Original Article

Technical efficiency, short-term clinical results and safety of a large-bore aspiration catheter in acute pulmonary embolism – A retrospective case study

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ABSTRACT

Background: Mechanical thrombectomy plays an important role in the management of acute pulmonary embolism (PE), either when rapid clot dissolution is needed or when thrombolytics are contraindicated. We describe our clinical and technical experience with the FlowTriever mechanical thrombectomy device in patients with acute PE. **Materials and Methods:** A retrospective analysis was performed on all cases of acute PE treated with the FlowTriever device at a single tertiary care hospital system during the trial period (November 2019–January 2020). Technical and clinical results, including complications, are reported. **Results:** Technical success was achieved in all eight successive cases (seven cases of submassive and 1 case of massive PE). Mean pulmonary artery pressure (MPAP) improved significantly after mechanical thrombectomy (27.8 ± 6.4 mmHg preprocedure; 20.5 ± 3.8 mmHg postprocedure; 7.3 ± 5.2 mmHg decrease after the procedure; $P = 0.016$). Hemoglobin levels did not change significantly after mechanical thrombectomy (11.8 g/dl ± 3.4 preprocedure; 9.9 g/dl ± 2.1 postprocedure; $P = 0.20$). Reduction in MPAP was achieved in 88% of cases (7/8) and hypoxia improved in all the nonintubated patients (7/7). Mortality observed in one patient with a massive central PE, was not related to the procedure. No mortality or procedural complications were observed in patients with submassive PE. **Conclusions:** The positive initial clinical experience and safety profile using the FlowTriever in the treatment of acute PE suggests, it has the potential to fill the unmet needs of a good mechanical thrombectomy device to treat massive and submassive high-risk PE especially when thrombolytics are contraindicated.

KEY WORDS: Chronic thromboembolic pulmonary arterial hypertension, FlowTriever, pulmonary embolism, right heart strain

INTRODUCTION

Pulmonary embolism (PE) is a major cause of morbidity and mortality, estimated to affect 1–2 persons/1000 annually

in the United States.[1,2] Appropriate PE risk stratification remains a critical step to direct clinical decision-making and hence reducing mortality. The American Heart Association (AHA)[3] and the European Society of Cardiology (ESC)[4] propose the following risk stratification.

Massive (American Heart Association) or high risk (European Society of Cardiology)

These PE patients are hemodynamically unstable (persistent hypotension with systolic blood pressure (SBP) of <90 mmHg or need for vasopressors). They constitute ~ 5% of the PEs but carry a very high mortality rate of >50%.[3]

Submassive (American Heart Association) or intermediate-risk (European Society of Cardiology)

These patients have right ventricular (RV) strain on echocardiography/computed tomography (CT) or RV injury (elevated cardiac biomarkers such as troponins or brain natriuretic hormone). The 2014 ESC Guidelines sub-stratifies intermediate-risk patients into low and high risk[5-7] based on a simplified PE severity index (sPESI) score [Table 1]. Submassive-high risk patients have a sPESI of ≥1 with both RV strain and injury. Sub-massive-low risk patients have a sPESI of ≥1 with either RV strain or injury or neither of these. As a group, they account for 35%–55% of the PE patients.[3,4,8,9] The mortality rates in these patients treated with anticoagulation (AC) alone ranges from 2% to 15%.[4,8,10-13]

Low risk (European Society of Cardiology and American Heart Association)

These patients are hemodynamically stable (SBP blood pressure ≥90 mmHg), without RV dysfunction or myocardial injury. Low-risk PE patients represent 55% of the PE population and have an excellent prognosis.

Systemic AC has long been the mainstay of treatment for acute PE but can take up to 24 h to become therapeutic[14] and does not dissolve or lyse the existing thrombus. In addition to systemic AC, the American College of Chest Physicians,[15] ESC,[4] and AHA,[16] make recommendations for systemic thrombolysis (ST) in patients with massive PE. However, guidelines on the use of adjunctive treatments, such as catheter-directed thrombolysis or mechanical thrombectomy in acute PE are limited. The decision for active thrombus removal is primarily driven by the severity of the PE and is secondarily influenced by the presence of patient-specific risk factors for bleeding, the extent and location of thrombus, operator expertise, individual physician preferences, and associated comorbidities.

