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Catheter-directed Therapies for Acute Pulmonary Embolism: It is Time to Establish a Role

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Abstract

Acute pulmonary embolism (PE) is associated with a broad spectrum of clinical severity. However, despite the varying presentations, therapy is primarily limited to anticoagulation. The only widely accepted exception to the use of anticoagulation alone is in those patients with massive acute PE, in whom systemic fibrinolysis is generally considered the most appropriate option. Unfortunately, there is a large group of patients without massive PE who do worse with heparin alone, and systemic fibrinolysis has not been consistently shown to be beneficial in these patients. The role of catheter directed therapies (CDT) needs to be further investigated for this all too common patient subset.

Keywords: Acute pulmonary embolism; Anticoagulation

Introduction

Acute pulmonary embolism (PE) is associated with a broad spectrum of clinical severity. However, despite the varying presentations, therapy is primarily limited to anticoagulation. The only widely accepted exception to the use of anticoagulation alone is in those patients with massive acute PE. Massive PE is defined as acute PE with sustained hypotension (systolic blood pressure <90 mm Hg for at least 15 minutes or requirement of inotropic support), pulselessness, or bradycardia with signs of shock [1]. In patients with massive PE and an acceptable risk of bleeding, systemic fibrinolysis is generally considered the most appropriate option [1,2]. In patients with massive PE and contraindications to systemic fibrinolysis, persistent shock despite systemic fibrinolysis, or shock likely to cause death before systemic fibrinolysis can take effect, surgical embolectomy has traditionally been offered [1,2]. However, the best surgical outcomes are achieved in only those centers with vast experience in embolectomy [3]. More recently, catheter-directed therapies (CDT) have gained momentum as an acceptable alternative in patients who would otherwise be offered surgical embolectomy [1-3].

Since systemic fibrinolysis is the least invasive approach, there have been extensive efforts to investigate its role outside of just those patients with massive PE, such as those with submassive PE [4,5]. Submassive PE has been defined as acute PE without hypotension but with either RV dysfunction or myocardial necrosis [3]. However, the risk of intracranial hemorrhage (ICH) with systemic fibrinolysis has attenuated the enthusiasm to extend this therapy to these patients.

The authors are of the mindset that rather than try to expand the role of systemic fibrinolysis, we as a community should be trying to establish a role for CDT. Unfortunately, at this point in time, the data for CDT are limited. Beyond mostly retrospective case series', we do not have a lot of guidance with regard to who may benefit from these interventions. Potential considerations are those patients with submassive PE or impending respiratory failure, both of which are patient groups who do not clearly meet current indications for therapy beyond anticoagulation but are undeniably at increased risk of adverse outcomes [1,2,6]. Escalation beyond anticoagulation seems warranted in these patients, and CDT may strike the appropriate balance between risk and benefit. CDT allows for the mechanical removal of thrombus with less procedural risk than surgical embolectomy and less bleeding risk than systemic fibrinolysis.

Many centers, including our institution, have had success with AngioJet (Possis, Minneapolis, MN) rheolytic thrombectomy (RT) combined with selective thrombolysis. The procedure is begun by accessing the common femoral vein with a 6 F sheath and then positioning a multipurpose guide catheter into the desired pulmonary artery (PA). Of note, our group relies heavily on computed tomography (CT) angiography to appropriately identify the pulmonary arteries to target. Selective angiography is then performed via the multipurpose catheter to identify the location and extent of thrombus. A 0.035” Wholey wire is then passed distal to the thrombus. The multipurpose catheter is subsequently removed in exchange for a 6 F 120 cm Angiojet Solent catheter, which is passed to the proximal aspect of the thrombus. The Solent catheter is connected to the AngioJet control unit and advanced back and forth through the thrombus in the pulse-spray mode. In the pulse-spray mode, approximately 5 mg of tissue plasminogen activator (tPA) is administered in 50 mL of half normal saline. After approximately 20 minutes of indwell time for the tPA, the catheter is changed to thrombectomy mode. In the thrombectomy mode, the catheter is passed back into the distal aspect of the thrombus. Thrombus is then aspirated via the Venturi effect as the catheter is pulled proximally. Pulse spray of tPA followed by thrombectomy can generally be repeated 3-5 times for a given pulmonary artery [3,7-10].

