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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Mechanical thrombectomy is associated with shorter length of hospital stay and lower readmission rates compared with conservative therapy for acute submassive pulmonary embolism: a propensity-matched analysis

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PURPOSE

To determine if mechanical thrombectomy (MT) for submassive pulmonary embolism (PE) positively impacts length of hospital stay (LOS), intensive care unit stay (ICU LOS), readmission rate, and in-hospital mortality compared with conservative therapy.

METHODS

This was a retrospective review of all patients with submassive PE who either underwent MT or conservative therapy (systemic anticoagulation and/or inferior vena cava filter) between November 2019 and October 2021. Pediatric patients (age <18) and those with low-risk and massive PEs were excluded from the study. Patient characteristics, comorbidities, vitals, laboratory values (cardiac biomarkers, hospital course, readmission rates, and in-hospital mortality) were recorded. A 2:1 propensity score match was performed on the conservative and MT cohorts based on age and the PE severity index (PESI) classification. Fischer's exact test, Pearson's χ^2 test, and Student's t-tests were used to compare patient demographics, comorbidities, LOS, ICU LOS, readmission rates, and mortality rates, with statistical significance defined as $P < 0.05$. Additionally, a subgroup analysis based on PESI scores was assessed.

RESULTS

After matching, 123 patients were analyzed in the study, 41 in the MT cohort and 82 in the conservative therapy cohort. There was no significant difference in patient demographics, comorbidities, or PESI classification between the cohorts, except for increased incidence of obesity in the MT cohort ($P = 0.013$). Patients in the MT cohort had a significantly shorter LOS compared with the conservative therapy cohort (5.37 ± 3.93 vs. 7.76 ± 9.53 days, $P = 0.028$). However, ICU LOS was not significantly different between the cohorts (2.34 ± 2.25 vs. 3.33 ± 4.49, $P = 0.059$). There was no significant difference for in-hospital mortality (7.31% vs. 12.2%, $P = 0.411$). Of those that were discharged from the hospital, there was significantly lower incidence of 30-day readmission in the MT cohort (5.26% vs. 26.4%, $P < 0.001$). A subgroup analysis did not demonstrate that the PESI score had a significant impact on LOS, ICU LOS, readmission, or in-hospital mortality rates.

CONCLUSION

MT for submassive PE can reduce the total LOS and 30-day readmission rates compared with conservative therapy. However, in-hospital mortality and ICU LOS were not significantly different between the two groups.

KEYWORDS

Embolectomy, lung, pulmonary, pulmonary embolism, submassive, thrombectomy

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The incidence of pulmonary embolism (PE) is estimated at 117 per 100,000 persons in the United States, with approximately 300,000 deaths attributed to PE annually.[1,2] Approximately 55% of patients with PE are at low mortality risk and can be managed with out-

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patient anticoagulation, whereas those with massive PE require treatment in an intensive care unit (ICU).[3-5] However, the management of patients with submassive PE is controversial. Unlike patients with massive PE, those with submassive PE are characterized as being hemodynamically stable but demonstrating signs of right heart strain on imaging and/or in laboratory values. Historically, the management of submassive PE has been systemic anticoagulation; however, management with systemic anticoagulation alone is associated with moderate self-reported functional impairment at 1 year after diagnosis of submassive PE.[6] With advancements in endovascular-based interventions, catheter-based thrombolysis with tissue plasminogen (tPA) or mechanical thrombectomy (MT) are often employed. Catheter-directed tPA has been successfully used in the past to treat submassive PE and prevent clinical and hemodynamic deterioration; however, it is associated with increased risk of hemorrhagic stroke and bleeding.[7-10] As a result, MT has gained popularity in recent years because of its ability to rapidly re-perfuse pulmonary circulation without the need for tPA or ICU admission.

