Catheter-Directed Embolectomy, Fragmentation, and Thrombolysis for the Treatment of Massive Pulmonary Embolism After Failure of Systemic Thrombolysis

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Chest 2008;134;250-254;
DOI 10.1378/chest.07-2846

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Catheter-Directed Embolectomy, Fragmentation, and Thrombolysis for the Treatment of Massive Pulmonary Embolism After Failure of Systemic Thrombolysis*

William T. Kuo, MD; Maurice A. A. J. van den Bosch, MD, PhD; Laurence V. Hofmann, MD; John D. Louie, MD; Nishita Kothary, MD; and Daniel Y. Sze, MD, PhD

Purpose: The standard medical management for patients in extremis from massive pulmonary embolism (PE) is systemic thrombolysis, but the utility of this treatment relative to catheter-directed intervention (CDI) is unknown. We evaluated the effectiveness of CDI as part of a treatment algorithm for life-threatening PE.

Methods: A retrospective review was performed on 70 consecutive patients with suspected acute PE over a 10-year period (from 1997 to 2006) who had been referred for pulmonary angiography and/or intervention. The criteria for study inclusion were patients who received CDI due to angiographically confirmed massive PE and hemodynamic shock (shock index, > 0.9). CDI involved suction embolectomy and fragmentation with or without catheter thrombolysis.

Results: Twelve patients were treated with CDI. There were seven men and five women (mean age, 56 years; age range, 21 to 80 years). Seven patients (58%) were referred for CDI after failing systemic infusion with 100 mg of tissue plasminogen activator, and five patients (42%) had contraindications to systemic thrombolysis. Catheter-directed fragmentation and embolectomy were performed in all patients (100%). Additionally, catheter-guided thrombolysis was performed in eight patients (67%). Technical success was achieved in 12 of 12 cases (100%). There were no major procedural complications (0%). Significant hemodynamic improvement (shock index, < 0.9) was observed in 10 of 12 cases (83%). The remaining two patients (17%) died secondary to cardiac arrest within 24 h. Ten of 12 patients (83%) survived and remained stable until hospital discharge (mean duration, 20 days; range, 3 to 51 days).

Conclusion: In the setting of hemodynamic shock from massive PE, CDI is potentially a life-saving treatment for patients who have not responded to or cannot tolerate systemic thrombolysis.

(CHEST 2008; 134:250–254)

Key words: pulmonary embolism; radiology intervention; shock; thrombolysis; thrombolytic therapy

Abbreviations: CDI = catheter-directed intervention; PE = pulmonary embolism; TNK = tenecteplase; tPA = tissue plasminogen activator

Massive pulmonary embolism (PE) is a common life-threatening condition. Although the true incidence is unknown, an estimated 530,000 cases of symptomatic PE and 150,000 cases of acute massive PE occur annually in the United States. The 30-day mortality rate for massive PE approaches 30%, and the presence of shock in these patients defines a threefold to sevenfold increase in mortality, with a majority of deaths occurring within 1 h of presentation. The standard medical management for patients in extremis from massive PE is systemic thrombolysis, but this treatment is associated with hemorrhagic risks, and some patients cannot receive systemic lysis due to contraindications. Furthermore, the safety and efficacy of systemic tissue plasminogen activator (tPA) [alteplase; Genentech; South San Fran...
cisco, CA) relative to catheter-guided intervention has not been firmly established. When the initial infusion of systemic thrombolysis fails to resolve hemodynamic shock, it is also unclear whether additional IV tPA should be administered vs treatment with alternative methods. If patients in extremis are not candidates for systemic thrombolysis, the remaining options are catheter-directed intervention (CDI) or open surgical embolectomy. CDI is considered to be much less invasive than open surgery; and for patients who are deemed to be poor surgical candidates, CDI is the only alternative treatment option. In this retrospective study, we evaluated the effectiveness of CDI (embolectomy, fragmentation, with or without local thrombolysis) as part of a treatment algorithm in our institution for the management of life-threatening PE.

**Materials and Methods**

This study was performed following institutional review board approval. A retrospective review was performed of 70 consecutive patients with suspected acute PE over a 10-year period (from 1997 to 2006) who had been referred to our department for pulmonary angiography and potential catheter intervention. The criteria for study inclusion were patients who received emergency CDI due to angiographically confirmed massive PE (Miller index score, > 0.6), with involvement of the central pulmonary arteries, and hemodynamic shock defined as a shock index (ie, heart rate/systolic BP) score of ≥ 0.9. CDI was performed, as part of an algorithm for treating massive PE, after the failure of therapy with systemic tPA or tenecteplase (TNK) [Genentech], at the operator’s discretion. Suction embolectomy was performed through an 8F or 9F guiding catheter, and fragmentation was achieved with either a 5F or 6F rotating pigtail catheter or a rheolytic thrombectomy device (AngioJet;Possis Medical; Minneapolis, MN). The insertion of an angioplasty balloon (diameter, 9 to 14 mm) was used adjunctively in some cases to achieve further clot disruption. Following fragmentation, catheter thrombolysis was accomplished by injecting the drug into and around the angiographically visible clot using either a pigtail catheter or an infusion catheter (Unifuse;Angiodynamics; Queensbury, NY).