Mechanical thrombectomy involves the removal of clots without the use of thrombolytics. Mechanical thrombectomy can be considered in patients with acute PE in the following circumstances:

- Massive PE, who are on hemodynamic support mechanisms, needing rapid clot dissolution to reduce the afterload on the heart and improve perfusion
- Submassive PE with right heart strain/injury to avoid clinical deterioration and provide rapid relief of symptoms
- In patients with massive or submassive PE with contraindications to thrombolytic therapy
- Prevention of chronic thromboembolic pulmonary arterial hypertension (CTEPH)-a potential but unproven rationale.

The FlowTriever device (Inari Medical Inc., Irvine, California) was approved at our institution, on a 3-month trial basis for mechanical thrombectomy in patients with acute PE. We evaluated the technical and clinical results of patients who underwent mechanical thrombectomy with the FlowTriever device and reported our data.

MATERIALS AND METHODS

All cases of acute PE treated with the FlowTriever device at a single tertiary care hospital system during the trial period (November 2019–January 2020) were retrospectively analyzed. Follow-up was available for each patient. The study received institutional review board approval with a waiver of informed consent. Immediate technical success was defined as the successful delivery of the device to the site of the clot, operation of the device, and removal of the device. Clinical success was defined in this study as an intraprocedural decrease in mean pulmonary artery pressure (MPAP). Any drop in hemoglobin levels postprocedure was also evaluated. Chart reviews of the hospitalization and any subsequent clinic or Emergency Room (ER) visits were performed to assess for immediate and delayed procedure-related outcomes and complications. The location of the clot [Figure 1a], the

Table 1: Simplified pulmonary embolism severity index score[7]

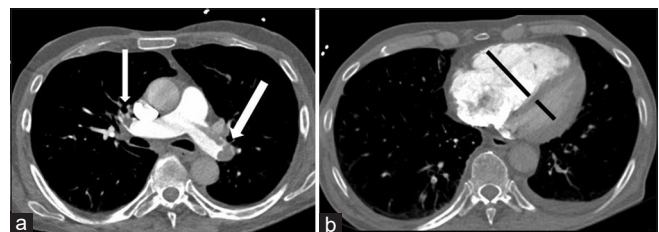| Parameter	Score
Age >80 years	1 point
History of cancer	1 point
History of chronic cardiopulmonary disease	1 point
Heart rate of >110 (beats/min)	1 point
SBP <100 (mmHg)	1 point
O_2 saturation <90%	1 point

SBP: Systolic blood pressure

Figure 1: (a and b) Acute bilateral PE. Axial contrast enhanced computed tomography scan showing filling defects (a) in both pulmonary arteries left > right (solid white arrows). The same patient with right heart strain (b) with the right ventricle twice the size of the left (black solid lines)

clot burden, RV dysfunction, and pulmonary hypertension were assessed on the CT angiograms performed during the hospital visit for acute PE. The right-to-left ventricular (RV: LV) ratio [Figure 1b] and pulmonary trunk were measured on axial CT angiography images per standard validated technique[17] and detailed in Table 2. PE was clinically stratified as massive or submassive based on the AHA criteria.[3]

The decision to offer mechanical thrombectomy to acute PE patients was made based on a multidisciplinary team consensus. Patients with centrally located PE who were clinically stratified as massive or submassive high risk were offered mechanical thrombectomy. Patients with isolated peripheral PE or those who were clinically stratified as low risk or submassive-low risk without signs of clinical deterioration were not offered mechanical thrombectomy.

All procedures were performed by 1 of the four interventional radiologists with 8, 6, 5, or 1 years of postfellowship experience.

Equipment

The FlowTriever is the first mechanical thrombectomy device with a US Food and Drug Administration indication for the treatment of acute PE. It consists of a compliant large-bore 20-French (F) aspiration guide catheter, also called T20 [Figure 2a], which tracks over a 0.035-inch guidewire to the level of the clot. Aspiration of the thrombus is performed by applying and subsequently releasing a vacuum within the system. The vacuum is created manually by a custom 60 cc syringe [Figure 2b] that is attached through a side-tube connector. Once the created vacuum is manually released, a powerful suction is initiated that allows the aspiration of large amounts of thrombus through the T20 into the 60 cc syringe. An additional part of the FlowTriever system, the FlowTriever catheter, which comes with multiple sizing options of self-expanding nitinol discs that can be advanced through the T20 to mechanically engage thrombus and help promote the release of clot from the vessel wall [Figure 2c].

