Catheter-directed clot fragmentation using the Cleaner^{TM} device in a patient presenting with massive pulmonary embolism

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ABSTRACT

Massive pulmonary embolism not amenable to systemic thrombolysis is a therapeutic challenge. Catheter directed clot fragmentation and thrombolysis have been efficacious in this setting. We describe successfully treating a massive pulmonary embolism with catheter-directed thrombolysis and clot fragmentation using local tPA, aspiration, and the Cleaner^{TM} device in a patient with an absolute contraindication to systemic thrombolysis.

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CASE REPORT

INTRODUCTION

Pulmonary embolus (PE) carries a significant mortality rate; however, not all pulmonary emboli are equal. The American Heart Association (AHA) recently released a stratification scheme for pulmonary emboli, categorizing them as massive, sub-massive, and low-risk, in order of decreasing mortality (1). Massive pulmonary emboli are defined by the AHA as those causing a systolic blood pressure of less than 90 mm Hg for greater than 15 minutes and/or requiring vasopressor support. Given the high mortality associated with hemodynamically significant PE and anticoagulation alone, the ACCP and AHA guidelines allow for consideration of escalation of therapy either through the administration of intravenous tPA, catheter directed therapy, or surgical embolectomy (1, 2).

In a meta-analysis performed by Kuo et al (3), catheter directed clot fragmentation and a variable amount of aspiration and local lysis in the setting of massive PE was associated with an 86% success rate. In the analysis, ~70% of interventionalists used a rotating pigtail catheter for clot fragmentation. Multiple other fragmentation techniques have been used in both Europe and the United States (3). Here, we report the use of the Cleaner^{TM} device (Rex medical, Athens, TX) to mechanically fragment a large clot in the right pulmonary artery in a patient presenting with a massive pulmonary embolism and intracranial hemorrhage.

CASE REPORT

A 40 year-old Caucasian male with acromegaly was admitted for a planned inter-hemispheric trans-callosal resection of a recurrent pituitary macroadenoma. He had numerous previous macroadenoma resections, and a history of unprovoked lower extremity DVT and pulmonary embolism treated with six months of anticoagulation and no inferior vena cava filter placement. Post operatively, he developed generalized tonic-clonic seizures and was found to have a sagittal vein thrombosis and a parasagittal frontal cortex acute hemorrhage. Given the hemorrhage, full dose anticoagulation was not initiated, but he was placed on 5000 units of subcutaneous unfractionated heparin twice daily for DVT prophylaxis. Serial CT imaging confirmed no progression of the hemorrhage.

On day 10 following his surgery, the patient developed acute shortness of breath and chest tightness. Objectively, he became tachycardic (HR 110) and tachypneic (RR 30), and desaturated on room air to 85%. An arterial blood gas revealed a pH of 7.46 (normal 7.40) with a pCO2 of 35mmHg (normal 40mmHg) and a pO2 of 59mmHg (normal>80mmHg) on a 100% FiO2 non-rebreather mask. His oxygen saturation only reached 92%. His blood pressure dropped from a baseline of 120/80 to 90/60. He was urgently sent for a chest CT which revealed an extensive pulmonary embolus filling the right and, to a lesser extent, left pulmonary arteries (Figure 1A-B). The pulmonary artery (PA), right atrium and right ventricle were distended (Figure 1C-D), and there was reflux of contrast into the IVC (Figure 1D). He had small infarcts in his right lung (Figure 1C). Another concerning finding was a large thrombus extending into the intra-hepatic inferior vena cava (Figure 1E). In addition, a Doppler study of his lower extremities confirmed the presence of left popliteal and left femoral thrombus. A transthoracic echocardiogram showed a severely dilated right ventricle and atrium with mild tricuspid regurgitation. Also noted was a dilated IVC without respiratory variability, implying a CVP >11mmHg (normal 0-2mmHg). The patient was immediately started on a heparin drip, and pulmonology, interventional radiology, and cardiothoracic surgery were consulted. Given the patient's hemodynamic instability, inability to tolerate a major surgery, and the absolute contraindication (intracranial bleeding) to systemic thrombolysis, a catheter-directed approach was chosen. The risks and benefits of this approach have been carefully discussed with the patient and he was fully consented for the procedure.

