Catheter-Based Therapies for Pulmonary Emboli

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KEYWORDS

• Catheter-directed therapy • Catheter-directed thrombolysis • Percutaneous intervention
• Pulmonary embolism • Thrombolysis • Transcatheter embolectomy • Transcatheter thrombectomy

KEY POINTS

- Acute pulmonary embolism remains a significant cause of mortality and morbidity, prompting care beyond anticoagulation for patients with massive and possibly submassive disease.
- Transcatheter therapies for acute pulmonary embolism consist of catheter-based thrombolysis directly into the clot, catheter-based thrombus debulking, and combinations of these.
- Evidence suggests that catheter-based thrombolysis at lower doses than standard systemic thrombolysis achieves an outcome including mortality that is variably the same or better at a lower bleeding risk.
- Catheter-based thrombus debulking consists of fragmentation and/or clot removal. This holds the promise of even faster hemodynamic improvement and can be used in patients with contraindications to thrombolysis, but no adequate or proved method or device is currently available.

INTRODUCTION

Although anticoagulation remains the mainstay of treatment of acute pulmonary embolism (PE), this disease still carries an estimated 30-day mortality of 9% to 11% and 3 month rate of 9% to 17%, with 100,000 to 200,000 deaths annually in the United States, concentrated in those with massive (high-risk) and less so in those with submassive (intermediate-risk) involvement.[1,2] Acute PE is believed the third most common cause of death in hospitalized patients and limited data suggest the possibility of long-term cardiopulmonary sequela even short of actual chronic thromboembolic pulmonary hypertension, which itself occurs in perhaps 1% to 4%.[3] Consequently, more advanced therapy should be considered in patients with massive and submassive involvement given their higher risk for these complications as long as the risks of such therapy are acceptable.

The acute goals of any therapy more aggressive than anticoagulation are to provide rapid relief of pulmonary arterial obstruction and restore pulmonary and systemic perfusion, reduce pulmonary artery pressure, reduce right ventricular compromise, and improve oxygenation. Options consist of systemic thrombolysis, catheter-based or catheter-directed therapies (CDT), surgical embolectomy, and extracorporeal membrane oxygenation.

TYPES OF TRANSCATHETER THERAPIES

Catheter-based therapies can be divided into catheter-directed thrombolysis, transcatheter mechanical thrombus debulking, and combinations of these. The rationale is to achieve clot reduction and clinical improvement with a lower bleeding risk than systemic thrombolysis and perhaps greater efficacy. Major limitations are the size and volume of clots, their age because older

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thromboemboli have started to organize and adhere to the vessel wall and be more resistant to pharmacologic or mechanical treatment, and the status of patients—considering individual risks for pharmacologic thrombolysis, level of cardiopulmonary instability, and the time available for any intervention.

General Concepts

Once a decision has been made to proceed with a transcatheter intervention, pulmonary artery catheterization becomes the first procedural step. Access usually is through a femoral or internal jugular vein and less commonly an upper extremity vein and should be done under ultrasound guidance to minimize punctures or inadvertent entry into a nearby artery, which increases the risk for access site bleeding. Two sheaths can be placed in one vein adjacent to each other if more than 1 catheter is needed for treatment. Right heart and pulmonary artery pressures should be obtained; at least the pulmonary artery value can be followed to determine patient response. Pulmonary angiography is usually done to visualize the emboli, but some proceduralists may skip this when a prior CT angiogram (CTA) permits confident guidance for thrombolysis. After the procedure, patients are followed in an intensive care setting, monitoring hemodynamics, respiratory status, and for possible complications related to the procedure, such as bleeding. An echocardiogram within 2 days is helpful in assessing response.

Catheter-Directed Thrombolysis

Systemic thrombolysis has been shown to accelerate dissolution of acute PE with more rapid lowering of pulmonary artery pressure and more rapid imaging response than anticoagulation along with reduced early mortality but at a cost of a higher risk of bleeding, most worrisomely, intracranially.[4,5] Furthermore, 30-day mortality is not always found reduced. Multiple contraindications exist for systemic thrombolysis, which are based on factors placing patients at higher risk for bleeding.[6] Absolute contraindications include past intracranial hemorrhage; recent ischemic stroke within the past 3 months; a central nervous system structural lesion; such as a tumor, major trauma or surgery within several weeks to months; and active bleeding. Relative contraindications include an ischemic stroke older than 3 months, oral anticoagulation, uncontrolled more severe hypertension, recent internal bleeding, pregnancy, advanced liver disease, and advanced age (variably >65–75 years). Depending on the patient, even absolute contraindications can become relative. A meta-analysis comparing systemic thrombolysis plus anticoagulation to just anticoagulation showed risks of major bleeding of 9.24% to 3.42% and of intracranial hemorrhage of 1.46% to 0.19%.[4]

Transcatheter thrombolysis directly into pulmonary thromboemboli has the theoretic advantages of supplying a high local concentration of the agent to a greater surface area of the clot yet at a lower dose than systemic administration and with lower systemic exposure. This should translate to greater efficacy with a lower risk of bleeding. Still, the 2016 guidelines for antithrombotic therapy for VTE disease by the American College of Chest Physicians recommend systemic thrombolysis over catheter-directed thrombolysis, reserving the latter as an option in patients at higher risk of bleeding or as a possible adjunct to catheter-assisted thrombus removal in patients with hypotension who have a high bleeding risk, have failed systemic thrombolysis, or have shock that is likely to cause death before systemic thrombolysis can take effect.[7] Typically, a multi-sidehole catheter is advanced into the clot in one lung or two catheters are used, one for each pulmonary artery (**Fig. 1**) and a fibrinolytic agent is infused, such as tissue plasminogen activator (TPA) at rates of 0.5-1 mg/hour per catheter when two catheters are used and 0.5-2 mg/hour if just one catheter is used. The duration of the infusion is usually 12-24 hours, giving average total doses of 20 to 28 mg.[8,9] Note that administering the thrombolytic agent proximal to the PE is believed to provide no benefit over systemic administration as the drug will preferentially course into unobstructed branches.[10] Systemic heparin is generally delivered at a subtherapeutic dose of 500-600 units/hour during the fibrinolytic instillation given concern over a greater potential for bleeding if fully anticoagulated.

In an attempt to further enhance the effectiveness and speed of clot dissolution, intrathrombotic fibrinolytic instillation can be combined with high-frequency, low intensity ultrasound waves delivered simultaneously with the drug through a multi-sidehole EkoSonic Endovascular System Infusion Catheter (EKOS Corp, Bothell, WA), which is called ultrasound-assisted or ultrasound-accelerated thrombolysis. The ultrasound disrupts and thins fibrin strands, increasing permeability and exposure to plasminogen activator sites deep in the clot (**Fig. 2**). This system has received an FDA indication for the treatment of pulmonary embolism.

The ULTIMA study randomized the use of ultrasound-assisted thrombolysis for acute intermediate