The relatively small number of centers who perform CDT and the lack of standardization of the approach are potential explanations for the scarcity of randomized control data. The authors acknowledge that multiple approaches are necessary. For example, if adjunctive tPA is contraindicated and clot burden persists despite RT, then other means of mechanical thrombectomy such as fragmentation or suction embolectomy (Angiovac catheter) may be needed [7]. The disadvantage of fragmentation is that it can lead to downstream embolization and paradoxically worsen PA pressures, particularly when concomitant aspiration is not employed [7]. The drawbacks of suction embolectomy are that it requires the insertion of large bore venous and arterial catheters via surgical cut-down. It also necessitates the initiation of cardiopulmonary bypass to effectively suction and filter blood before returning it to the body [3]. The distribution of thrombus also impacts the decision of what catheter-based approach to use. If clot burden is primarily sub-segmental, then mechanical thrombectomy may not be adequate. In such a situation, local tPA delivered over a period of time via an indwelling infusion catheter may be needed [7]. Recent data specifically suggest a benefit to ultrasound-assisted local tPA infusion. Low-energy application of ultrasound via the EKOS device (EkoSonic Endovascular) dissociates fibrin stands and allows for more effect thrombolysis, resulting in infusions of lower-dose and lesser duration [3,7]. In fact, the recently published ULTIMA (Ultrasound Accelerated Thrombolysis of Pulmonary Embolism) trial showed that standardized ultrasound-assisted thrombolysis was superior to heparin alone in reversing RV dilatation at 24 hours without an increase in bleeding complications [11]. This was the first randomized trial to evaluate a catheter-based intervention for the treatment of acute PE and will hopefully serve as a catapult for further investigation. Table 1 is a summary of available catheter-directed modalities.

Modality	Mechanism	Advantages	Disadvantages
Rheolytic thrombectomy	High velocity saline jet suctions thrombus via the Venturi effect	Highly effective for removing thrombus proximal to segmental pulmonary arteries with experienced operator	Can cause bradyarrhythmias and/or bronchospasm
Thrombus fragmentation	Direct clot fragmentation	- Inexpensive - Widely available	Can result in distal embolization and paradoxically elevate PA pressures
Rotational thrombectomy and aspiration	High-speed rotating screw within catheter creates negative pressure, causing aspiration of thrombus from catheter tip into lumen	Reportedly effective thrombus removal [12]	Limited experience with this technique [12]
Suction (aspiration) thrombectomy	Direct removal of thrombus via aspiration	Highly effective for removing thrombus proximal to segmental pulmonary arteries	- Requires surgical cut-down for insertion of large bore catheters - Requires cardiopulmonary bypass
Catheter-directed thrombolysis	Local administration of low-dose thrombolytic	- Allows for a lower dose of thrombolytic - Effective for distal clot	Elevated bleeding risk even with local thrombolysis
Ultrasound accelerated thrombolysis	Combination of ultrasound therapy for fibrin fragmentation along with local thrombolysis	- Allows for a lower dose of thrombolytic than even standard catheter-directed thrombolysis - Effective for distal clot	
Pulmonary artery angioplasty +/- stenting	Thrombus fragmentation with balloon inflation	- Readily available	- Risk of injury to pulmonary artery (dissection, perforation) - Risk of distal embolization

Table 1: Summary of Available Catheter-Directed Therapies for PE (modified from Wasfy et al. [7]).

Despite the presence of multiple options for CDT, this should not preclude the development of an algorithm that can serve as a framework for implementing CDT in a standardized fashion. This also should not preclude further investigation into the predictors of suboptimal outcomes in patients with acute PE, as these predictors may serve as the foundation for future studies looking at CDT. There are enough centers now who offer these interventions that it should be feasible to try to consolidate our experiences and implement a standardized protocol. It is only when a uniform protocol is in place and a specific patient group is identified that we can begin to investigate in whom CDT may be beneficial, as there undoubtedly is a large group of patients in whom anticoagulation alone is just not enough.

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