Intraprocedurally, the cardiac anesthesia team administered moderate sedation and analgesia without intubation. Due to low systolic pressures, the patient required intermittent boluses of phenylephrine. The operators (A.K.S. and C.I) used the combination of a 5 French pigtail catheter and Bentson 0.035 inch wire through a 9 French, 55 cm sheath to access the pulmonary artery. The PA pressure was transduced through the pigtail catheter and found to be 39/19 mmHg (normal less than 30/12mmHg); next, a pulmonary angiogram, at a rate of 10 ml/sec using a total of 20 ml Omnipaque 300 (GE Healthcare, Pewaukee, WI USA), was performed (Figure 1F), demonstrating complete occlusion of the right pulmonary artery with no visible blood flow into the branches. Scattered emboli were identified in the left pulmonary circulation as well. An Amplatz 0.035 Inch wire was advanced into a segmental branch of the right pulmonary artery, and the sheath was advanced over the wire into the right PA. A total of 12 mg of Alteplase, in 2 separate aliquots, were delivered directly into the clot via the pigtail catheter. Between these doses, pigtail catheter rotation through the clot was attempted, but was ineffective due to the catheter slipping out of the clot and into the main pulmonary artery. Additionally, aspiration was performed through a 7 Fr aspiration catheter, removing a small amount of thrombus. Follow-up angiography through the sheath in the right PA demonstrated mildly improved right lung perfusion with persistent significant thrombus in the upper and lower lobe branches (Figure 2A). The patient's hemodynamics did not significantly improve at this time. Next, the Cleaner™ device was advanced through the sheath and activated in both the upper and lower lobe branches (Figure 2B, Interactive supplemental files). To prevent perforation of the pulmonary artery, the sheath was advanced over wire into each branch before the Cleaner device was loaded. Once the Cleaner was in appropriate position within the sheath, the sheath was retracted, leaving the Cleaner in the pulmonary artery branch. This technique avoided unprotected advancement of the Cleaner tip. After Cleaner deployment, repeat right PA angiography was performed through the sheath, demonstrating improved pulmonary perfusion during both the arterial and parenchymal phases (Figure 2C). At this point, the patient's arterial pO2 improved to 103 mm Hg, and his systolic blood pressure rose to > 100 mm Hg. The completion PA pressure was 29/12 mm Hg. The catheters and wires were removed, and hemostasis was achieved with manual pressure.

After completion of the procedure (step by step approach, Figure 3), the patient maintained excellent oxygenation and an adequate blood pressure without vasopressor support. His heart rate decreased to < 100 beats/minute. Over the course of next few days, the patient remained stable with decreasing O2 requirements, eventually breathing comfortably on room air by day 7. He was transitioned to oral anticoagulants and began inpatient physical therapy. The hypercoagulability workup has been negative, but given the patient's repeated episodes of VTE in peri-operative settings, 6 months of anticoagulation has been prescribed. The patient continued to recover as an outpatient, and at two-months follow-up, he had no new episodes of shortness of breath, was not using supplemental oxygen, and had no complications related to anticoagulation therapy.

