding risk; retrieval of IVC filter, if appropriate; screening for the development of chronic pulmonary hypertension in patients at risk; and completion of a hypercoagulable profile, when indicated.

**CONCLUSIONS**

At this time, there is not enough evidence to strongly support routine utilization of any of the previously discussed techniques in the management of submassive or massive PE, beyond anticoagulation. Most PE patients should continue to be treated conservatively, with aggressive treatment options reserved for those at high- or intermediate-high-risk without contraindications. Several studies have shown benefit from systemic fibrinolysis in this patient population, at the expense of an increased bleeding risk. Currently, CDF with use of the EKOS catheter is the only FDA-approved catheter-based therapy for use in treatment of acute PE, although adequate comparative studies are lacking. Other catheter-based therapies focus on direct thrombus removal without use of fibrinolytic agents and may be an option for patients who either cannot receive fibrinolysis or cannot wait for CDF to take effect. Although some centers have reported favorable outcomes with surgical embolectomy as a first-line management of intermediate-high- and high-risk PE, it is reasonable to reserve it for patients with massive PE and shock, who have contraindications to fibrinolysis, who have failed other treatments, or who have concomitant intracardiac thrombus or paradoxical embolus.

**FIGURE 6** EkoSonic Endovascular Device

The 5.2-F infusion catheter (A), which contains 3 lumens: 1 each for the inner ultrasound cable, drug infusion, and normal saline as a coolant. The inner cable (B) is shown with ultrasound crystals (arrows). Ultrasound energy separates fibrin strands, allowing for enhanced thrombus penetration of fibrinolytic agent. Images from EKOS Corporation.
Until appropriate studies fill knowledge gaps, we recommend utilization of multidisciplinary PERTs and collection and sharing of data in registries or formal studies. We have provided sample algorithms and pathways to coordinate response to PE and encourage multidisciplinary decision making. Similar to a “Code Stroke” or “Code STEMI,” PE should be considered as a “lung attack,” and appropriate resources utilized. Formation of hospital-based PERT programs and collaboration across multiple institutions through the National PERT Consortium can provide the foundation for global prospective registries and much-needed randomized trials.

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REFERENCES


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