Most patients with an acute pulmonary embolism (PE) will have an uncomplicated clinical course once effective levels of anticoagulation are obtained. However, in PE patients presenting with low systemic arterial blood pressure or with signs of reduced organ perfusion, the overall 3-month mortality rate is approximately 50%, with acute right ventricular failure as the most common cause of early death. In these patients, rapid reperfusion of the pulmonary arteries facilitates reversal of right ventricular failure and, therefore, is potentially life-saving. This issue of Cardiology Rounds focuses on catheter interventions in patients with massive PE.

Reperfusion therapy options

Systolic blood pressure (SBP) at the time of PE diagnosis is the most powerful predictor of early death. In 2392 patients in the International Cooperative Pulmonary Embolism Registry (ICOPER), the 90-day mortality rates were:

- 52.4% (95% CI, 43.3-62.1) in patients with massive PE and an SBP < 90 mm Hg; and
- 14.7% (95% CI, 13.3-16.2) in those with a preserved SBP ≥ 90 mm Hg (Figure 1).1,2

Among the 108 patients with massive PE, the diagnosis was first established at autopsy in 15%. In ICOPER, potentially life-saving treatment, including thrombolysis, catheter thrombectomy, or surgical embolectomy, was withheld in two-thirds of the patients with massive PE.

In patients with massive PE, systemic thrombolysis1 or surgical embolectomy,1 in addition to anticoagulation, are standard treatments. Thrombolysis with a continuous intravenous infusion of 100 mg recombinant tissue plasminogen activator (r-tPA) over 2 hours is approved by the Food and Drug Administration (FDA) for patients with massive PE. However, approximately one-third are not eligible for thrombolysis because of contraindications, such as recent surgery, trauma, stroke, or advanced cancer.1 PE thrombolysis is accompanied by a particularly high risk of bleeding complications. Among 304 patients from the ICOPER who received PE thrombolysis, 66 (21.7%) suffered major bleeding and 9 (3.0%) had intracranial bleeding.2 At the Brigham and Women’s Hospital, 104 PE patients received a continuous intravenous infusion of 100 mg r-tPA over 2 hours from 1996-2004.6 Major bleeding occurred in 20 (19.6%), and systemic hypotension, cancer, diabetes mellitus, and elevated INR were identified as independent predictors of major hemorrhage.
Several tertiary care centers perform emergency surgical embolectomy in patients with massive PE and contraindications to thrombolysis.4 This operation mandates a median sternotomy, incision of the main pulmonary artery, and circulatory arrest with cardiopulmonary bypass. In the 2 largest PE registries, surgical embolectomy was used in only 1% of patients with massive PE and cardiogenic shock.2,5

The only alternative to thrombolysis or surgical embolectomy for reversing PE-related right heart failure and cardiogenic shock is percutaneous catheter thrombectomy.7,8 Catheter thrombectomy may be particularly useful if contraindications to thrombolysis are present or if surgical embolectomy is not feasible.

**Indications for catheter intervention**

Catheter intervention in massive PE patients aims at removing obstructing thrombi from the main pulmonary arteries and reversing right ventricular failure and hemodynamic instability.

The indications for catheter thrombectomy have not been clearly defined by the North American or the European consensus guidelines. The following 3 criteria should be fulfilled when considering catheter thrombectomy in a patient with acute PE:

1. hemodynamic instability, defined as a SBP of ≤90 mm Hg, a drop in SBP of ≥40 mm Hg for ≥15 minutes, or ongoing administration of catecholamines for systemic arterial hypotension;
2. subtotal or total filling defect in the left and/or right main pulmonary artery by chest computed tomography (CT) or by conventional pulmonary angiography;
3. failed thrombolysis or the presence of at least one of the following contraindications to thrombolysis:
   - active bleeding
   - history of intracranial bleeding, head injury, ischemic stroke, brain tumor, or neurosurgery
   - surgery, delivery, organ biopsy, puncture of a non-compressible vessel within 10 days
   - gastrointestinal bleeding within 15 days
   - major trauma within 15 days
   - active cancer with known hemorrhagic risk
   - platelets <50,000 or INR >2.0
   - pregnancy.

Surgical embolectomy rather than catheter thrombectomy should be considered in the presence of free-floating cardiac thrombi or in patients with paradoxical embolism from a large atrial septal defect.

**Percutaneous catheter devices**

An ideal percutaneous PE thrombectomy catheter should be:

- highly maneuverable to allow rapid right heart passage and advancement into major pulmonary arteries
- effective in removing obstructing thrombi from main pulmonary arteries to facilitate rapid improvement in hemodynamics
- safe without causing damage to cardiac structures and pulmonary arteries, and without causing significant blood loss, distal thrombus embolization, or mechanical hemolysis.

**The Greenfield embolectomy catheter**

The Greenfield embolectomy device (Boston Scientific/Meditech, MA) is a 10-French, steerable catheter with a 5-mm or 7-mm plastic suction cup at the tip (Figure 2). This device – the first catheter designed to treat massive PE – has been available for >3 decades. The major disadvantage is that it has to be inserted through a venotomy via the femoral or jugular vein and cannot be introduced with a guide wire. The device removes centrally-located fresh embolus by manual suction with a large syringe and requires retrieval of the device and the thrombus as a unit through the venotomy site. In the hands of Dr. Greenfield, the device has been successful in extracting pulmonary thrombus in 76% of patients, with significant improvement in hemodynamics.9,10 The 30-day mortality rate was 30%. A risk of the device is the loss of the entrapped thrombus when removing it from the pulmonary circulation, which can result in embolization and hemodynamic deterioration.
Mortality in this series was 20%. One disadvantage is the risk of macroembolization, which may cause further deterioration in hemodynamics when a large centrally-located non-obstructive thrombus breaks and embolizes into a previously nonobstructed branch.

