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## Catheter Interventions in Massive Pulmonary Embolism

By NILS KUCHER, M.D.

**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).<sup>1,2</sup>

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 thrombolysis<sup>3</sup> or surgical embolectomy,<sup>4</sup> 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.<sup>5</sup> 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.<sup>2</sup> 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.<sup>6</sup> Major bleeding occurred in 20 (19.6%), and systemic hypotension, cancer, diabetes mellitus, and elevated INR were identified as independent predictors of major hemorrhage.



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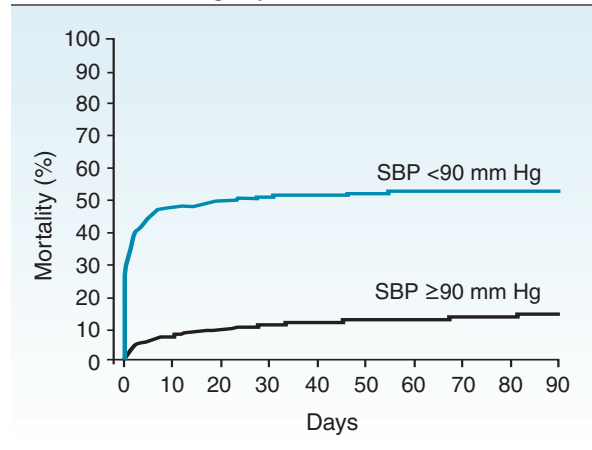
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**Figure 1: Cumulative mortality through 90 days in 108 patients with systolic blood pressure (SBP) <90 mm Hg and in 2,284 patients with SBP ≥90 mm Hg at presentation**



Several tertiary care centers perform emergency surgical embolectomy in patients with massive PE and contraindications to thrombolysis.<sup>4</sup> 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.<sup>2,5</sup>

The only alternative to thrombolysis or surgical embolectomy for reversing PE-related right heart failure and cardiogenic shock is percutaneous catheter thrombectomy.<sup>7,8</sup> 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  $\leq 90$  mm Hg, a drop in SBP of  $\geq 40$  mm Hg for  $\geq 15$  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.<sup>9,10</sup> 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.

**Figure 2: The Greenfield pulmonary embolism suction embolectomy catheter device.** The device is introduced without a guide wire by steering the catheter tip with a joystick (located next to the handle bar)



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### *Balloon angioplasty and stents*

Balloon angioplasty of obstructing emboli has been used for many years in an attempt to restore pulmonary blood flow and improve hemodynamics.<sup>11,12</sup> Balloon angioplasty using balloon sizes of 6 mm to 16 mm results in compression of the embolus to the vessel wall, but also in the partial fragmentation of the thrombus with distal embolization. Most patients treated with balloon angioplasty also receive local thrombolysis, which results in a decrease in pulmonary artery pressure over time. Therefore, it is unknown whether balloon angioplasty without concomitant thrombolysis is effective. Self-expanding wallstents<sup>13</sup> and self-expandable Gianturco Z stents<sup>14</sup> have also been used in patients with massive PE and failed thrombolysis or failed thrombus fragmentation.

### *Pigtail rotational catheter*

The rotatable pigtail catheter (Cook Europe, The Netherlands) is a modified 5-French pigtail catheter with a radiopaque tip, with 10 side holes for contrast material injection. An oval side hole in the outer aspect of the pigtail loop allows direct passage of a guide wire through the hole to act as a central axis around which the catheter rotates. The catheter is rotated bimanually to break apart large fresh clots; its pigtail tip breaks the clot into multiple smaller fragments that embolize distally in the pulmonary circulation. In 20 patients with massive PE, catheter intervention with the pigtail rotational catheter resulted in a 33% recanalization rate by fragmentation alone, but the catheter was more effective using adjuvant thrombolytic therapy with r-tPA.<sup>15,16</sup>

Mortality in this series was 20%. One disadvantage is the risk of macroembolization,<sup>17</sup> which may cause further a deterioration in hemodynamics when a large centrally-located non-obstructive thrombus breaks and embolizes into a previously nonobstructed branch.

### *Amplatz thrombectomy device (ATD)*

The Amplatz 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.<sup>18</sup> 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.

