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Catheter based therapies in massive pulmonary embolism

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Pulmonary embolism (PE) is the third most common cardiovascular disease claiming 100,000 deaths annually in the United States (U.S.). It also the leading cause of preventable deaths in hospitalized adults [1]. Risk stratification remains the essential first step to tailor PE treatment. Majority of the radiologically diagnosed acute PE are low risk with mortality rate <2% [2]. High risk PE occur in only 5% of all hospitalized PE patients, but are associated with very high mortality rates (18% to 64%) [3]. Systemic thrombolysis has been the cornerstone therapy in such patients with high risk PE as long as their bleeding risk is acceptable [4]. Thrombolytic use in massive PE is associated with lower risk of mortality, lower subsequent risk of developing chronic thromboembolic pulmonary hypertension and also improves the quality of life [5]. However, these benefits are observed at the expense of an increased risk of bleeding [6]. In a meta-analysis of 16 randomized controlled trials, systemic thrombolytic therapy was associated with nearly three times higher risk of major bleeding and four times higher risk of intracranial hemorrhage compared with anticoagulation alone [6]. In an effort to mitigate bleeding complications from systemic thrombolytics, contemporary practice has seen a lot of enthusiasm around catheter based thrombus removal techniques in an effort to provide similar efficacy benefit of thrombus resolution without the added bleeding risk with systemic thrombolysis [7,8].

Goal is to resolve the acute cor pulmonale by relieving the central pulmonary vascular obstruction, but with exposure to lower bleeding risk. Aspiration thrombectomy was first described by Greenfield et al. in 46 patients with massive PE, with reductions in mean pulmonary artery pressure by 8 mm-hg and improvement in cardiac output by 40% immediately following the procedure [9]. Later, Tajima et al. demonstrated that pretreatment with low dose thrombolytics promoted clot lysis and improved aspiration [10]. In this context, Gregorio et al. now report this contemporary series of high risk PE patients undergoing pharmaco-mechanical thrombectomy using the Indigo CAT-8 catheter, Penumbra inc. (Alameda, CA, U.S.) [11]. Key findings from this report include: Pharmaco-mechanical thrombus removal is effective in patients with high risk PE. Significant hemodynamic improvement was noted in all patients, with normalization of PA pressures at 30 days in >90% of those who survived. Thirty-day mortality rate of 11% (6/54) in a high risk PE cohort is comparable to prior reports [9,12]. Table 1 summarizes key reports of percutaneous thrombectomy in PE patients thus far.

These results suggest a possible synergistic effect of low dose thrombolytic therapy and aspiration thrombectomy. Similar treatment strategy is proven in patients with proximal DVT, but data on such an approach in massive PE is scant: this report from Gregorio et al. is therefore encouraging and at least hypothesis generating. Recently reported ATTRACT randomized controlled trial suggested a reduced incidence of moderate to severe post thrombotic syndrome with pharmaco-mechanical thrombectomy in patients with proximal DVT [13]. Next steps should include rigorous investigation of pharmaco-mechanical thrombectomy in PE patients.

IVC filters were routinely placed in all patients in this series. Routine use of inferior vena cava (IVC) filters prior to pharmaco-mechanical thrombectomy in this report is another controversial topic with very little evidence either way at this time. IVC filter placement has the upside of reducing more embolization in the acute setting, with the downside of adverse long-term consequences if the filter is not removed in follow up [14, 15]. While six in-hospital deaths reported among study participants, including three deaths during thrombo-aspiration and one during thrombolytic infusion is comparable to prior reports in this very high risk patient population [9,12]; future investigation looking at incorporating prompt mechanical circulatory support in patients who are decompensating rapidly is also warranted.

In conclusion, current societal guidelines do not recommend catheter-based therapies in patients with high risk PE unless systemic thrombolytic therapy is contraindicated (class IIa recommendation) [4]. This limited application stems from the lack of large trials, leaving a void in our ability to rapidly adopt and implement such therapies. In

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Table 1
Key studies of percutaneous thrombectomy in patients with pulmonary embolism.

Study	Device	PE patient population	Success rate	Mortality rate
Aspiration thrombectomy				
Greenfield et al.[a]	Greenfield suction catheter®, Boston Scientific, Marlborough, MA, USA	High risk-46	76%	30.4%
Dumantepe et al.[b]	Aspirex® (Straub Medical, Wangs, Switzerland)	High risk-11; Intermediate risk-25	97.2%	5.5%
Liu et al.[c]	Straub Rotarex®, Straub Medical, Wangs, Switzerland	High risk-14	64.2%	No deaths reported.
FLARE[d]	FlowTriever®, Inari Medical, Irvine, CA, USA	Intermediate risk-106	100%	<1%
Al-Hakim et al.[e]	AngioVac®, AngioDynamics, Latham, NY, USA.	High risk-4; Intermediate risk-1	40%	80%
Gregorio et al.[f]	Indigo CAT 8®, Penumbra Inc., Alameda, CA, USA	High risk-54	100%	11.1%
Rheolytic thrombectomy				
Margheri et al.[g]	AngioJet®, Boston Scientific, Boston, MA, USA	High risk-8; intermediate risk-12; low risk-5	100%	16%
Fava et al.[h]	Hydrolyzer®, Cordis, FL, USA	High risk-11	100%	9%
Fava et al. (unreported)	Oasis®, Cordis, FL, USA	NR	80%	No deaths reported
Thrombus fragmentation				
Schmitz-Rode et al.[i]	Pigtail fragmentation catheter®, William Cook Europe, Denmark	High risk-10	80%	20%
Kawahito et al.[j]	Fogarty Balloon Catheter®, Edward Lifesciences, Irvine, CA, USA	High risk-5	100%	No deaths reported.
Barjaktarevic et al.[k] (case report)	Cleaner®, Rex medical, Athens, TX, USA	High risk-1	NA	NA
Muller-Hulsbeck et al.[l]	Amplatz thrombectomy device®, Microvena, White Bear Lake, MN, USA	High risk-9	100%	No deaths reported

Footnotes: - FLARE- FlowTriever Pulmonary Embolectomy Clinical Study.
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the real-world, systemic thrombolytic therapy is withheld in at least 70% of patients with massive PE [1,16]. We need to generate more evidence informing our use of novel treatment strategies such as pharmaco-mechanical thrombectomy in patients with PE. Nonetheless, pulmonary embolism continues to be a widely prevalent and highly morbid clinical condition. Its treatment is an evolving paradigm, while we wait for more conclusive evidence, these reports with novel treatment strategies continue to show promise. We should incorporate all available therapies in our tool kit and continue to manage these very sick PE patients in a multidisciplinary thoughtful fashion [17].

Disclosures

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Aggarwal V: None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.04.029.

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