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Safety of the Inari FlowTriever device for mechanical thrombectomy in patients with acute submassive and massive pulmonary embolism and contraindication to thrombolysis

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ABSTRACT

Objectives: This report evaluates the safety of percutaneous mechanical thrombectomy with the Inari FlowTriever System (Inari Medical, Irvine, California) for the treatment of acute massive/submassive pulmonary embolism (PE) specifically in therapeutically anticoagulated patients with contraindication to thrombolysis.

Material and Methods: A single-center retrospective chart review was performed on patients with contraindication to thrombolysis and massive/submassive PE who underwent FlowTriever thrombectomy between 2017 and 2019. Primary outcomes included procedure or device-related complications within 30 days of discharge. Secondary outcomes included technical and clinical success defined by improvement in mean pulmonary artery pressure (PAP), oxygen saturation, and heart rate.

Results: Thirteen patients with contraindication to thrombolysis received FlowTriever thrombectomy with technical success achieved in all cases. Zero major or minor adverse events, technical complications, delayed procedure-related complications, or deaths within 30 days of hospital discharge occurred. Mean PAP decreased significantly by 19.1% (32.5 ± 13.3 mmHg to 26.3 ± 12.4 mmHg; $P = 0.0074$, 95% confidence interval (CI) 2.0–10.5 mmHg). Oxygen saturation improved post-procedure (increased 3.9 ± 3.8%; $p = 0.0032$, 95% CI 1.6–6.1%) as did heart rate (decreased 22.2 ± 17.0 bpm; $P < 0.001$, 95% CI 11.9–32.4 bpm). Anticoagulation was maintained throughout every procedure and all patients were closed with purse-string suture only.

Conclusion: FlowTriever mechanical thrombectomy appears safe for acute PE in therapeutically anticoagulated patients with contraindications to thrombolytic therapy. These patients may experience immediate hemodynamic improvements similar to those reported in other studies. Further data are needed to prospectively evaluate long-term safety in this population.

Keywords: Mechanical thrombectomy, Pulmonary embolism, Thrombolysis

INTRODUCTION

In the treatment of acute pulmonary embolism (PE), there are subsets of patients, such as those with recent trauma or surgery, for which thrombolysis is absolutely or relatively contraindicated due to increased bleeding risks.[1] Percutaneous mechanical thrombectomy procedures remove thrombus without thrombolytic drugs and thus may be a preferable treatment approach for these patients. The FlowTriever System (Inari Medical, Irvine, California) is a mechanical

thrombectomy device designed specifically to extract thrombus from large vessels such as the pulmonary arteries. The system consists of a 16, 20, or 24 Fr guide catheter with large bore syringe for aspiration thrombectomy with optional self-expanding nitinol mesh discs to disrupt thrombus. The 16 Fr catheter can be used through the 20 or 24 Fr catheters to reach more distal branches.

FlowTriever outcomes data are small but growing. The pivotal FLARE study was a prospective multicenter trial that enrolled 106 patients and showed that the FlowTriever was safe and effective for patients with intermediate-risk PE, with significant improvement in the right ventricular (RV) function and minimal bleeding complications.[2] The FLARE trial evaluated a substantial number of patients but was limited in that it specifically excluded patients who were hemodynamically unstable requiring vasopressors, had any contraindication to thrombolysis, or had undergone recent surgery. Another recent single-center retrospective study of 46 patients found the FlowTriever System safe and effective for acute massive/submassive PE, but only 26% of patients in this study had a contraindication to thrombolysis.[3] The present chart review supplements these recent data by evaluating the safety of FlowTriever thrombectomy to treat acute submassive/massive PE patients who were excluded from the FLARE trial, specifically those with contraindication to thrombolytic therapy regardless of hemodynamic stability or recent surgery.

MATERIAL AND METHODS

Study design

After the Institutional Review Board (IRB) approval was obtained, a single-center retrospective chart review was performed for patients with submassive or massive PE, contraindication to thrombolytic therapy, therapeutically anticoagulated and treated with the FlowTriever from 2017 to 2019 by a single operator. A total of 13 patients were identified: Five with relative and eight with absolute contraindications to thrombolysis.[1,4]