**Amplatzer thrombectomy device (ATD)**

The Amplatzer Thrombectomy Device (Bard-Microvena, MN) is a 7-French catheter with a distal metal can housing an impeller mounted on a drive shaft. The high speed of the impeller creates a vortex of circulating blood, pulling the clots toward the impeller, which pulverizes and recirculates fresh thrombus. The ATD cannot be used in combination with a guide wire; therefore, a guiding catheter is advanced close to the pulmonary embolus and the ATD is introduced through the catheter. Initial experience with the ATD device resulted in clinical improvement in a limited number of patients, with improvement in symptoms and SBP. There is the risk of severe hemoptysis with the ATD and it is unclear whether it is the result of perforation, dissection, or reperfusion injury. Because of the recirculation of macerated blood and thrombus, the ATD always causes some degree of transient mechanical hemolysis.

**Hydrodynamic thrombectomy catheter devices**

None of the currently available hydrodynamic catheter devices were designed for treatment of the large-sized pulmonary arteries, but they have been successfully used in small case series of patients with massive PE. The AngioJet Xpeedior (Possis, MN) is a 6-French, over-the-wire catheter and probably the most efficacious catheter among the hydrodynamic devices (Figure 3). However, since AngioJet was not designed to treat vessels >12 mm in diameter, it is also of limited effectiveness in the therapy of massive PE. However, minor improvements in pulmonary perfusion are often sufficient to improve hemodynamics and clinical outcomes in these critically-ill patients.

**Aspirex pulmonary embolism thrombectomy catheter**

The 11-French Aspirex catheter thrombectomy device (Straub Medical, Switzerland) was specifically designed and developed for percutaneous interventional treatment of PE in pulmonary arteries, ranging from 6-14 mm in caliber. The central part of this over-the-wire catheter system is a high-speed rotational coil within the...
catheter body that creates negative pressure through an L-shaped aspiration port at the catheter tip, macerates aspirated thrombus, and removes macerated thrombus (Figure 4). The catheter is connected to a motor via an electromagnetic clutch. A small control unit ensures steady motor speed at 40,000 rpm.

The aspiration capacity of the Aspirex device was adjusted to remove thrombus from obstructed major pulmonary arteries and minimize the risk of vascular collapse and vessel wall entrapment. The design of the Aspirex catheter does not allow recirculation of aspirated blood or thrombus. In static in-vitro tests using human blood samples, aspiration with the Aspirex device was not associated with an increase in plasma free hemoglobin.27 The Aspirex device was effective and safe in animal experiments.27

Currently, a multinational registry is investigating device effectiveness and safety using a compassionate-use protocol for massive PE patients (an example is described in Figure 5) according to the above-mentioned inclusion criteria. The Aspirex device will be available in the United States once the FDA has approved it.

Catheter-directed fibrinolysis

Catheter-directed thrombolytic therapy with intrapulmonary administration of a fibrinolytic
drug has been used by several authors.\textsuperscript{28-31} Local fibrinolysis is occasionally used in combination with catheter thrombectomy, particularly if recanalization of main pulmonary arteries by catheter thrombectomy is incomplete. It accelerates clot lysis and achieves rapid reperfusion of the pulmonary arteries. The technique requires positioning of an infusion catheter within the embolus, with injection of a bolus of thrombolytic drug, followed by a continuous infusion. The following intrapulmonary thrombolytic regimens have been used in combination with a therapeutic infusion of unfractionated heparin in patients with massive PE: urokinase 250,000 IU/h over 2 hours, followed by urokinase 100,000 IU/h for 12-24 hours; alteplase bolus of 10 mg followed by 20 mg/h over 2 hours, or 100 mg over 7 hours.

**Complications of catheter thrombectomy**

Rare catheter thrombectomy complications include pericardial tamponade and pulmonary hemorrhage. The most serious complication is perforation or dissection of a major pulmonary arterial branch that may cause massive pulmonary hemorrhage and immediate death. The myocardium of the right ventricle, particularly the right ventricular outflow tract, is thin and fragile, and caution is warranted when advancing any device into the pulmonary arteries. The interventionalist must be able to perform emergent pericardiocentesis in case of perforation and should be familiar with measures to achieve rapid reversal of anticoagulation. To minimize the risk of perforation or dissection, thrombectomy should be performed only in the main and lobar pulmonary arteries, not in segmental pulmonary arteries. The procedure should be terminated as soon as hemodynamic improvement is achieved, regardless of the angiographic result.

Device-related complications also include blood loss and mechanical hemolysis, or arrhythmia from catheter passage through the right heart. Other complications include bleeding from heparin anticoagulation, contrast-induced nephropathy, anaphylactic reaction to iodine contrast, and vascular access complications, such as hematoma, pseudoaneurysm, or atrioventricular (AV) fistula.

**Conclusion**

Acute massive PE has an exceptionally high mortality rate with right ventricular failure being the most common cause of early death. Multidisciplinary disease management programs – involving emergency medicine specialists, cardiologists, and cardiovascular surgeons – help in diagnosing this life-threatening entity and rapidly initiating the appropriate treatment. Thrombolysis is standard therapy for patients for whom the risk of bleeding is not substantially increased. In patients who cannot receive thrombolysis, catheter thrombectomy or surgical embolectomy are promising alternatives for effectively reversing right ventricular failure and improving the clinical outcome of these critically-ill patients.

**Samuel Z. Goldhaber, MD**, was guest editor for this issue of *Cardiology Rounds*.

**Reference List**


Disclosure: Dr. Kucher receives research grants from Pfizer and Sanofi-Aventis and consults for Straub Medical.