Catheter-Based Reperfusion Treatment of Pulmonary Embolism
Rolf P. Engelberger, MD; Nils Kucher, MD

Case Presentation: A 76-year-old man with a history of hemicolecotomy for colon cancer 10 days previously was admitted because of syncope and severe shortness of breath. On physical examination, the patient was hemodynamically unstable, with a systolic arterial pressure of 80 mm Hg, a heart rate of 124 beats per minute, and distended jugular veins. He was agitated and unable to speak full sentences. His respiratory rate was 28 breaths per minute, and oxygen saturation was 80% on room air. Contrast-enhanced computed tomography showed a filling defect of the left main pulmonary artery, complete occlusion of the left lower lobe pulmonary artery, and right ventricular enlargement (right-to-left ventricular dimension ratio of 1.4) (Figure 1). After administration of unfractionated heparin and fluids, the systemic arterial systolic pressure dropped to 75 mm Hg, and an infusion with norepinephrine was initiated.

How should these 2 cases be further evaluated and treated?

Reperfusion Therapy
Acute pulmonary embolism (PE) is a life-threatening condition with an estimated overall mortality rate of ≈15% at 3 months.2 Massive (or high-risk) PE is defined as acute PE with sustained systemic arterial hypotension (usually systolic arterial pressure 90 mm Hg), cardiogenic shock, or the need for cardiopulmonary resuscitation; the in-hospital mortality rate may exceed 50%.3 Submassive (or intermediate-risk) PE is associated with preserved systemic arterial pressure, but with right ventricular dysfunction on echocardiography or with elevated cardiac biomarkers; the in-hospital mortality rates between 6% and 8%.4,5 Patients with low-risk PE are hemodynamically stable and have neither right ventricular dysfunction nor elevated cardiac biomarkers; these patients usually have excellent short-term prognosis once therapeutic levels of anticoagulation are established.6

A scientific guideline statement from the American Heart Association7 provides detailed recommendations on the management of acute PE, including suggestions on the use of reperfusion therapy, ie, systemic thrombolysis, catheter interventions, and surgical embolectomy (Figure 2). Thrombolysis with a 2-hour continuous intravenous infusion of 100 mg of recombinant tissue plasminogen activator is approved by the Food and Drug Administration for patients with massive PE and may be considered in patients with submassive acute PE judged to have clinical evidence of adverse prognosis. However, a meta-analysis including 13 randomized clinical trials of fibrinolysis versus heparin...
treatment alone showed no significant reduction in recurrent PE or death. In addition, systemic thrombolysis has absolute and relative contraindications. Absolute contraindications include any prior intracranial hemorrhage, known structural intracranial cerebrovascular disease (eg, arteriovenous malformation), known malignant intracranial neoplasm, ischemic stroke within 3 months, suspected aortic dissection, active bleeding or bleeding diathesis, recent surgery involving the spinal canal or brain, or significant closed-head or facial trauma with radiographic evidence of bony fracture or brain injury. Relative contraindications are age ≥75 years; current use of anticoagulation therapy; pregnancy; puncture of a noncompressible vessel; traumatic or prolonged cardiopulmonary resuscitation (>10 minutes); internal bleeding (within 2–4 weeks); history of chronic, severe, and poorly controlled hypertension or severe uncontrolled hypertension on presentation; dementia; remote (>3 months) ischemic stroke; and major surgery within 3 weeks. It is therefore not surprising that up to two thirds of the patients with massive PE do not receive systemic thrombolysis.

Furthermore, even in selected patients without absolute contraindications to thrombolysis, up to 20% of major hemorrhages and 3% to 5% of intracranial bleeding complications have been reported. Surgical embolectomy requires cardiopulmonary bypass for extracting centrally obstructing pulmonary emboli and is an alternative reperfusion treatment option if absolute contraindications to thrombolysis are present and if performed in an experienced center. According to a meta-analysis on case studies of surgical embolectomy, the pooled mortality rate of 19% from the last decade has substantially improved compared with the pooled mortality rate of 35% before 1990. This observation may likely be attributed to improved surgical techniques and to a change in patient selection.

**Indications for Catheter Intervention**

**Thrombus Fragmentation**

The aim of this technique is to reduce pulmonary vascular resistance by mechanically disrupting thrombus into smaller fragments. Thrombus fragmentation can be achieved by manual rotation of a pigtail catheter or with peripheral balloon angioplasty catheters.

Contemporary Catheter Techniques

**Percutaneous catheter-based interventions are appropriate if systemic full-dose thrombolysis is contraindicated or urgent recanalization of PE is warranted, and if performed in an experienced center. The goal of the catheter intervention is the removal of the obstructing thrombi from the main or lower lobe pulmonary arteries, to facilitate right ventricular recovery, and to improve symptoms and survival.** Since the first description of the Greenfield embolectomy device in 1971, several catheter-based techniques have been introduced.