DISCUSSION

Hemodynamically unstable or "massive" pulmonary embolus is a serious and often complicated medical emergency to manage. Mortality is high and rises stepwise in accordance with the degree of hemodynamic compromise. From the MAPPET database, the mortality associated with death from a PE was 15% with hypotension, 25% with cardiogenic shock, and 65% with cardiopulmonary arrest (4). The ACCP guidelines recommend systemic thrombolysis for hemodynamically unstable patients, and highlight the potential detriment of waiting to give IV tPA until vasopressors are initiated (5). Unfortunately, there is a significant risk of bleeding from systemic lysis, with a 20% incidence of major bleeding and a 3% to 5% risk of hemorrhagic stroke (6, 7). A large percentage of patients with high risk pulmonary embolus (up to 70%) are considered not to be candidates for its use (6). Accordingly, the ACCP recommends catheter-based treatment in select hypotensive patients who are not candidates for systemic lysis, for whom systemic lysis has failed, or for those who are too hemodynamically compromised to wait for systemic lysis to take effect. (2).

The patient described above had contraindications to administration of systemic tPA, but clearly required treatment escalation since heparin treatment and vasopressor support did not lead to hemodynamic stability. Given the high surgical risk of open thrombectomy, percutaneous techniques to re-canalize the pulmonary trunk were considered. Initially, our plan was to use mechanical fragmentation with a pigtail catheter and deliver local boluses of tPA. While there was some concern that local tPA would still have systemic effects and exacerbate the patient's intracranial bleed, we justified its use given the patient's hemodynamic deterioration and our ability to administer direct intra-thrombus doses, thereby limiting the dose required and minimizing systemic delivery. Our decision to use the Cleaner arose from the overall lack of efficacy of pigtail fragmentation. Moreover, while there was some angiographic improvement after tPA and aspiration, the patient remained hemodynamically unstable. The Cleaner device was used off-label because the distal end of the wire has a sinusoidal shape that has a variable 4000 RPM radius of rotation based on the size of the vessel and a relatively atraumatic tip, theoretically favorable mechanical characteristics for the pulmonary circulation. Overall, there is a paucity of mechanical devices to either remove or create channels through thrombus. The most available device, the Angiojet, is associated with hemolysis and hemodynamic collapse (3), and now has a black box warning from the United States Food and Drug Administration for use in the pulmonary artery.

Our experience with the Cleaner device was encouraging; it remained within the clot during activation, unlike the pigtail catheter. No bradycardia, tachycardia, hemolysis, or hemodynamic instability was noted during or after its use. It should be noted that while the device is FDA approved for arterio-venous fistula and graft de-clotting, it is not FDA approved for use in the pulmonary circulation. Additionally, during device activation, the patient temporarily coughed vigorously, which is unsurprising given the proximity to carinal cough receptors.

Given the number of agents used during the case, the patient's positive outcome cannot be solely attributed to deployment of the Cleaner. However, temporally speaking, the patient's hemodynamics rapidly improved immediately following its use. Moreover, there was improved perfusion, albeit modest, on the post-Cleaner deployment angiograms. It is important to note that complete thrombus clearance in the acute setting is frequently unnecessary; often, creating channels through the clot to improve perfusion is enough to improve the patient's hemodynamics, after which anticoagulation facilitates clot resolution. If the patient did not have an absolute contraindication, a tPA infusion catheter could have been placed into the clot at the end of the procedure to hasten thrombolysis.

The extensive thrombus in the IVC was certainly a concern to the team, but no catheter-based device was present that could effectively remove the clot. Fortunately, anticoagulation was sufficient to prevent further clinical deterioration in this patient.

Catheter-directed thrombolysis and fragmentation offer several advantages in this type of patient. First, it allows a much lower dose of Alteplase to be administered because the drug is given directly into the clot. For this patient, it is conceivable that the procedure could have been accomplished without any Alteplase; however, given his worsening hemodynamics, a low dose (12 mg) as opposed to the standard dose of 100 mg peripherally was used to accelerate clot lysis. Second, seemingly modest angiographic improvement led to substantial improvement in hemodynamic stabilization, a common finding in the treatment of massive PEs. Tools such as the Cleaner can be used to perform a combination of fragmentation and aspiration without significant morbidity, as compared with open surgery.