Procedural details

A standard weight-based heparin infusion was started in all patients at the time of PE diagnosis and maintained throughout each procedure with additional IV boluses as required. After gaining access through the right common femoral vein, pulmonary pressures were obtained, and angiography was performed. After confirmation of significant thrombus burden, the right groin access site was dilated to accept a 22 or 24 Fr dry seal sheath (Gore, Flagstaff, AZ). The FlowTriever 20 Fr aspiration catheter was then advanced over a 0.035" 260 cm angle short-tipped stiff Glidewire (Terumo, Shibuya, Japan) into the affected pulmonary artery and thrombectomy was performed. Pulmonary angiography was repeated as needed. Once technical success (indicated by subjective decrease in thrombus burden) was achieved, the catheter was retracted into the main pulmonary artery and post-thrombectomy pulmonary artery pressure (PAP) was obtained. In some patients, a retrievable Gunther Tulip IVC filter (Cook, Bloomington, Indiana) was placed. The dry seal sheath was removed, and hemostasis was achieved at the site with a purse-string suture and manual compression.

Definitions and endpoints

Pre-treatment risk factors, procedural details, and post-procedure findings were collected. Primary outcomes were defined as any adverse event or procedure-related complication within 30 days of hospital discharge. Complications were defined as device-related death, minor/major bleeding (including access site complications), treatment-related clinical deterioration, and pulmonary, vascular, or cardiac injury. Secondary outcomes included technical success and clinical success as defined by reduction in mean PAP, oxygen requirements, and heart rate while on the operating table.

Statistical analysis

Continuous variables are given as mean with standard deviation, discrete variables as median with range, and categorical variables as count with percentage. A two-tailed paired *t*-test was used to compare pre- and post-procedure data, which included PAP and vital signs.

RESULTS

Baseline demographics and clinical data

Baseline characteristics are summarized in Table 1. The average age was 62 years old, with eight females and five males. A medical history in this cohort included three patients with a previous deep venous thrombosis (DVT), 12 with hypertension, four with previous stroke or transient ischemic attack, and one with prior PE. Pre-procedure laboratories identified four patients with concomitant DVT, four with elevated B-type natriuretic peptide (> 400 pg/mL), and 10 with elevated troponin I (> 0.04 ng/mL). Only one patient had D-dimer collected during workup, which was elevated (> 500 ng/mL).

Three patients presented with massive PE and 10 with submassive PE. Of the three massive PEs, two required vasopressor support and one experienced cardiac decompensation before thrombectomy. The emergency department and intensive care unit were the most common referral sources with four patients presenting from each. Two patients decompensated in the operating room, two presented

as inpatients on general wards, and one as an outpatient. All patients had a contraindication to thrombolysis: Five with bleeding disorders, four with recent intracranial or spinal surgery, one recent head trauma, one recent stroke, one intracerebral hemorrhage, and one intracranial neoplasm.

Computed tomography (CT) angiography was obtained within 48 h before each procedure, and RV to left ventricular (LV) ratio was calculated in cross-section using these CT scans. All patients had right heart strain with a pre-procedure RV/LV of 1.39 ± 0.25. Pulmonary thrombus burden was categorized as unilateral, central only, bilateral only, or central and bilateral, with central thrombus confined to the pulmonary trunk or main pulmonary arteries. Central and bilateral thrombus was present in five patients, and bilateral thrombus alone was present in the other eight patients. Only two patients had follow-up imaging as repeat CT is not standard of care at our institution. An elevated simplified PE severity index ≥ 1 was recorded in 12 patients.

Procedural characteristics

FlowTriever procedure details are outlined in Table 2. Nine patients received monitored anesthesia care, two conscious sedation, and two general anesthesia. The two general anesthesia patients had both sustained intraoperative massive PEs – one became hypoxic during a lumbar fusion and the other sustained cardiac arrest during an orthopedic knee revision. Both patients required vasopressors pre- and periprocedurally.

Technical success was achieved in a single session for 100% of cases (n = 13). A median of seven aspirations was applied to each patient, with thrombus extracted on at least one aspiration from every patient, and thrombus was extracted for every aspiration in nine of the patients. Figure 1 shows representative images of the large thrombus burden typically extracted from these patients. Anticoagulation was maintained throughout each procedure, and all patients were closed using only a purse-string suture with manual compression.

Safety outcomes

In regard to the primary safety outcomes, zero major or minor adverse events or technical complications were observed using either a 22 or 24 Fr sheath and large caliber thrombectomy catheter. No delayed procedure-related complications were observed or deaths within 30 days of hospital discharge.

Table 1: Baseline demographics and clinical data.