For patients with absolute contraindications to thrombolysis, contemporary catheter intervention techniques can be separated into 4 categories: (1) thrombus fragmentation, (2) rheolytic thrombectomy, (3) suction thrombectomy, and (4) rotational thrombectomy (Table 1). For patients without absolute contraindications to thrombolysis, 2 approaches are being used: (1) conventional catheter-directed thrombolysis (CDT) and (2) pharmacomechanical thrombolysis (PMT).
Figure 2. Suggested algorithm for the management of acute pulmonary embolism according to the scientific statement of the American Heart Association with the corresponding levels of evidence. The size of the treatment effect is expressed as Class I to III (I: Benefit $\geq$ Risk; IIa: Benefit $>$ Risk; IIb: Benefit $=$ Risk; III: Risk $>$ Benefit) and the certainty of the treatment effect as level A to C (A, data derived from multiple randomized clinical trials or meta-analyses; B, single randomized trial or nonrandomized studies; C, case studies, consensus opinion of experts, or standard of care). Biomarker $-$, negative test results for troponin or natriuretic peptides; biomarker $+$, positive test results for troponin or natriuretic peptides; BP, systolic arterial pressure; CPR, cardiopulmonary resuscitation; ECHO $-$, normal right ventricular function by echocardiography; ECHO $+$, moderate or severe right ventricular dysfunction by echocardiography; IVC, inferior vena cava; PE, pulmonary embolism.

Rheolytic Thrombectomy
A high-pressure saline jet within the AngioJet® device generates a pressure gradient by Bernoulli’s principle, enabling the removal of thrombus fragments. This device also permits local ablating the removal of thrombus fragments without the need for surgical cut down. Because bleeding complications seem to occur less frequently with catheter-directed than with full-dose systemic thrombolysis, this approach is often performed in patients with submassive and massive PE in the presence of relative contraindications to systemic thrombolysis. Fibrinolytic agents are usually administered as a continuous infusion; a bolus can be considered at the time of catheter placement in patients who are hemodynamically unstable. Various drug regimens have been used, eg, recombinant tissue plasminogen activator at a dose of 0.5–2.0 mg per hour per catheter for less than 24 hours (bolus dose of 2–5 mg per catheter).

Pharmacomechanical Thrombolysis
PMT is defined as the combination of CDT with a mechanical catheter intervention technique. The combination of thrombus fragmentation or aspiration with CDT may be particularly useful for patients with hemodynamic instability. Another PMT approach is the Power Pulse spray technique for intraclot delivery of low doses of thrombolytic agents, facilitating rheolytic thrombectomy with the AngioJet device. Ultrasound-enhanced thrombolysis may be considered as PMT and is a combination of CDT with a sophisticated catheter system that uses high-frequency, low-power ultrasound. Ultrasound itself cannot dissolve thrombus, but enhances fibrinolysis by causing reversible disaggregation of uncrosslinked fibrin fibers, thereby increasing thrombus permeability for the thrombolytic drug. In addition, ultrasound pressure waves augment the penetration of thrombolytic drug.
Combined techniques eg, Pigtail fragmentation (5F) plus Aspirex* 8F, 10F thrombectomy.
require continuous hemodynamic and electrocardiographic monitoring. Duplex ultrasonography of the common femoral vein is useful to rule out suspected concomitant iliofemoral DVT.

In our opinion, it is important to obtain complete right heart hemodynamic measurements before and after completion of the procedure for monitoring the treatment effect (Table 2).

The amount of iodine contrast agent should be kept as low as possible and depends mainly on the hemodynamic status and the size of the selected vessel. Despite lower contrast agent requirements with digital subtraction angiography, this technique is not routinely recommended, because most patients with massive PE cannot hold their breath. Nonselective angiography with large (>30 mL) amounts of contrast agent via power injector should be avoided due to the risk of worsening right ventricular failure. To minimize the risk of pulmonary artery perforation, the main and lower lobe pulmonary arteries should be considered for treatment, and segmental branches with a diameter of <6 mm should not be approached.27

### Cases, Continued

In addition to treatment with dose-adjusted unfractionated heparin, a catheter intervention was selected in both cases. For the first case, bilateral

![Figure 3](image-url)

**Figure 3.** Left, Conventional pulmonary angiogram from the first case showing a subtotal filling defect of the left main pulmonary artery and complete occlusion of the lower lobe pulmonary artery (giant embolus delineated by white arrow heads). Middle, fluoroscopic image of the chest showing placement of two 12-cm treatment zone EkoSonic 6F devices with radio-opaque treatment zone markers and ultrasound elements. Right, Conventional pulmonary angiogram after completion of ultrasound-enhanced fibrinolysis showing residual thrombus (white arrow heads) and a recanalized left lower lobe pulmonary artery.