The degree of pulmonary involvement was assessed before and after CDI, based on a consensus interpretation by two radiologists, using the scoring system of Miller et al. The Miller score ranges from 0 to 34 with higher scores reflecting greater pulmonary involvement. The Miller index (ie, Miller score divided by 34) ranges from 0 to 1.0, with massive PE defined as a Miller index of > 0.6. Technical success was defined as a reduction in the baseline Miller index following treatment. Hemodynamic status was assessed by calculating the shock index (ie, heart rate/systolic BP) before and after CDI, with severe impairment defined as a shock index of ≥ 0.9, which is an indicator and value previously described as useful in identifying and assessing critically ill patients. Significant hemodynamic improvement was defined as achieving a shock index < 0.9. Clinical success was defined as the stabilization of hemodynamic parameters, the resolution of shock, complete weaning off ventilatory and inotropic support, and survival until discharge from the hospital.

Major procedural complications from CDI were defined as follows: hemorrhage requiring transfusion; perforation of cardiopulmonary structures; anaphylaxis from contrast injection; induction of right heart block; further increase in pulmonary hypertension; worsening hypoxia; exacerbation of shock; and/or death during the procedure. Minor procedural complications were defined as follows: transient catheter-induced arrhythmia; mild contrast reactions; catheter-related infection; and small hematomas not requiring transfusion. The data were analyzed using the Student t test for the comparison of paired samples. A p value of < 0.05 was considered to be statistically significant.

**Results**

Twelve patients with massive PE were referred for treatment. There were seven men and five women with a mean age of 56 years (age range, 21 to 80 years). Risk factors for PE included preexisting deep venous thrombosis, right atrial thrombus, or both. Prior to CDI, pulmonary hypertension was documented in 11 of 12 patients (92%). Right ventricular strain was documented in 10 of 12 patients (83%). Nine of 12 patients (75%) were managed with ventilatory support, and 6 of 12 (50%) patients required inotropic/pressor support in addition to intubation. All patients (100%) were in hemodynamic shock.

Seven of 12 patients (58%) were referred for CDI after no response (ie, no resolution of shock) to the administration of 100 mg of IV tPA. A large retroperitoneal hemorrhage requiring transfusion developed in one of seven patients (14%) who were being treated with systemic thrombolysis. Five of 12 patients (42%) had contraindications to systemic thrombolytic therapy and were referred directly for CDI without receiving IV tPA.

Catheter-directed fragmentation and suction embolectomy were emergently performed in all cases (100%). In 2 of 12 patients (17%), the insertion of an
angioplasty balloon (diameter, 9 to 14 mm) was used adjunctively to facilitate clot disruption. The choice and dose of the thrombolytic agent was at the discretion of the operator. Catheter-guided thrombolysis was performed in 7 of 12 patients (58%). Five of these seven patients received tPA (mean dose, 20 mg; dose range, 10 to 30 mg), and the remaining two patients received TNK (mean dose, 12 mg; dose range, 5 to 20 mg). Rheolytic thrombectomy was attempted in three patients but completed in only two. One patient could not tolerate activation of the rheolytic catheter, due to the induction of transient bradycardia, and was treated with standard CDI. Technical success was achieved in 12 of 12 patients (100%), and there were no major procedural complications (0%). Minor complications developed in 2 of 12 patients (17%) [groin hematoma, which resolved without requiring transfusion, 1 patient; transient bradycardia during the activation of the rheolytic catheter, 1 patient]. In this latter patient, the rheolytic thrombectomy device was switched off after 15 s, resolving the arrhythmia; standard catheter techniques were resumed with success. Following treatment, 10 of 12 patients (83%) were additionally managed with placement of an inferior vena cava filter for PE prophylaxis.

Posttreatment angiography showed an increase in pulmonary perfusion in all patients (100%), with the mean Miller index improving from 0.88 to 0.47 ($p < 0.01$). Figure 1 demonstrates one case in this series. In the nine patients who underwent pulmonary pressure measurements before and after CDI, the average systolic pulmonary pressure improved from 57.6 to 44.0 mm Hg ($p < 0.05$). Significant hemodynamic improvement (shock index, <0.9) was observed in 10 of 12 (83%) patients following CDI. Two of 12 patients (17%) who failed to show significant hemodynamic improvement died secondary to cardiac arrest within 24 h of treatment. Clinical success was achieved in 10 of 12 patients (83%) [mean stay, 20 days; range, 3 to 51 days]. The results are summarized in Table 1.