Characteristics	Patient values (n=13)
Age (years) – mean±SD	61.9±13.3
Female – *n* (%)	8 (61.5)
BMI (kg/m^2) – mean±SD	32.9±5.3
Ethnicity – *n* (%)	
White/Caucasian	7 (53.8)
Black/African American	4 (30.8)
Other	1 (7.7)
Not given	1 (7.7)
Previous medical history – *n* (%)	
Hypertension	12 (92.3)
Stroke/TIA	4 (30.8)
DVT	3 (23.1)
Pulmonary embolism	1 (7.7)
Concomitant DVT – *n* (%)	4 (30.8)
Elevated troponin (>0.04 ng/mL) – *n* (%)	10 (76.9)
Elevated BNP (>400 pg/mL) – *n* (%)	4 (30.8)
Elevated D-dimer (>500 ng/mL) – n/N (%)	1/1 (100)
Contraindication to thrombolysis – *n* (%)	
Bleeding disorder	5 (38.5)
Recent intracranial or spinal surgery	4 (30.8)
Head trauma or recent stroke	2 (15.4)
Intracerebral hemorrhage	1 (7.7)
Intracranial neoplasm	1 (7.7)

BMI: Body mass index, BNP: B-type natriuretic peptide, DVT: Deep vein thrombosis, TIA: Transient ischemic attack

Table 2: Procedural characteristics.

Characteristics	Patient values (n=13)
Anesthesia – *n* (%)	13 (100)
Monitored anesthesia care	9
Conscious sedation	2
General anesthesia	2
Femoral access – *n* (%)	13 (100)
Number of FlowTriever aspirations per patient – median (IQR)	7 (4–7)
Percent of aspirations with thrombus retrieved – median (IQR)	100% (85–100%)
Patients with thrombus extracted on at least 1 aspiration – *n* (%)	13 (100)
Patients with thrombus retrieved on every aspiration – *n* (%)	9 (69.2)
Technical complications – *n* (%)	0 (0)
Anticoagulation pre-procedure – *n* (%)	12 (92.3)
UFH	10 (76.9)
LMWH	1 (7.7)
VKA (Coumadin)	0 (0)
DOAC	1 (7.7)
ICU length of stay, days – median (IQR)	3 (2–6)
Hospital length of stay, days – median (IQR)	10 (8–13)
Adverse events – *n* (%)	0 (0)
Major bleeding events – *n* (%)	0 (0)

IQR: Interquartile range, UFH: Unfractionated heparin, LMWH: Low-molecular-weight heparin, VKA: Vitamin K antagonist, DOAC: Direct-acting oral anticoagulants, ICU: Intensive care unit

Effectiveness outcomes

The secondary outcomes of immediate post-procedure hemodynamic improvements are presented in Figure 2. Reduction in mean PAP and heart rate and increase in oxygen saturation post thrombectomy were all clinically and statistically significant. Figure 3 shows a 12″ segment of thrombus extracted from one of the patients that received post-procedure imaging. The pre-procedure CT shows thrombus at the main pulmonary artery bifurcation, as well as more distally into the right pulmonary artery. The 7-week post-procedure CT shows no thrombus at the bifurcation but a small remnant thrombus in the right pulmonary artery. This patient's RV/LV decreased from 1.13 to 0.87 after FlowTriever thrombectomy.

DISCUSSION

FlowTriever thrombectomy offers an attractive advanced therapeutic option for this cohort of patients while minimizing bleeding risks. The FlowTriever can provide rapid hemodynamic improvements with high technical success without complications or adverse events despite the majority of patients having prior recent stroke, head trauma, intracranial hemorrhage, or recent surgery. Post-procedure improvements in mean PAP, heart rate, and oxygen saturation were all statistically significant and clinically relevant. These findings are particularly important in this cohort of patients with excessive right heart strain because PE hemodynamic dysfunction has been associated with negative clinical outcomes such as decreased cardiac function, chronic pulmonary hypertension, or increased 30-day mortality.[5-8]