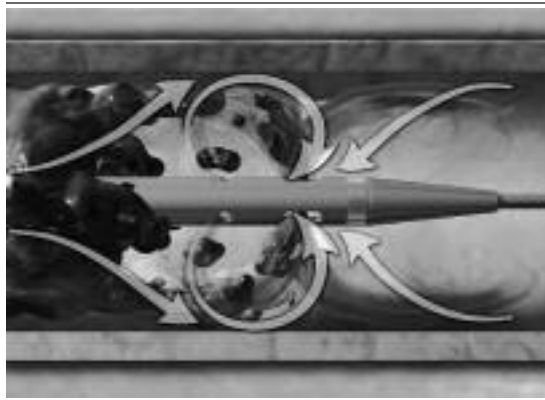
### *Hydrodynamic thrombectomy catheter devices*

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.<sup>18-26</sup> 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

**Figure 3:** The Angiojet Xpedior catheter device removes thrombus in vessels up to 12 mm in dimension by reversed high-pressure saline injection (Venturi effect)

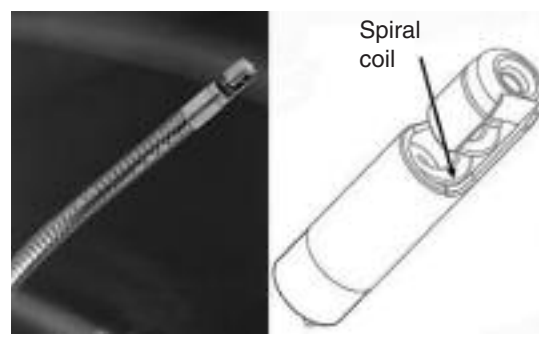


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catheter body that creates negative pressure through an L-shaped aspiration port at the catheter tip, macerates aspirated thrombus, and removes macerated thrombus (Figure 4). The catheter is connected to a motor via an electromagnetic clutch. A small 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 asso-

**Figure 4:** The flexible catheter tip of the Aspirex Pulmonary Embolism thrombectomy device



Left panel: high-speed rotation of the internally located spiral coil permits aspiration, mazeration, and removal of thrombus through the aspiration port (right panel).

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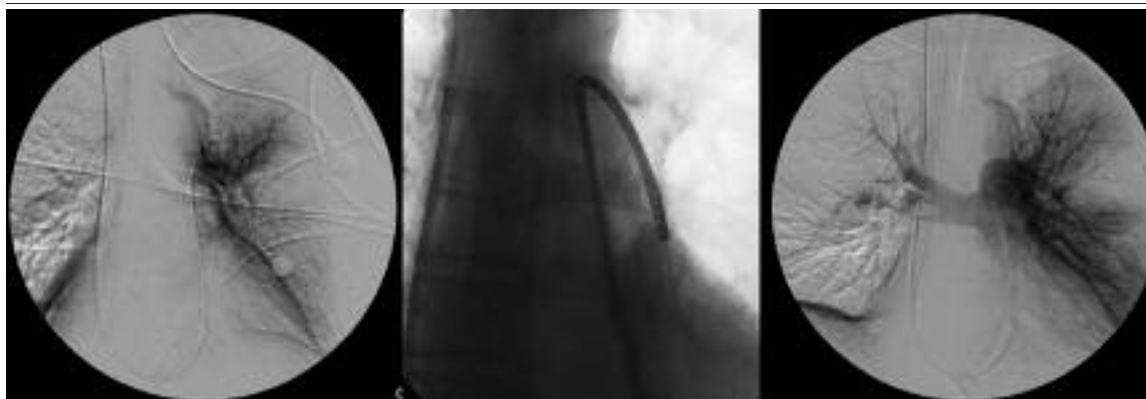
ciated with an increase in plasma free hemoglobin.<sup>27</sup> The Aspirex device was effective and safe in animal experiments.<sup>27</sup>

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

**Figure 5:** A 62-year-old man presented 13 days after gastric cancer surgery with sudden onset of syncope, profound dyspnea, and hypoxia requiring emergent mechanical ventilation. Initial systemic BP was 97/64 mm Hg and heart rate was 133 BPM. Systemic thrombolysis did not improve hemodynamic instability.



**Left panel:** The patient was taken to the catheterization laboratory and angiography via the right jugular vein demonstrated complete obstruction of the left main pulmonary artery.

**Middle panel:** The thrombotic occlusion was crossed using a 0.035-inch guide wire and Aspirex thrombectomy was performed.

**Right panel:** Final angiography showed recanalization of the left main pulmonary artery. After thrombectomy, systemic pressure increased to 149/63 mm Hg and mean pulmonary artery pressure decreased from 36 to 24 mm Hg.

drug has been used by several authors.<sup>28-31</sup> 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.