### Table 1—Outcome Data Relative to CDI In 12 Patients With Acute PE*

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>CDI</th>
<th>Catheter tPA/TNK</th>
<th>IVC Filter</th>
<th>Shock Index Before</th>
<th>Shock Index After</th>
<th>Systolic Pulmonary Pressure, mm Hg Before</th>
<th>Systolic Pulmonary Pressure, mm Hg After</th>
<th>Miller Index Before</th>
<th>Miller Index After</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>62/F</td>
<td>5F pigtail, 14-mm balloon, 8F sheath</td>
<td>15 mg RPA, 5 mg LPA</td>
<td>Yes</td>
<td>1.5</td>
<td>0.7</td>
<td>NM</td>
<td>1.00</td>
<td>0.47</td>
<td>Survival</td>
<td></td>
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<tr>
<td>80/M</td>
<td>5F pigtail, 8F sheath</td>
<td>No</td>
<td>Yes</td>
<td>0.9</td>
<td>0.6</td>
<td>0.94</td>
<td>0.47</td>
<td>Survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>58/M</td>
<td>6F pigtail, 9-mm balloon, 9F sheath</td>
<td>15 mg RPA, 5 mg LPA</td>
<td>No</td>
<td>1.2</td>
<td>0.5</td>
<td>40</td>
<td>29</td>
<td>1.00</td>
<td>0.47</td>
<td>Survival</td>
</tr>
<tr>
<td>54/M</td>
<td>5F pigtail, 8F sheath</td>
<td>No</td>
<td>Yes</td>
<td>1.1</td>
<td>0.8</td>
<td>60</td>
<td>54</td>
<td>0.88</td>
<td>0.47</td>
<td>Survival</td>
</tr>
<tr>
<td>50/M</td>
<td>6F pigtail, 9F sheath</td>
<td>TNK: 2.5 mg RPA; 2.5 mg LPA</td>
<td>Yes</td>
<td>0.9</td>
<td>0.4</td>
<td>57</td>
<td>47</td>
<td>0.76</td>
<td>0.35</td>
<td>Survival</td>
</tr>
<tr>
<td>59/M</td>
<td>5F pigtail, 8F sheath</td>
<td>No</td>
<td>Yes</td>
<td>1.1</td>
<td>0.7</td>
<td>53</td>
<td>47</td>
<td>0.85</td>
<td>0.41</td>
<td>Survival</td>
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<tr>
<td>70/F</td>
<td>6F rheolytic thrombectomy catheter (AngioJet), 9F sheath</td>
<td>No</td>
<td>Yes</td>
<td>1.1</td>
<td>0.7</td>
<td>40</td>
<td>35</td>
<td>1.00</td>
<td>0.85</td>
<td>Survival</td>
</tr>
<tr>
<td>64/F</td>
<td>5F pigtail, 8F sheath</td>
<td>5 mg RPA, 15 mg LPA</td>
<td>No</td>
<td>1.7</td>
<td>1.1</td>
<td>61</td>
<td>48</td>
<td>0.56</td>
<td>0.21</td>
<td>Death</td>
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<tr>
<td>57/F</td>
<td>5-cm infusion catheter, 9F sheath (failed rheolytic thrombectomy [AngioJet])</td>
<td>TNK: 10 mg RPA; 10 mg LPA</td>
<td>Yes</td>
<td>1.4</td>
<td>0.7</td>
<td>73</td>
<td>38</td>
<td>0.91</td>
<td>0.44</td>
<td>Survival</td>
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<tr>
<td>63/M</td>
<td>5F pigtail, 8F sheath</td>
<td>20 mg RPA, 10 mg LPA</td>
<td>Yes</td>
<td>1.6</td>
<td>0.8</td>
<td>80</td>
<td>30</td>
<td>0.91</td>
<td>0.35</td>
<td>Survival</td>
</tr>
<tr>
<td>22/M</td>
<td>6F rheolytic thrombectomy catheter (AngioJet), 9F sheath</td>
<td>5 mg RPA, 5 mg LPA</td>
<td>Yes</td>
<td>2.7</td>
<td>1.5</td>
<td>59</td>
<td>32</td>
<td>0.85</td>
<td>0.35</td>
<td>Death</td>
</tr>
<tr>
<td>71/F</td>
<td>5-cm infusion catheter, 8F sheath</td>
<td>TNK: 5 mg RPA; 5 mg LPA</td>
<td>Yes</td>
<td>1.4</td>
<td>0.8</td>
<td>44</td>
<td>0.94</td>
<td>0.21</td>
<td>Survival</td>
<td></td>
</tr>
</tbody>
</table>

*F = female; M = male; NM = not measured (due to impending hemodynamic collapse); RPA = right pulmonary artery; LPA = left pulmonary artery; IVC = inferior vena cava.