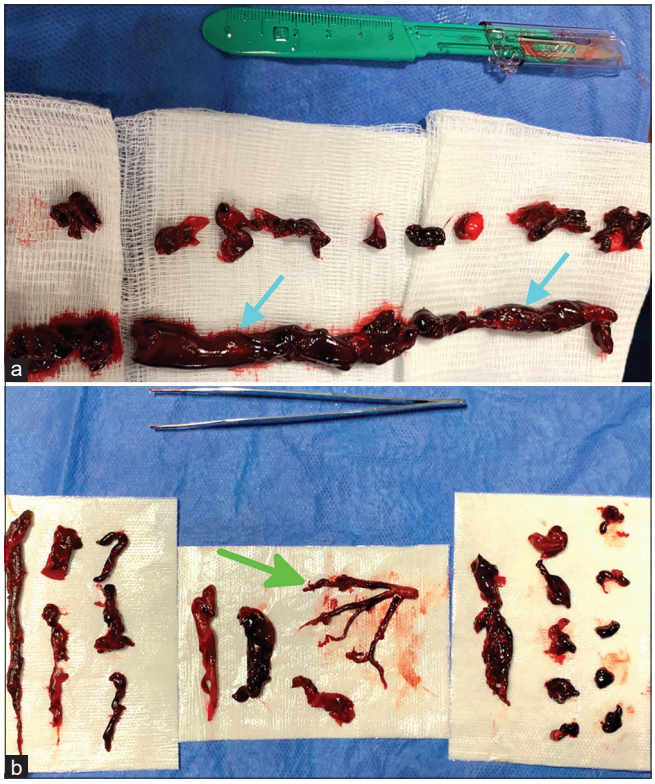

Figure 1: Representative thrombus extracted from (a) a 71-year-old male with recent diagnosis of pancreatic cancer and (b) a 69-year-old female with recent lumbar spinal fusion who both presented with sudden onset dyspnea. (a) The continuous thrombus segment at the bottom (blue arrow) was approximately 6″ long. (b) Representative thrombus with a cast of the distal pulmonary artery segments (green arrow).

Although this study investigated a small sample size for a safety study, the results show great promise in that zero major or minor adverse events, technical complications, delayed procedure-related complications, or deaths within 30 days of hospital discharge were observed. The pivotal FLARE trial evaluated significantly more patients but documented four patients with six major adverse events (MAEs) including one with major bleeding and pulmonary vascular injury; one with a ventricular fibrillation event requiring intubation and coronary angioplasty before resuming thrombectomy; and two patients with respiratory deterioration peri- and post-procedurally requiring intubation. In addition, the authors observed 14 patients (including the four with MAEs) who experienced 26 total serious adverse events within 30 days of index thrombectomy.[2] The other recent single-center retrospective study observed two MAEs and two deaths within 30 days of thrombectomy.[3] The MAEs included a submassive PE with self-limited hemoptysis requiring intubation and the other was a massive PE with a decrease in hematocrit requiring two units of packed red blood cells. The two deaths observed were a submassive PE with pancreatic cancer and a massive PE with prior severe anoxic brain injury resulting in cardiac arrest before thrombectomy.[3] The most significant limitation of the present study is the small sample size for a safety study. Both of the above-mentioned trials reported MAEs in roughly 4% of patients (3.8% and 4.3%, respectively). Assuming the same rate, this study would require approximately twice the sample size to observe a single MAE. Further data are required from this population of interest to draw more concrete conclusions; however, the present data are encouraging.

Nevertheless, despite only evaluating high-risk patients with contraindication to thrombolytic drugs, the hemodynamic improvements in this report are consistent with those from the previous FlowTriever thrombectomy studies.[2,3] For PE patients without these restrictions, thrombolysis is an alternative treatment option when an advanced intervention is warranted.[9,10] However, this therapeutic option comes with a risk of serious complications. Systemic thrombolysis has been shown to reduce both mortality and hemodynamic deterioration compared to anticoagulation alone, but has been associated with major bleeding.[11] The ULTIMA and