An accurate risk stratification of patients with acute submassive PE can help guide the management and level of care. In the current climate of ballooning healthcare costs, the appropriate stratification and treatment of submassive PE can help appropriately allocate intensive care and maximize healthcare cost-effectiveness through efficacious treatment for patients. The PE severity index (PESI) is a validated tool to help stratify patients with acute PE based on the risk of 30-day mortality.[11]

Recent data suggest that MT for PE is safe and effective.[12-14] However, the impact of MT compared with that of conservative therapy for submassive PE has not been well studied. Therefore, the purpose of the current study was to determine the impact of MT using the FlowTriever device (INARI Medical, Irvine, CA, USA) for submassive PE on length of hospital stay (LOS), ICU stay (ICU LOS), readmission rates, and in-hospital mortality rates compared with anticoagulation therapy alone.

Main points

- Pulmonary embolism (PE) thrombectomy is a safe and effective therapy for the management of acute submassive PEs.
- PE thrombectomy can provide prompt reperfusion of the pulmonary vasculature and have an immediate clinical benefit.
- PE thrombectomy reduces length of hospital stay compared with anticoagulation therapy.
- PE thrombectomy reduces 30-day readmission rates compared with anticoagulation therapy.

Methods

Patient selection

After obtaining Institutional Review Board (IRB) approval (2004777), a detailed retrospective review of patients with PE who underwent MT between November 2019 and October 2021was performed. Similarly, patients who were treated conservatively [systemic therapy with/without an inferior vena cava (IVC) filter] between June 2017 and October 2021were retrospectively reviewed for comparison. Patients with massive PE, low-risk PE, pediatric patients (age <18 years), and those that had undergone catheter-directed or systemic thrombolysis with tPA were excluded from both groups (Figure 1). The remaining patients were categorized as an MT cohort (those treated with MT) and conservative therapy cohort (those treated with systemic anticoagulation).

Variables assessed

Basic patient demographics and comorbidities such as a history of diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, chronic lung disease, obstructive sleep apnea, asthma, smoking, coronavirus disease, and malignant neoplastic disease were recorded. Patient vitals and laboratory values including cardiac biomarkers such as troponin and/or brain natriuretic peptide (BNP) at the time of the PE diagnosis were collected. Patients were determined to have right heart strain/injury based on imaging or biomarker (elevated troponin or BNP compared with baseline) elevation. For all hemodynamically stable patients with a diagnosis of PE, the right ventricle to left ventricle ratio (RV:LV) and maximum pulmonary artery (PA) distance was measured by the primary authors and senior author. Patients with an RV:LV >0.9 and/or echocardiogram evidence of moderate-to-severe right heart strain were determined to have a submassive PE and were included in the study. Finally, PESI was calculated for each patient and stratified into five categories as described by Aujesky et al.[11]

The primary endpoints of the current study were to compare the LOS and mortality rate between the conservative therapy cohort and MT cohort. Therefore, the total LOS and ICU LOS was calculated for each patient. Finally, the incidence of 30 day readmission rates was also determined for both cohorts.

Mechanical thrombectomy procedure

At the time of PE diagnosis, systemic anticoagulation was started in all patients prior to performing MT. The FlowTriever device is the first MT device approved by the US Food and Drug Administration for the treatment of