The Cleaner™ has not been approved for use in the treatment on pulmonary embolism. However, based on our experience, it may have value as a clot fragmentation device in difficult cases such as this one. Randomized controlled clinical trials to compare the various treatment modalities in the setting of massive pulmonary embolus are difficult to conduct. However, insights can still be obtained through prospective observational studies, such as the PERFECT registry (8) that is currently ongoing.

TEACHING POINT

The Cleaner™ may be of use as an additional mechanical clot fragmentation device during catheter directed therapy in the setting of massive pulmonary embolus.

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FIGURES

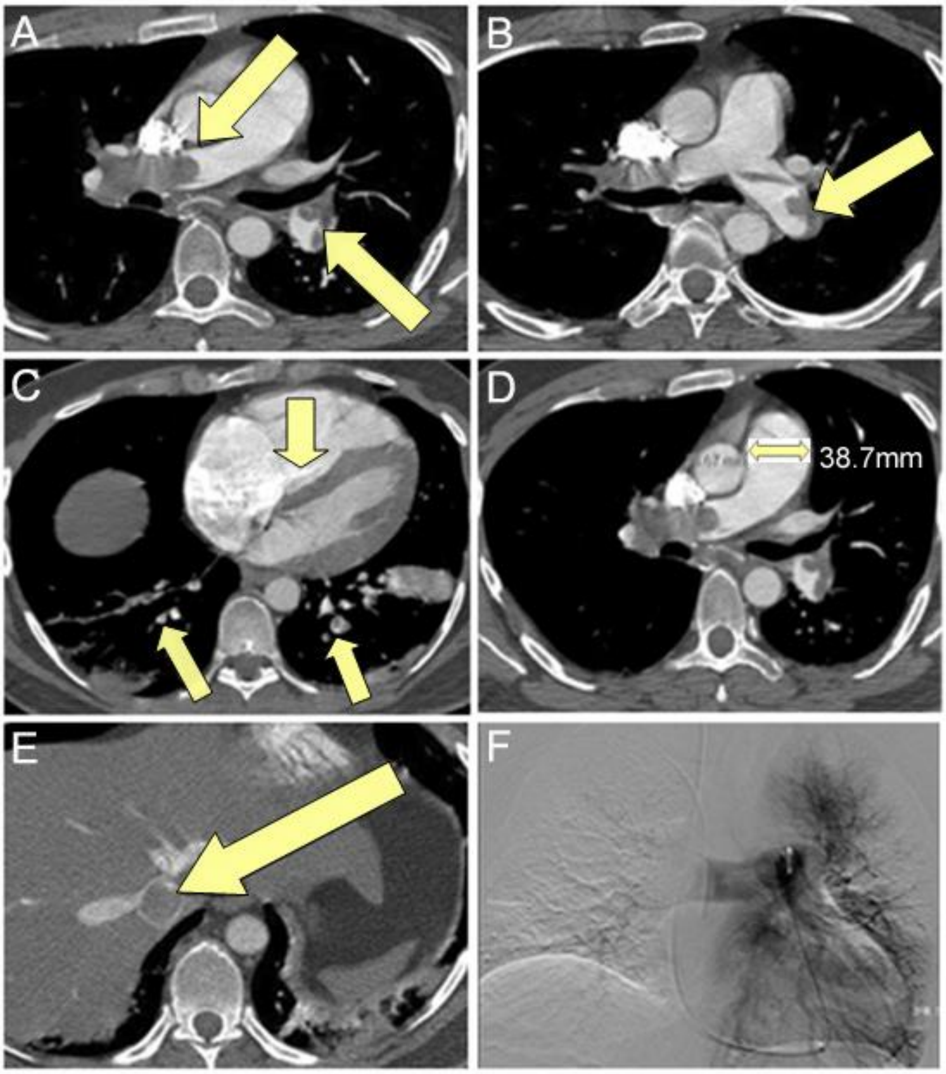

Figure 1: 40 year old male patient with high clinical suspicion of acute PE. Axial images from a pulmonary arterial phase contrast-enhanced chest CT (GE scanner, mA: 490, kVP: 120, slice thickness: 1.25mm, 140 cc Omnipaque 300) A) and B) Large, expansile, central thrombus in the right pulmonary artery, and eccentric non-occlusive acute thrombus in the left pulmonary artery extending to the lower lobe branch. C) Enlarged right atrium and right ventricle with septal bowing toward the left ventricle with bilateral subsegmental emboli and evidence of small infarcts in the right lower lobe. D) Enlarged main