Procedure

Systemic AC initiated at the time of PE diagnosis was continued throughout the thrombectomy procedure with additional heparin boluses administered to mainta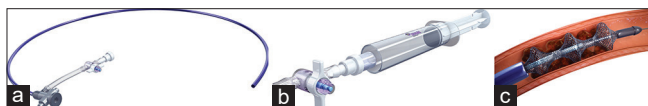in the activated clotting time around 250 s. Inferior vena cava (IVC) filters were not deployed prior to thrombectomy in any of the cases. Conscious sedation was used in most cases, with appropriate hemodynamic monitoring. General anesthesia is not preferred in patients undergoing pulmonary embolectomy[18] and was used only in one patient who required mechanical ventilation before the procedure. Vital signs were monitored and recorded by nurses throughout the procedure. Supplemental oxygen requirements (defined as oxygen required to maintain saturation >90%), fluoroscopy time, and procedural time were obtained from the initial and final nursing charting, performed at the start and close of the case. Hemoglobin levels were obtained before the procedure and within 24 h after the procedure. The right common femoral vein was accessed in all cases, with ultrasound-guidance, followed by insertion of a 6-F sheath, using the Seldinger technique. A 5-F angled Pigtail catheter was advanced over a 0.035-inch guidewire through the right heart and used to select the pulmonary trunk. Baseline main pulmonary artery (PA) pressures were measured, and an initial pulmonary angiogram was performed through the catheter. The guidewire was advanced distally into a lobar or segmental PA and then exchanged for an Amplatz Super Stiff (Boston Scientific, Marlborough, Massachusetts) 1-inch floppy tip guidewire. Following serial dilations, the initial 6-F sheath was exchanged for a 22-F DrySeal Introducer sheath (GoreFlagstaff, Arizona), which was advanced into the IVC. The T20 was advanced over the wire into a main or lobar PA with the thrombus [Figure 3a], and the inner dilator was removed. Aspiration thrombectomy was performed multiple times until the angiographic resolution of central clot was achieved; intermittent pulmonary arteriography was obtained through the T20, as needed [Figure 3b]. The aspirated thrombus was manually expelled from the syringe onto a towel on the side table to reuse the syringe for the next aspiration [Figure 3c]. Repeat PA pressures were measured, and the device was withdrawn. The access site was closed with a purse-string suture. Deployment of the nitinol discs was not required to engage the clot in any of our procedures.

Figure 2: (a-c) Flowtriever catheter-based mechanical thrombectomy device and its components. Flowtriever (a) is a 20 F catheter which is designed to aspirate clot by creating a vacuum using a proprietary 60 cc syringe (b) attached to a side port. The device also comes with three braided nitinol disks to engage clot and pull it into the aspiration guide catheter (c), as needed in difficult cases with adherent clot. Used with permission of Inari Medical, Irvine CA

Figure 3: (a-c) Thormbectomy with T20. The initial pulmonary angiogram (a) showing a filling defect in right upper pulmonary artery (white arrow) with poor perfusion of the upper lobe. The postthrombectomy angiogram (b) through the T20 (black arrow), showing resolution of the filling defect in the right upper lobe pulmonary artery (white arrow) with good perfusion in the upper lobe. The extracted clot laid out on the procedure table (c)

RESULTS

Patient demographics, clinical data, and initial imaging findings are summarized in Table 2. Technical success was achieved in all eight cases (100%). Seven (87.5%) cases of submassive and 1 (12.5%) cases of massive PE were treated. Clinical outcome measures, including MPAP and change in hemoglobin levels, were compared using the Wilcoxon matched-pairs signed-rank test on GraphPad Prism Version 8 (GrapPad Software, San Diego, CA, USA). MPAP improved significantly after mechanical thrombectomy (27.8 ± 6.4 mmHg preprocedure; 20.5 ± 3.8 mmHg postprocedure; 7.3 ± 5.2 mmHg decrease after procedure; a 26.3% drop, ($P = 0.016$) [Figure 4]. Hemoglobin levels did not change significantly after mechanical thrombectomy (11.8 g/dl ± 3.4 mmHg preprocedure; 9.9 g/dl ± 2.1 mmHg postprocedure; 1.8 g/dl ± 1.9 mmHg decrease after the procedure; $P = 0.20$). Reduction in MPAP was achieved in 88% of cases (7/8), and a reduction in oxygen requirement was observed in 100% of nonintubated patients (7/7). Mean fluoroscopy time was 23.1 ± 10.5 min, and the mean procedure time was 86.3 min ± 16.4 min. Mortality was observed in one patient with a massive central PE, however not related to the procedure. No mortality or procedural complications were observed in patients with sub-massive PE.