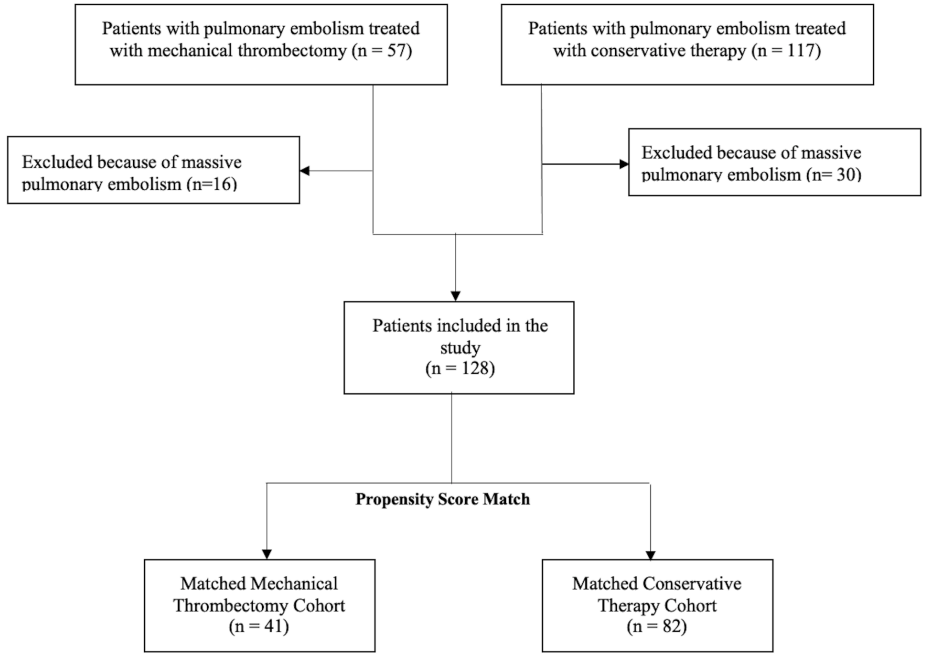

Figure 1. Flowchart of inclusion and exclusion criteria.

acute PE and was thus used to perform MT on all acute submassive PEs included in the study (Figure 2a). The technical procedure for MT has been previously described by Yasin et al.[14] Briefly, the right common femoral vein was accessed in all cases. A 5F angled pigtail catheter was advanced through the right heart and was used to select the pulmonary trunk. Baseline main PA pressures were measured, and an initial pulmonary angiogram was performed through the catheter to identify the extent and location of the PE (Figure 2b). Subsequently, 20/24F FlowTriever devices were used for aspiration thrombectomy. The procedure endpoint was decided based on a combination of post-procedure PA angiograms (Figure 2c), PA pressures, and the response of the patient's clinical status following aspiration thrombectomy. The access site was closed with a purse-string suture. Throughout the procedure, additional heparin boluses were administered to maintain the activated clotting time of approximately 250 s.

Research ethics standards compliance

This original research was completed under an IRB approved protocol. Due to the retrospective nature of the study, informed consent was not required. The IRB number is 2004777. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical analysis

Retrospective analysis can be confounded by selection bias; therefore, a propensity score matching algorithm was used to create similar groups for the conservative therapy and MT cohorts. In this study, a 2:1 propensity score match was used based on age and PESI classification. The matched cohorts were compared for patient demographics, comorbidities, vitals, cardiac biochemical markers, radiographic features of right heart strain (through computed tomography scan or echocardiography), PESI classification, LOS, ICU LOS, mortality rate, and readmission rates using Fisher's exact test or Pearson's χ^2 test for categorical variables and Student's t-tests for continuous variables. All statistical analyses were performed using the R program (r-project.org), with statistical significance set at $P < 0.05$.

Results

Patient characteristics

After matching based on PESI classification and age, 123 patients were analyzed in the study, with 82 in the conservative therapy cohort and 41 in the MT cohort. The patient characteristics, imaging findings of right heart strain, elevated cardiac biochemical markers, and PESI classifications are outlined for both cohorts in Table 1. There was no significant difference in patient demographics, comorbidities, or imaging findings of right heart strain between the two cohorts except an increased incidence of obesity in the MT cohort ($P = 0.013$) and hypertension in the conservative therapy cohort ($P = 0.024$). The incidence of elevated cardiac biochemical markers from baseline was higher in patients who underwent MT (100% vs. 72%, $P < 0.001$). There was no difference in IVC filter placement during hospital stay and PESI classification between the cohorts.

Outcomes assessed

Patients in the MT cohort had a significantly shorter LOS compared with the conservative therapy cohort (5.37 ± 3.93 vs. 7.76 ± 9.53 days, $P = 0.029$; Table 2). However, ICU LOS was not significantly different between the cohorts (2.34 ± 2.25 vs. 3.33 ± 4.49 , $P = 0.062$; Table 2). There was no significant difference for in-hospital mortality (7.31% vs. 12.2%, $P = 0.411$; Table 2). Of those that were discharged from the hospital, there was significantly lower incidence of 30-day readmission in the MT cohort (5.26% vs. 26.4%, $P < 0.001$; Table 2). A subgroup analysis of PESI classifications revealed that PESI scores had no significant impact on LOS, ICU LOS, readmission, or in-hospital mortality rates.