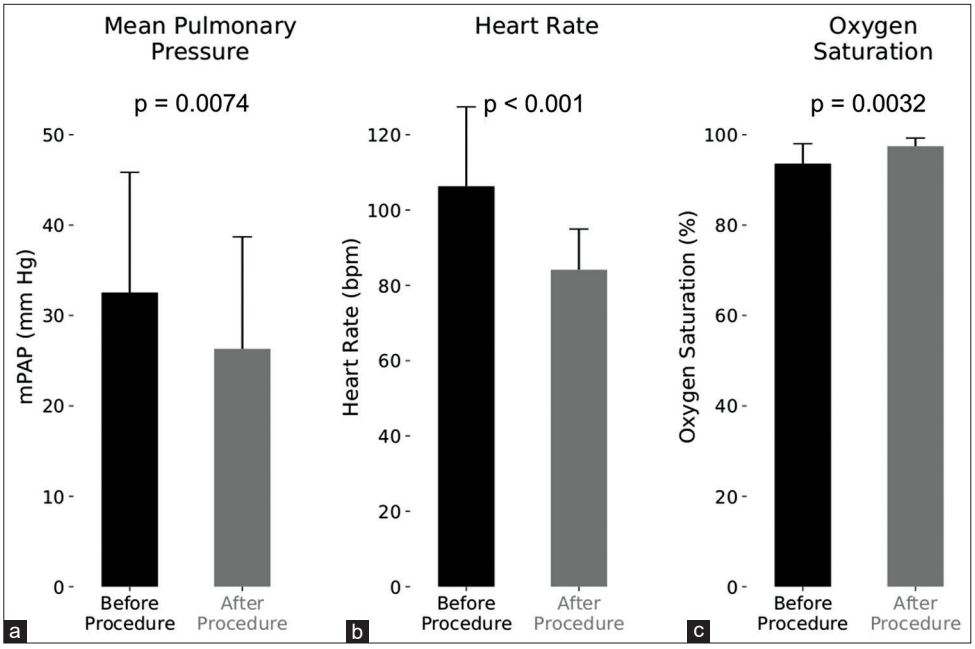

Figure 2: Hemodynamic improvements before and after FlowTriever thrombectomy. (a) Average reduction in mean pulmonary artery pressures of 19.1%, from 32.5 mmHg to 26.3 mmHg (P = 0.0074, 95% CI 2.0–10.5 mmHg reduction). (b) Average heart rate decreased from 106 bpm to 84 bpm (P = 0.00052, 95% CI 11.9–32.4 bpm reduction). (c) Mean oxygen saturation increased from 93.6% to 97.5% (P = 0.0032, 95% CI 1.6–6.1% increase).

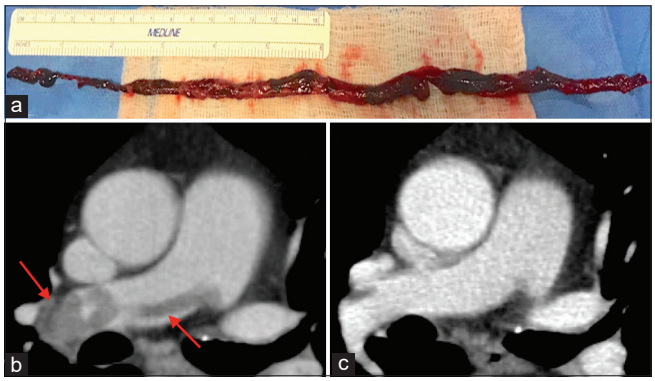

Figure 3: A 55-year-old male with recent hemicolectomy for colon cancer who presented with sudden onset dyspnea. (a) Approximately 12 in thrombus aspirated from the right pulmonary artery. (b) Pre-procedure contrast-enhanced computed tomography (CT) cross-section showing right and central portions of the bilateral thrombus (red arrow) before thrombectomy. (c) Post-procedure contrast-enhanced CT cross-section showing minor residual thrombus in the right pulmonary artery 7 weeks after thrombectomy.

SEATTLE II trials showed that catheter-directed thrombolysis was effective in reducing the RV/LV ratio but was still associated with major bleeding, even in reduced doses.[12-14] A meta-analysis of 26 thrombolytic trials between 1971 and 2018 concluded with moderate certainty that thrombolytic therapy reduced mortality in submassive PE patients (risk ratio 0.61, 95% CI 0.40–0.94), but also determined with high certainty that thrombolytics increased major bleeding events (risk ratio 1.89, 95% CI 1.46–2.46).[15] Thrombolytic bleeding risks are eliminated in mechanical thrombectomy which make the FlowTriever System a promising treatment option for intermediate and higher risk PE, including thrombolytic eligible patients, presuming comparable effectiveness to thrombolytics.

The limitations of this study include the small sample size as previously discussed, retrospective data analysis, and lack of randomization. Furthermore, all patients were treated at the same institution which limits direct extrapolation to a more general PE patient population. However, it is notable that the rapid hemodynamic improvements and lack of major bleeding are consistent with the increasing body of evidence that shows FlowTriever thrombectomy as a safe and effective PE treatment and warrants future and ongoing studies.

CONCLUSION

This retrospective review of a single-center experience with FlowTriever thrombectomy demonstrated that this therapeutic approach could provide safe and effective reperfusion treatment for acute submassive and massive PE patients with contraindication to thrombolytic therapy, whereby advanced treatment would otherwise be limited. FlowTriever thrombectomy can rapidly improve cardiac parameters without the complications associated with thrombolysis. Larger studies and further data are needed to prospectively evaluate long-term safety and effectiveness in this patient population.

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Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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