pulmonary artery as measured on the CT chest (38.67mm) E) A lower axial image during the same contrast phase demonstrates expansile thrombus filling the inferior vena cava with reflux into the hepatic veins. F) Preliminary digital subtraction (6 frames/second, AP projection) pulmonary angiography through a 9 Fr sheath positioned in the pulmonary artery via right internal jugular vein access demonstrates occlusive thrombus in the right pulmonary artery and scattered large thrombi in the left pulmonary circulation, with no perfusion to the right lung.

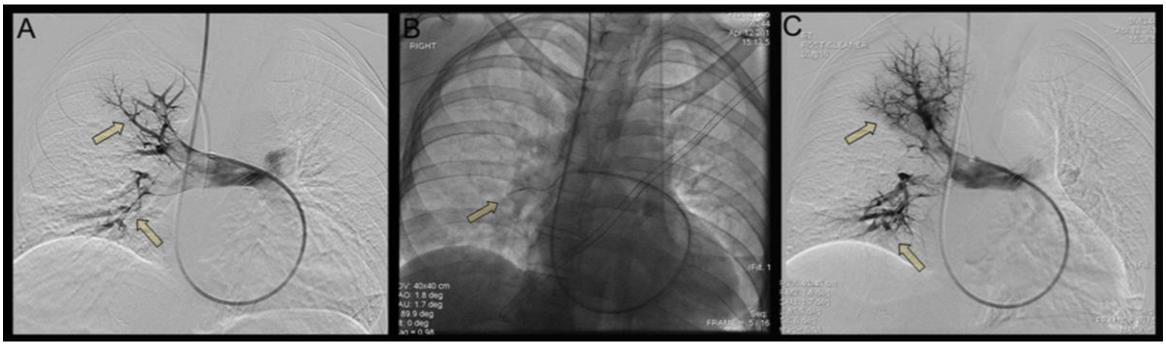

Figure 2: 40 year old male patient with acute massive PE. A) Parenchymal phase digital subtraction angiography (6 frames/second, AP projection) after administration of Alteplase and aspiration, demonstrating significant thrombus in the right pulmonary artery and its upper and lower lobe branches with mildly improved perfusion. B) Spot fluoroscopic image of the Cleaner device being deployed in the right lower lobe pulmonary artery through the 9 Fr sheath. C) Parenchymal phase digital subtraction angiography (6 frames/second, AP projection) after use of the Cleaner™ device, demonstrating more lobar and segmental branch opacification and greater perfusion to the upper and lower lobes. Overall fluoroscopy time for the case was 32 minutes, with a dose area product of 20157 cGy cm^2.