Discussion

This retrospective study utilized a propensity scoring algorithm to compare MT with conservative therapy for patients with submassive PE with regards to LOS, in-hospital mortality rates, and 30-day readmission rates. The study found that patients treated with MT had a significantly shorter overall LOS and decreased incidence of 30-day readmission compared with conservative therapy. However, there was no significant difference in ICU LOS or in-hospital mortality rates. Notably, the study did not find a correlation

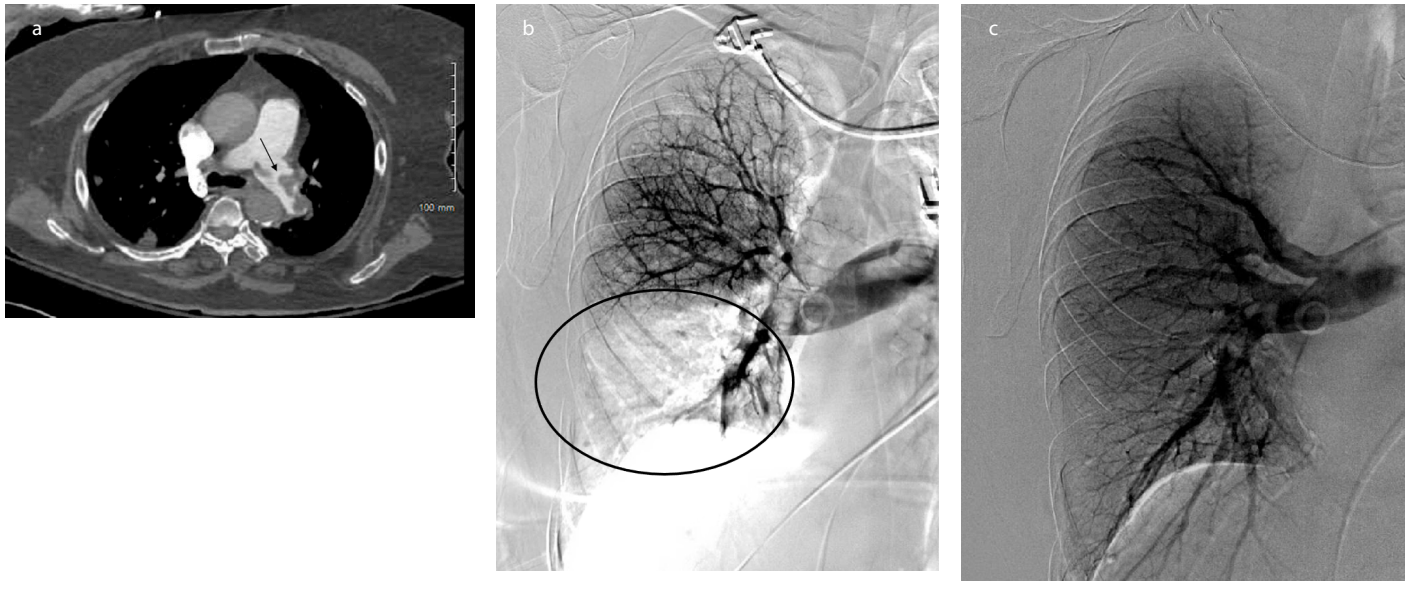

Figure 2 (a) Helical computed tomography scan of the pulmonary arteries, demonstrating a large clot burden within the left pulmonary artery (black arrow). **(b)** Pulmonary angiogram revealing a large filling defect within the right lower lobar pulmonary artery (black oval). **(c)** Post mechanical thrombectomy pulmonary angiogram demonstrating. the complete opacification of the right lower lobar pulmonary artery.

between PESI classifications and LOS, ICU LOS, 30-day readmission rates, or in-hospital mortality rates for acute submassive PE.