No blood transfusions were administered. Only two patients with submassive PE were briefly admitted to the intensive care unit, due to transient preprocedural hypotension and chest pain, respectively. No thrombolytics were used intra-procedurally to achieve a reduction in PA pressures. Two of the eight patients have since been seen in the clinic with the return to baseline activity, normal exercise tolerance, echocardiographic, and CT findings postprocedure.

DISCUSSION

Our initial experience using the Inari FlowTriever device yielded 100% technical success, no procedure-related
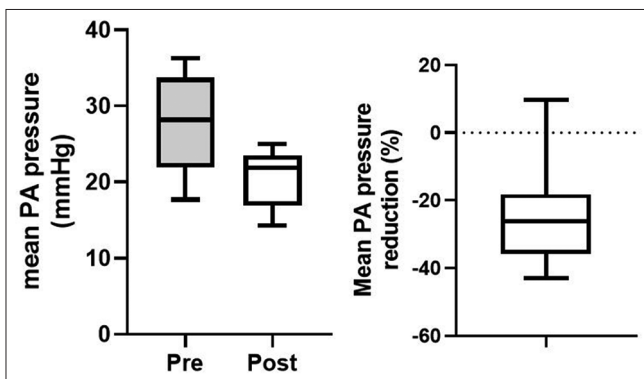

Figure 4: Change in mean pulmonary artery pressure pre- and post-procedure. Mean pulmonary artery pressure improved significantly after mechanical thrombectomy (27.8 ± 6.4 mmHg prior to procedure; 20.5 ± 3.8 mmHg postprocedure; 7.3 ± 5.2 mmHg decrease after procedure; a 26.3% drop, [$P = 0.016$])

Table 2: Baseline patient demographics, risk stratification, pre-procedural Imaging, labs, key results and complications

Age/gender	PE classification	RV/LV ratio	PA pressure (mmHg) Preprocedure	PA pressure (mmHg) Postprocedure	Preprocedure dysfunction per echo	Postprocedure dysfunction per echo	BNP (pg/ml)	Troponin (ng/ml)	Preprocedure H and H	Postprocedure H and H	Complications
73/female	Sub-massive	1.3	60/22	45/15	Moderate	Not available	360	0.05	14	11	None
68/male	Sub-massive	1.7	49/22	31/11	Severe	Not available	2974	0.33	17	11	None
42/female	Sub-massive	1.2	51/16	41/11	Mild	Normal	3224	0.06	7	6.9	None
63/male	Sub-massive	2	46/20	33/19	Severe	Mild	Not obtained	1.50	14	13	None
61/female	Sub-massive	1.3	35/9	25/9	Not available	Mild	2235	0.04	7.8	7	None
58/female	Sub-massive	2	50/6	44/12	Not available	Normal	356	0.10	13	11	None
66/male	Massive	2	67/21	51/9	Moderate	Not available	7007	0.70	11	10	Death
72/female	Sub-massive	2.7	45/16	32/9	Severe	Normal	1905	0.03	10.4	9.6	None

BNP: Brain natriuretic peptide, H and H: Hemoglobin and hematocrit, PA: Pulmonary artery, RV: Right ventricle, LV: Left ventricle, PE: Pulmonary embolism

complications, and a statistically significant drop in MPAP. Improvement in supplemental oxygenation requirements was seen in all the nonintubated patients within 48 h after the procedure. The single mortality that occurred was not procedure-related and occurred in a patient with massive PE, presumably due to an inherently poor prognosis associated with this type of PE and delay in the intervention (as the patient was initially found unresponsive in the field before eventual transfer to our hospital). At the time of arrival, required four vasopressors, had renal failure and lactic acidosis.