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**Table 2.** Suggested Step-By-Step Approach for the Catheter Intervention Procedure in Patients With Acute Pulmonary Embolism

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>1.</td>
<td>Prepare the patient for standard cardiac catheterization in the catheterization laboratory.</td>
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<tr>
<td>2.</td>
<td>Obtain venous access at the common femoral vein using a standard sheath.</td>
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<tr>
<td>3.</td>
<td>Administer a bolus of 80 units per kilogram of intravenous unfractionated heparin. In patients with heparin pretreatment (bolus or infusion), adjust further heparin dosing according to the activated clotting time (target 250–350 s). In patients who received a therapeutic dose of low molecular weight heparin within 12 hours, procedural unfractionated heparin may not be required, particularly not in patients who are candidates for catheter-directed thrombolysis.</td>
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<tr>
<td>4.</td>
<td>Perform right heart catheterization and obtain hemodynamic measurements.</td>
</tr>
<tr>
<td>5.</td>
<td>Perform selective conventional cineangiography of the occluded pulmonary artery by injecting a total of 10–15 mL of contrast medium at a rate of 5–8 mL/s using the left anterior oblique view (LAO 20°) for the left pulmonary artery or right anterior oblique view (RAO 20°) for the right pulmonary artery. The tip of the catheter should be placed proximally to the thrombotic occlusion within the right or left main pulmonary artery, to be confirmed by a non-damped pressure tracing.</td>
</tr>
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<td>6.</td>
<td>Cross the embolic occlusion using a standard diagnostic catheter and an angle-tipped exchange-length hydrophilic 0.035-inch guide wire (e.g., Terumo Glidewire with torque device). A manual injection of 1 or 2 mL of contrast medium through the diagnostic catheter may be required to confirm successful passage of the embolic occlusion and a safe position of the catheter tip within a large lower lobe segmental branch.</td>
</tr>
<tr>
<td>7.</td>
<td>Introduce the desired catheter treatment device directly over the 0.035-inch wire into the obstructed pulmonary artery. For the use of specific thrombectomy devices, follow the instructions of the manufacturer.</td>
</tr>
<tr>
<td>8.</td>
<td>Repeat steps 5–7 if treatment of contralateral pulmonary embolism is required.</td>
</tr>
<tr>
<td>9.</td>
<td>Repeat step 4 after completion of treatment for assessing the treatment effect on hemodynamic measurements.</td>
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ultrasound-enhanced thrombolysis was immediately initiated with the administration of 26 mg t-PA over 15 hours (3-mg bolus per device, 10-mg continuous infusion per device over 15 hours) (Figure 3). At completion of the infusion, the patient had improved his hemodynamic measurements: systolic blood pressure 115 mm Hg, heart rate 84 beats per minute, and oxygen saturation 90% on 3 L of supplemental oxygen. Follow-up angiography showed complete reperfusion of the left pulmonary artery and residual nonobstructive thrombus in both pulmonary arteries. The mean pulmonary artery pressure decreased from 39 to 27 mm Hg, and cardiac output increased to from 3.1 to 4.7 L/min. For the second case, it was decided to select a catheter intervention without thrombolysis by using a combined mechanical approach with bilateral pigtail fragmentation and rheolytic thrombectomy. Two thrombectomy runs were performed in both main pulmonary arteries with the AngioJet 6F device. During thrombectomy, the device was advanced at a speed of approximately 5 mm per second. Each thrombectomy run consisted of 2 parts: 1) thrombectomy during 15 seconds from proximal to distal and 2) thrombectomy during 15 seconds from distal to proximal. At completion of the procedure, there was residual thrombus and modest improvement in flow in both pulmonary arteries. The patient remained hypotensive, with a systolic arterial pressure of 85 mm Hg and heart rate of 115 beats per minute. Mean pulmonary artery pressure remained elevated at 35 mm Hg (baseline 37 mm Hg), and cardiac output remained low at 3.2 L/min (baseline 3.0 L/min). Over the next 24 hours, the patient slowly improved, and the norepinephrine infusion was successfully weaned. Both patients were discharged alive on anticoagulant therapy.

Disclosures

Dr Kucher reports being a consultant for EKOS Corp and MEDRAD and having received honoraria from Sanofi-aventis, Boehringer Ingelheim, and Bayer. Dr Engelberger reports no conflict.

References

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