Venous thromboembolism (VTE) is a major healthcare burden worldwide and is responsible for significant healthcare resource utilization. Acute PE is one of the most feared entities of VTE and is associated with increased patient mortality, long-term morbidity, and healthcare costs.[15,16] Recently, Shalaby et al.[15] queried the National Inpatient Sample database and determined that patients with acute PE had an in-hospital charge of approximately US$ 30,000. Similarly, PE is associated with decreased aerobic functional capacity in half the patients 1 year after their PE diagnosis and has a negative impact on quality of life.[6,17] Current guidelines regarding the management of acute submassive PE recommend anticoagulation therapy with observation and/or the escalation of care based on hemodynamic instability.[18] In addition to conservative therapy with anticoagulation, catheter-based thrombolysis has been shown to be efficacious but is associated with an increased risk of bleeding.[7,9,10] As a result, patients undergoing catheter-based thrombolysis require ICU admission for close monitoring, which can substantially increase healthcare costs. Additionally, about 30% of patients with PE have an absolute or relative contraindication to systemic or catheter-directed thrombolysis.[18,19] However, MT provides a unique opportunity to evacuate the PE with immediate patient benefits as a result of prompt reperfusion.[14] Consequently, the current study sought to compare the clinical benefits to patients of MT with conservative treatment with anticoagulation therapy.

A diagnosis of PE often increases the complexity of care, leading to an increase in LOS, and it can be a barrier to timely discharge. Therefore, prompt diagnosis and the appropriate management of PE is crucial to ensure optimal patient outcomes in a timely manner. However, the appropriate management for submassive PE in not well established. The current study compared MT and conservative therapy for submassive PE and determined that patients undergoing MT for submassive PE had a significantly shorter LOS compared with conservative therapy (5.4 vs. 7.8 days, $P = 0.026$). However, the current study did not identify any difference in the length of ICU stay between the cohorts. Recently, Buckley and Wible[13] compared patients with PESI classification 4 or 5 who underwent MT with those receiving conservative therapy and found that patients who underwent MT had a shorter ICU LOS with no significant impact on overall LOS. This discrepancy in findings regarding ICU stay may be because of the difference in institutional protocols following MT. In our institution, patients who are admitted to the ICU or a

Table 1. Adjusted comparison of patient characteristics between mechanical thrombectomy and conservative therapy

Patient characteristics	Mechanical thrombectomy, n = 41, (%)	Conservative therapy, n = 82, (%)	Adjusted *P* value
Age, years (SD)	58.58 ± 14.18	59.28 ± 16.24	**0.762**
Sex, male	16 (39)	47 (57.3)	**0.066**
Obesity	30 (73.2)	41 (50)	**0.013***
Diabetes mellitus	9 (21.9)	26 (19.2)	**0.259**
Hypertension	15 (36.6)	48 (58.5)	**0.024***
Congestive heart failure	4 (9.8)	6 (7.3)	**0.644**
Coronary artery disease	4 (9.8)	11 (13.4)	**0.558**
Chronic lung disease	3 (7.3)	16 (19.5)	**0.081**
Obstructive sleep apnea	6 (14.6)	14 (17.1)	**0.731**
History of cancer	11 (26.8)	19 (23.1)	**0.659**
Tobacco use	10 (24.4)	34 (41.5)	**0.064**
SARS-CoV-2 infection	5 (12.2)	3 (3.7)	**0.071**
Imaging and laboratory characteristics of submassive pulmonary embolism			
RV:LV ratio	1.55 ± 0.39	1.51 ± 0.58	**0.672**
Main pulmonary artery distance, mm	32.73 ± 5.89	31.28 ± 4.61	**0.168**
Evidence of right heart strain in CT scan	39 (95.1)	70 (85.4)	**0.113**
Elevated troponin or BNP from baseline	41 (100)	59 (71.9)	**<0.001***
IVC filter placement during hospital stay	4 (9.8)	16 (19.5)	**0.174**
PESI category			
PESI 1	5 (12.2)	11 (13.4)	**0.842**
PESI 2	5 (12.2)	10 (12.2)	**1.000**
PESI 3	9 (22)	15 (18.3)	**0.631**
PESI 4	9 (22)	13 (15.6)	**0.412**
PESI 5	13 (31.7)	33 (40.2)	**0.363**

*Signifies statistically significant finding; SD, standard deviation; SARS, severe acute respiratory syndrome; CoV-2, coronavirus 2; RV:LV, right ventricle to left ventricle ratio; CT, computed tomography; BNP, brain natriuretic peptide; PESI, pulmonary embolism severity index.

step-down unit are readmitted to ICU care after the MT before the de-escalation of care is considered by the primary team.