AC alone does not dissolve thrombus. Patients presenting with massive PE need to be treated in a critical care setting and often require prompt aggressive measures such as ST, catheter-based therapy, or mechanical circulatory support to prevent further deterioration.[3,4,15,19] Although ST is usually indicated for these patients, bleeding complications are always a concern, and at least a third have some contraindication to systemic thrombolytics.[20] Moreover, up to 10% of patients who receive ST remain in shock.[21] In patients with submassive high-risk PE, advanced endovascular therapies can be used to expedite symptom resolution and avert possible deterioration toward the higher risk category from progressive right-sided heart failure. There have been three prospective studies demonstrating that catheter-directed lysis (CDL) can effectively lyse pulmonary arterial thrombi, improve pulmonary blood flow at 48 h, and rapidly restore RV function.[22-24] Although, none of the studies reported major intracranial hemorrhage, one of them reported 10% of patients who received CDL experienced significant extracranial bleeding complications.[24] In addition to acute outcomes, long-time sequelae are a concern when treating PE patients. CTEPH, a condition found in about 4% of patients at 2-year follow-up, is a severe complication, which frequently requires major surgery.[25] In addition, a higher proportion of patients suffer chronic disability without resting pulmonary hypertension, referred to by some as the post-PE syndrome and by others as a chronic thromboembolic disease.[26] Preventing these chronic morbidities is another yet to be investigated rationale for aggressive interventional treatment in patients with sub-massive PE. Mechanical thrombectomy is particularly valuable in patients with coagulopathies and/or contraindications to thrombolytics, as it achieves active thrombus removal, without the use of thrombolytics, largely eliminating the risks of major intra and extracranial hemorrhage.

Thrombus maceration may be performed with a pigtail catheter, guidewire, or with peripheral balloons, sized smaller than the arterial lumen. However, these techniques are unreliable, lack control, and are associated with the risk of distal embolization. The AngioVac cannula (Angiodynamics Inc., Latham, NY) is a veno-veno bypass system designed to aspirate intravascular material. The inflow cannula is a 22F suction catheter, accessed through femoral or internal jugular veins. The outflow cannula (16F–20F, at the operator's discretion) returns blood to the body through a separate femoral or internal jugular vein access. The system requires a perfusionist to be present during the procedure, which adds to the time required to assemble a team. Moreover, there have been reports of difficulty navigating the AngioVac through the right side of the heart to the PA from its bulk and inflexibility.[27] The Penumbra system (Penumbra Inc., Alameda, CA) is a suction aspiration system initially used in the endovascular treatment of stroke. The Penumbra INDIGO CAT 8 system (Penumbra, Inc., Alameda, CA, USA) is a flexible 8-F aspiration catheter, which is connected to a continuous suction vacuum system. A wire separator in the catheter lumen facilitates clot retrieval. The Penumbra system lacks the means to return blood to the patient and can lead to significant blood loss if not embedded in the clot.[28] In addition, the smaller size catheter potentially limits the amount of clot extracted.

Although the FlowTriever is a large catheter (20F), it had no problems tracking over a stiff wire into the target location. With each aspiration, blood loss is limited to 60cc, even if unexpectedly, no thrombus would be retrieved due to suboptimal device placement. We did not experience any significant blood loss from the aspiration process in our case series and no cardiac injury or other device-related complications. We demonstrated significant improvement in PA pressures and O$_2$ requirements in all our nonintubated patients without significant complications, as previously reported.[29] The FlowTriever has been evaluated in a prospective single-arm multicenter trial (FLARE; NCT02692586)[10] and more recently, in a retrospective study.[29] Our case series adds to this initial body of evidence. The major limitation of our study was its small sample size, single institute experience, retrospective nature, and lack of a control arm. It still provides valuable insights as a real-world early experience highlighting the potential of FlowTriever to quickly treat PE with acute improvement in both PA pressures and oxygenation status.

CONCLUSIONS

We report a positive initial clinical experience and a good safety profile using the FlowTriever in treatment of acute PE. It appears to fill the unmet need for a dedicated mechanical thrombectomy device to treat massive and submassive high-risk PE. Prospective randomized studies are needed to validate these initial observations, to assess the potential long-term impact on the development of chronic-PE syndrome, and evaluate this therapy against other catheter-directed and pharmacological approaches.

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Conflicts of interest
There are no conflicts of interest.

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