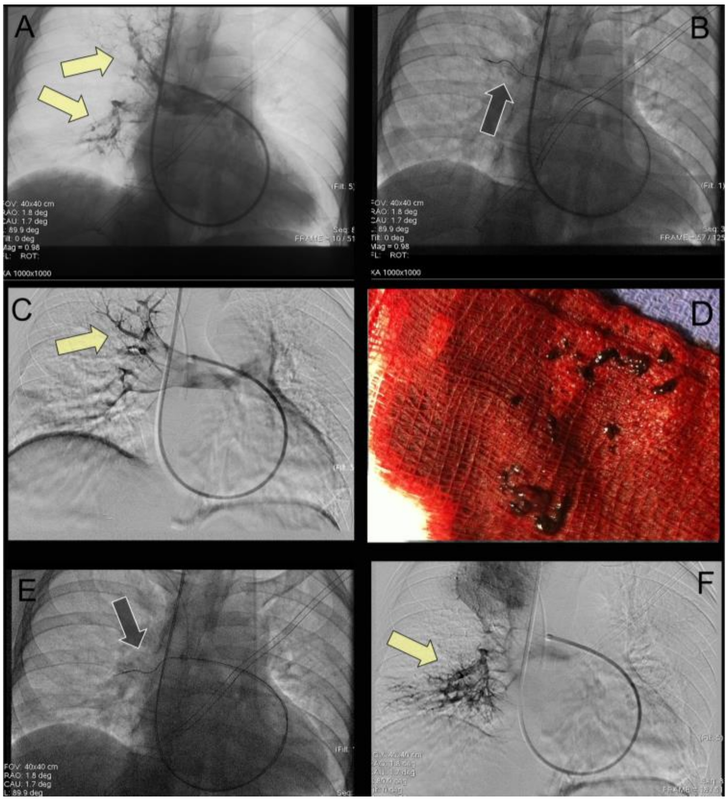

Figure 3: Percutaneous thrombectomy procedure: A 5 French pigtail catheter was inserted over a 0.035 Bentson wire and its tip advanced selecting the main pulmonary artery. The sheath was advanced over Amplatz wire 0.035 Inch with its tip in the right pulmonary and an angiogram with 10 ml/sec of 20 ml Omnipaque contrast was performed from this position. These injection rates and volumes were used during all remaining angiograms. A) The right pulmonary angiogram, before the alteplase thrombolysis/mechanical thrombectomy, showed large filling defect in the main right pulmonary artery with poor right pulmonary perfusion (arrows pointing at hypoperfused upper and lower right lung arteries). Pressure in the main pulmonary artery, before the alteplase thrombolysis/ mechanical thrombectomy, was 39/19 with mean of 24 mm Hg. At this point, right pulmonary catheter-directed thrombolysis using 6 mg of alteplase diluted in 10 ml sterile water injected over 2 minutes was performed. Right pulmonary mechanical thrombolysis using rotational pigtail (5 French) catheter was then performed under fluoroscopic guidance and cardiopulmonary monitoring. B) Right upper lobe pulmonary mechanical thrombolysis using the Cleaner™ Argon device (arrow) was performed under fluoroscopic guidance and cardiopulmonary monitoring. C) Right pulmonary angiogram showing improved perfusion of right upper pulmonary arteries (arrow) D) Dark clotted blood was removed via the aspiration catheter in the amount of 70 ml E) Right lower lobe pulmonary mechanical thrombolysis using the Cleaner device (arrow) under fluoroscopic guidance and cardiopulmonary monitoring F) Completion right pulmonary angiogram after the alteplase thrombolysis/ mechanical thrombectomy, showing significant decrease in the filling defect in the right lower pulmonary arteries. Respiratory and heart rates were improved and the pressure in the main pulmonary artery, after the alteplase thrombolysis/ mechanical thrombectomy, was 28/12 with mean of 19 mm Hg.