With the transition from fee-for-service to bundled payments, there is increasing institutional pressure to reduce the risk of readmissions in patients admitted for elective or urgent procedures. Readmission within 30 days is often a major contributor to healthcare costs, and factors that can reduce the risk of short-term readmissions are being studied across many medical specialties. The diagnosis of VTE, especially PE, has been shown to dramatically increase the risk of increasing short-term readmission rates.[20-22] In a European VTE registry, the readmission rate within 1 year of VTE diagnosis was approximately 25%.[23] Similarly, Chen et al.[24] determined that a perioperative diagnosis of PE following major respiratory, cardiovascular, or musculoskeletal surgery was associated with an increased risk of 30-day readmission compared with a diagnosis of perioperative PE. Therefore, optimizing care for patients with PE is of paramount importance for improving patient outcomes and reducing readmission rates. In the current study, the management of acute submassive PE with MT was associated with lower readmission rates compared with conservative management alone. This is in contrast to the findings of Buckley and Wible[13], who did not identify a significant difference in readmission rates between MT and conservative therapy cohorts. Finally, the present study did not find a statistically significant difference in in-hospital mortality rates between the two cohorts but identified a trend toward decreased risk of mortality in the MT cohort ($P = 0.059$). This finding is consistent with that of Buckley and Wible[13], who demonstrated a significantly reduced mortality rate for patients that underwent MT compared with conservative therapy. Notably, however, the study conducted by Buckley and Wible[13] did not match patients in the two cohorts, and a few patients in the conservative therapy cohort underwent systemic or catheter-based thrombolysis, which adds heterogeneity to the data.

There are several notable limitations to the present study that should be considered when interpreting the findings. Although the present study is the only moderately sized study with robust propensity score matching between cohorts, there likely exists variables that were not controlled for. Despite matching, only a few variables were not equal between the two cohorts, such as elevated biomarkers, which could impact the findings of our study. Additionally, due to the retrospective nature of the study, the findings are limited to shorter LOS and decreased readmission rates with MT compared with conservative therapy as opposed to establishing a cause-and-effect relationship. The lack of mortality benefits with MT compared with conservative therapy may be because of the relatively small sample size. In addition, the study did not evaluate the time interval from PE diagnosis to when thrombectomy was performed, which might have affected the potential benefits of MT for the inclusion of patients who presented early versus those who presented later for thrombectomy.

Finally, for the purposes of this study, a propensity score analysis was utilized to match patients in both cohorts by age and PESI classification, and independent statistical analyses were utilized to compare differences in baseline characteristics and outcomes. There is a lack of consensus regarding the appropriate use of statistical analysis for estimating the treatment effect in propensity-matched groups. It has been suggested that outcomes can be directly compared between propensity-matched cohorts using independent statistical analysis.[25] Therefore, in the current study, a Pearson's χ^2 test and Student's t-tests were performed to compare outcomes between propensity-matched MT and conservative therapy cohorts for submassive PEs.

In conclusion, MT for submassive PE can reduce total LOS and 30-day readmission rates compared with conservative therapy. However, in this study, in-hospital mortality and ICU LOS were not significantly different between the two groups.

Table 2. Adjusted comparison of primary outcomes between mechanical thrombectomy and conservative therapy

Outcomes	Mechanical thrombectomy	Conservative therapy	Adjusted *P* value
Readmission rate	2	19	**<0.001***
In-hospital mortality	3	10	**0.411**
ICU stay	2.34 ± 2.25	3.33 ± 4.49	**0.062**
LOS stay	5.37 ± 3.93	7.76 ± 9.53	**0.029***

*Signifies statistically significant finding; ICU, intensive care unit; LOS, length of hospital stay.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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