**DISCUSSION**

In this case series, 12 patients in extremis from massive PE were treated with CDI with a clinical success rate of 83% and with no major procedural complications (0%). As part of a treatment algorithm, CDI was emergently performed in five patients (42%) who could not receive systemic tPA due to contraindications and in seven patients (58%) who had already not responded to systemic...
thrombolytic therapy. When CDI was performed with local thrombolysis, a lower dose of the thrombolytic agent was used (average dose: tPA, 20 mg; TNK, 12 mg) vs the standard systemic tPA infusion dose of 100 mg.

Although there is no established protocol for CDI of PE, the authors used a rotating pigtail catheter for fragmentation and a guiding sheath for suction embolectomy in most cases. The manual rotation of a pigtail catheter has previously been described as an effective technique for treating massive PE. The largest retrospective series (59 consecutive PE patients treated with CDI), reported by De Gregorio et al. in 2002, showed the safety and effectiveness of CDI using a rotating pigtail catheter with local thrombolysis when used as the primary treatment for massive PE. The advantage of the rotating pigtail is the wide availability of this catheter and its relative low cost when compared to mechanically driven thrombectomy devices. Furthermore, the minor complication of transient bradycardia secondary to the activation of the rheolytic thrombectomy catheter (AngioJet; Possis Medical) prompted the elimination of this device from subsequent treatment regimens.

There are several inherent advantages to the use of CDI for the treatment of PE. Mechanical fragmentation and suction embolectomy can achieve immediate debulking and fragmentation of an occlusive thrombus in the main pulmonary circulation, and a lower dose of the thrombolytic agent is needed for treatment. Targeted drug delivery requires a lower overall dose of the thrombolytic agent since the drug is concentrated in the culprit embolus and is not wasted in the systemic circulation. Following fragmentation, a greater surface area of the thrombus is exposed to the lytic agent and a smaller amount of the drug is needed to achieve lysis. Another benefit is that treatment can be monitored in real time with follow-up angiography. Finally, successful treatment can be accomplished predominantly by mechanical catheter techniques in some cases, with little or no need for the injection of a thrombolytic agent. Three patients in our series were successfully treated without the use of any systemic or local thrombolytic agents, and two patients required only a small dose of a catheter-injected lytic agent for treatment.

There is currently no widely accepted protocol for CDI, as many operator-dependent and institution-dependent variations exist; however, a systematic review analyzing a variety of CDI methods showed that they were all generally safe and effective with no significant difference between techniques and with low complication rates. Nevertheless, catheter-directed therapy requires an interventionalist with the appropriate expertise not only to perform treatment but also to monitor and adjust the treatment as necessary.

Figure 1. A 57-year-old woman presented in extremis from massive bilateral PE. The patient was referred to the Interventional Radiology Department when there was no response to IV infusion of 100 mg of tPA. Both lungs were treated emergently with CDI, including 20 mg of local TNK. Pulmonary angiograms of the left lung, before and after CDI, are shown. Top, a: left pulmonary angiogram demonstrates a persistent massive PE, despite treatment with systemic tPA, and flow into the left lung is severely compromised. Bottom, b: following CDI, left lung perfusion is improved. Similar maneuvers were performed in the right lung (not shown) with good results and resolution of shock. Reproduced with permission from Sze et al.
such maneuvers but also to recommend CDI in the appropriate clinical scenario as part of the PE treatment algorithm.

Although CDI involves catheterization of the pulmonary arteries, it is much less invasive than open surgical embolectomy. When patients are poor candidates for systemic thrombolysis and surgical embolectomy, CDI may be the only viable treatment option and should be pursued if available. Nevertheless, a multidisciplinary approach is desired to determine the best treatment for patients with life-threatening PE. In the event of a failed catheter intervention, surgical backup treatment should be considered if there are no contraindications. The authors believe that the integration of CDI into the treatment algorithm for PE has the potential to improve mortality rates from massive PE. The criteria for using CDI in our study was limited to patients presenting in hemodynamic shock, but Goldhaber\textsuperscript{12} has recommended that catheter interventions should be initiated in patients with acute PE, if possible while systemic arterial pressure is preserved and before pressor dependence ensues. Prospective large-scale studies are needed to further validate the safety and effectiveness of CDI and to determine its ideal role in the management algorithm for PE. In conclusion, CDI appears to be a potentially life-saving treatment for patients in extremis from massive PE. In the setting of hemodynamic shock from massive PE, CDI may be performed with or without local thrombolysis and may be useful in patients who have not responded to or cannot tolerate systemic thrombolysis.

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