Endovascular Technique	Rheolytic embolectomy	Rotational embolectomy	Aspiration embolectomy	Thrombus fragmentation	Catheter-directed thrombolysis
Commonly used devices	AngioJet (Possis, Minneapolis, MN) Oasis (Medi-tech/ Boston Scientific, Natick, MA) Hydrolyser (Cordis, Bridgewater, NJ)	Rotarex and Aspirex (Straub Medical AG in Wangs, Switzerland), Cleaner™ (Rex medical, Athens, TX)	The Greenfield suction embolectomy catheter (Medi-tec/ Boston Scientific, USA)	Fogarty arterial Balloon embolectomy catheter (Edwards Lifescience Corp, Irvine , CA) Pigtail rotational catheter (Cook-Europe, the Netherlands)	ClearWay™ RX infusion catheter (Atrium Medical Corporation, Hudson, NH)
Mechanism of Action	Injecting pressurized saline through the catheter's distal tip +/- a lytic agent; the fragments of clot are then sucked back into an exhaust lumen of the catheter for disposal	A high-speed rotational coil within the catheter body creates negative pressure through an L-shaped aspiration port at the catheter tip, macerating the thrombus and removing it by aspiration	Suctioning thrombus through a large-lumen catheter by applying negative pressure	Manually rotating a standard pigtail catheter or performing balloon sweeps with a balloon angioplasty catheter	Local thrombolysis with tPA or tenecteplase Requires positioning of an infusion catheter within the embolus, with injection of a bolus of thrombolytic drug, followed by a continuous infusion.
Advantages	- Percutaneous embolectomy is a minimally invasive interventional therapy without the need for cardiopulmonary bypass - It can rapidly reverse acute right ventricular failure and cardiogenic shock - Catheter thrombectomy represents the only reperfusion strategy when contraindications to thrombolysis are present or when surgical embolectomy is not feasible or not readily available - In comparison to thrombolysis, catheter thrombectomy causes fewer systemic bleeding complications, including the most serious complication of intracranial hemorrhage				
	These catheters can be placed over the guidewire so are easily placed to target destination	Combines the benefits of fine thrombus fragmentation with aspiration	This has been the first and oldest technique available Large open end which allows large pieces of clot to be removed	Mechanical techniques that are effective and do not require specialized equipment or instruments.	Lower doses of the thrombolytic agent are used (average doses of tPA 10-20 mg vs. systemic tPA infusion dose of 100 mg as a standard) Local delivery of the drug protects it from deactivation by circulating inhibitors and achieves higher drug concentration at the site of thrombosis
Disadvantages	- Major but extremely rare complications include severe pulmonary hemorrhage and pericardial tamponade. Perforation or dissection of major PA branch not uncommon and can be fatal. More common complications include arrhythmia, tricuspid or pulmonary valve regurgitation, vascular access complications, and anaphylactic reaction to iodine contrast. Bleeding may occur at any site from anticoagulation with intravenous unfractionated heparin. Renal failure may occur due to the use of iodine contrast for pulmonary angiography, particularly in patients with preexisting renal dysfunction. - Absolute contraindications for percutaneous transcatheter treatment basically remain the same as those for thrombolysis in general - Only operators experienced with these techniques should perform catheter-based intervention. Interventionalists must be comfortable managing cardiogenic shock, bradyarrhythmias, anticoagulation, and cardiac tamponade - As compared to surgical embolectomy, percutaneous approach offers less control of hemodynamics in case of severe complications - In general, this approach is not effective once the thrombus is adherent and begins to organize - Literature limited to uncontrolled, small series and case reports				
	It is not designed for the use in the large-sized main pulmonary arteries The rheolysis can result in profound and life-threatening arrhythmias	Prolonged aspiration may potentially cause hemodynamic deterioration in patients with PE-related shock due to blood loss	Catheter is difficult to manipulate due to its size and stiffness	The risk of distal embolization and further deterioration in hemodynamics when a large centrally-located non-obstructive thrombus breaks and embolizes into a previously unobstructed branch	Major bleeding complication rates vary from 5-11% based on some studies; most bleeds occur at puncture site

Table 1: Commonly used endovascular techniques for percutaneous thrombectomy

ABBREVIATIONS

ACCP - American College of Chest Physician
AHA - The American Heart Association
CVP - central venous pressure
DVT - deep venous thrombosis
HR - Heart rate
IVC - inferior vena cava
PA - pulmonary artery
PE - Pulmonary embolus
pO2 - arterial partial pressure of oxygen
RR - Respiratory rate
tPA - Tissue plasminogen activator

KEYWORDS

Pulmonary embolism; catheter-directed thrombolysis; clot fragmentation; Cleaner^{TM} device