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### Reference List

1. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Massive pulmonary embolism. *Circulation* 2006;113:577-82.
2. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet* 1999;353:1386-9.
3. Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. *Eur Heart J* 2000;21:1301-36.
4. Aklog L, Williams CS, Byrne JG, et al. Acute pulmonary embolectomy: a contemporary approach. *Circulation* 2002; 105:1416-9.
5. Kasper W, Konstantinides S, Geibel A, et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. *J Am Coll Cardiol* 1997;30:1165-71.
6. Fiumara K, Kucher N, Fanikos J, Goldhaber SZ. Predictors of major hemorrhage following fibrinolysis for acute pulmonary embolism. *Am J Cardiol* 2006;97:127-9.
7. Kucher N, Goldhaber SZ. Management of massive pulmonary embolism. *Circulation* 2005;112:e28-e32.
8. Uflacker R. Interventional therapy for pulmonary embolism. *J Vasc Interv Radiol* 2001;12:147-64.
9. Greenfield LJ, Proctor MC, Williams DM, Wakefield TW. Long-term experience with transvenous catheter pulmonary embolectomy. *J Vasc Surg* 1993;18:450-458.
10. Greenfield LJ, Kimmell GO, McCurdy WC, 3rd. Transvenous removal of pulmonary emboli by vacuum-cup catheter technique. *J Surg Res* 1969;9:347-52.
11. Handa K, Sasaki Y, Kiyonaga A, et al. Acute pulmonary thromboembolism treated successfully by balloon angioplasty: a case report. *Angiology* 1988;8:775-778.
12. Fava M, Loyola S, Flores P, Huete I. Mechanical fragmentation and pharmacologic thrombolysis in massive pulmonary embolism. *J Vasc Interv Radiol* 1997;8:261-266.
13. Haskal ZJ, Soulen MC, Huetti EA, Palevsky HI, Cope C. Life-threatening pulmonary emboli and cor pulmonale: Treatment with percutaneous pulmonary artery stent placement. *Radiology* 1994;191:473-475.
14. Koizumi J, Kusano S, Akima T, et al. Emergent Z stent placement for treatment of cor pulmonale due to pulmonary emboli after failed lytic treatment: Technical considerations. *Cardiovasc Intervent Radiol* 1998; 21:254-255.

15. Schmitz-Rode T, Janssens U, Duda SH, et al. Massive pulmonary embolism: percutaneous emergency treatment by pigtail rotation catheter. *J Am Coll Cardiol* 2000;36:375-80.
16. Schmitz-Rode T, Janssens U, Schild HH, et al. Fragmentation of massive pulmonary embolism using a pigtail rotation catheter. *Chest* 1998;114:1427-36.
17. Schmitz-Rode T, Janssens U, Hanrath P, et al. Fragmentation of massive pulmonary embolism by pigtail rotation catheter: possible complication. *Eur Radiol* 2001;11:2047-9.
18. Uflacker R, Stange C, Vujic I. Massive pulmonary embolism: preliminary results of treatment with the Amplatz thrombectomy device. *J Vasc Interv Radiol* 1996;7:519-528.
19. Reekers J, Kromhout J, van der Wall K. Catheter for percutaneous thrombectomy: first clinical experience. *Radiology* 1993;188:871-874.
20. Fava M, Loyola S, Huete I. Massive pulmonary embolism: treatment with the hydrolyser thrombectomy catheter. *J Vasc Interv Radiol* 2000;11:1159-64.
21. Sharafuddin MJA, Hicks ME. Current status of percutaneous mechanical thrombectomy. Part I: general principles. *J Vasc Interv Radiol* 1997;8:911-921.
22. Sharafuddin MIA, Hicks ME. Current status of percutaneous mechanical thrombectomy. Part II: devices and mechanisms of action. *J Vasc Interv Radiol* 1998;9:15-31.
23. Muller-Hulsbeck S, Grimm J, Leidt J, Heller M. In vitro effectiveness of mechanical thrombectomy devices for large vessel diameter and low-pressure fluid dynamic applications. *J Vasc Interv Radiol* 2002;13:831-39.
24. Koning R, Cribier A, Gerber L, et al. A new treatment for severe pulmonary embolism. *Circulation* 1997;96:2498-2500.
25. Voigtlander T, Rupprecht HJ, Nowak B, et al. Clinical application of a new rheolytic thrombectomy catheter system for massive pulmonary embolism. *Cathet Cardiovasc Intervent* 1999;47:91-6.
26. Zeni PT Jr, Blank BG, Peeler DW. Use of rheolytic thrombectomy in treatment of acute massive pulmonary embolism. *J Vasc Interv Radiol* 2003;14:1511-5.
27. Kucher N, Windecker S, Banz Y, et al. Percutaneous catheter thrombectomy device for acute pulmonary embolism. *Radiology* 2005;236:852-8.
28. Molina HE, Hunter DW, Yedlick JW, et al. Thrombolytic therapy for post operative pulmonary embolism. *Am J Surg* 1992;163:375-381.
29. Gonzales-Juanatey JR, Valdes L, Amaro A, et al. Treatment of massive pulmonary thromboembolism with low intrapulmonary dosages of urokinase: short term angiographic and hemodynamic evolution. *Chest* 1992;102:341-346.
30. Vujic I, Young JWR, Gobien RP, et al. Massive pulmonary embolism treatment with full heparinization and topical low-dose streptokinase. *Radiology* 1983;148:671-675.
31. Verstraete M, Miller GAH, Bounameaux H, et al. Intravenous and intrapulmonary recombinant tissue-type plasminogen activator in the treatment of acute massive pulmonary embolism. *Circulation* 1988;77:353-360.



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